RELATIONSHIPS BETWEEN ENVIRONMENTAL RISK FACTORS, PARASITIC INFECTIONS AND HEALTH OUTCOMES IN AN URBAN AFRICAN SETTING

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ABSTRACT

The relationships between parasitic infections, environmental and living conditions, and health outcomes were studied in subdivisions of lower (LSES) and higher (HSES) socio-economic status in Lubumbashi, Zaire. The two LSES subdivisions had higher prevalences of Plasmodium infection and higher rates of stunting, abdominal pain and low packed cell volume (PCV) than the HSES subdivision. The prevalence and intensity of Ascaris lumbricoides and Trichuris trichiura was not associated with socio-economic status. Maternal education was a significant predictor of A. lumbricoides intensity in both LSES and HSES subdivisions. Factors related to poor sanitation were risk factors for A. lumbricoides in LSES subdivisions, whereas a high ratio of relatives to immediate family members per household predicted high intensity infection in the HSES subdivision. The risk of stunting was higher in children with A. lumbricoides, that of wasting was higher in children with A. lumbricoides or T. trichiura whereas the risk of kwashiorkor was high with T. trichiura but very reduced in those with A. lumbricoides. The four most common clinical conditions were diarrhea, abdominal pain, fever and low PCV. Hookworm infection, T. trichiura infection, young age and residence in LSES subdivisions were determinants of diarrhea. T. trichiura infection, young age and living in a LSES subdivision were risk factors for abdominal pain. Plasmodium infection and young age were associated with fever. LSES was predictive of low PCV. No combination of parasites had antagonistic or synergistic effects on clinical indicators examined. Based on this study, it is suggested that

similar drug control programs can be effectively used in both LSES and HSES subdivisions, and there is no reason to believe that treatment for one parasite will increase the risk of infection with another. Although maternal education should be improved in all subdivisions, attention to sanitation, crowding and diet in the LSES subdivisions, and to the role of relatives and visitors in parasite transmission in the HSES subdivision should be priorities.

RESUME

Les liens existant entre les infections parasitaires, les facteurs environnementaux, et les affections morbides ont été examinés dans trois zones de la ville de Lubumbashi au Zaïre. La prévalence de paludisme, de nanisme, de douleur abdominale et d'anémie, était plus élevée dans les deux zones populaires (zone à niveau socio-économique bas) que dans la zone résidentielle (zone à niveau socio-économique élevé). La prévalence et la charge ascaridaire et trichocéphalaire n'étaient pas liées au niveau socio-économique des zones. Par contre, le niveau de scolarisation des mères était significativement lié à la charge ascaridaire dans toutes les zones. Hormis le niveau de scolarisation des mères, d'autres déterminants de la charge ascaridaire dans les zones populaires, étaient liés à la promiscuité ou aux mauvaises conditions hygiéniques, alors que dans la zone résidentielle, ils étaient plutot liés au rapport de nombre des membres de famille élargie sur celui des membres de famille restreinte par maison. Le nanisme était élevé chez les enfants infectés d'Ascaris; la fonte, chez ceux infectés d'Ascaris ou de Trichocéphale. Le kwashiorkor était plus élevé chez les enfants infectés de Trichocéphale mais moins élevé chez ceux infectés d'Ascaris. Les affections morbides communes étaient la diarrhée, la douleur abdominale, la fièvre et l'anémie. La diarrhée était liée aux ankylostomes, au Trichocéphale, à l'âge et à la zone de résidence; la douleur abdominale, au Trichocéphale, à l' âge et à la zone de résidence; la fièvre, au paludisme et à l' âge. Cependant, l'anémie n'était liée qu' à la zone de résidence. Les infections mixtes n'ont révelé aucun effet synergique ou antagoniste sur les

affections morbides.

Ce travail suggère qu' une chimiothérapie semblable dans les trois zones serait possible et que le traitement d' une espèce parasitaire ne pourra ni augmenter, ni réduire le risque d'infection avec d'autres espèces. Bien que le niveau de scolarisation des mères soit le factor le plus important pour le contrôle des infections d'origine parasitaire à Lubumbashi, l' hygiène publique, la sous alimentation, et la promiscuité dans les zones populaires ainsi que l'examen du rôle des membres de famille élargie et des visiteurs dans la dynamique de transmission parasitaire en zones résidentielles sont aussi importants.

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TABLE OF CONTENTS

LIST OF TABLES

CHAPTER III

CHAPTER IV

CHAPTER V

LIST OF FIGURES

CHAPTER V

LIST OF APPENDICES

STATEMENT OF AUTHORSHIP

My Co-supervisors Drs Marilyn E. Scott and Katherine Gray-Donald, are co-authors on all the chapters that are presented in this thesis. However, the field and laboratory work, data analysis and manuscript preparation were carried out by myself. Dr Kalumba-Konglo Olela has been made co-author in the last two chapters for his contribution in clinical investigations and anthropometric measurement, although he was a paid project physician and used a protocol that was designed by myself. Laboratory assistants did all the work related to parasite identification and eggs counting, under my supervision. Although they were all trained and experienced laboratory technicians, I conducted a one week intensive training on basic medical parasitology including the transect egg counting technique with them. I designed the study protocol and conducted face to face interviews with the mothers or care givers. I made observations in households and recorded major characteristics. I also met and interviewed local health authorities and political leaders. I did the speciation of malaria slides at the Centre for Tropical Diseases at Montreal general Hospital under the supervision of Evelyne Kokoskin-Nelson. Data analysis, interpretations of results and the writing of the chapters were all done by myself under the supervision of Drs Marilyn E. Scott and Katherine Gray-Donald. Dr Marilyn E. Scott also supervised for a short period field work in Zaire.

These details on authorship are presented to conform to the regulations of the Faculty of Graduate Studies and Research, McGill University.

Also required is the following passage: "Candidate have the option of including, as part of the thesis, the text of one or more papers submitted or to be submitted for publication, or the clearly-duplicated text of one or more more published papers. These texts must be bound as an integral part of the thesis.

If this option is chosen, connecting texts that provide logical bridges between the different papers are mandatory. The thesis must be written in such a way that it is more than a mere collection of manuscripts.

The thesis must still conform to all other requirements of the "Guidelines for Thesis Preparation". The thesis must include: table of contents, an abstract in English and French, an introduction which clearly states the rationale and objectives of the study, a comprehensive general review of the literature, a final conclusion and summary, and a thorough bibliography or reference list.

Additional material must be provided where appropriate (e.g. in appendices) and in sufficient detail to allow a clear and precise judgement to be made of the importance and originality of the research reported in the thesis.

In the case of manuscripts co-authored by the candidate and others, the candidate is required to make an explicit statement in the thesis as to who contributed to such work and to what extent. Supervisors must attest to the accuracy of such statements. Since the task of examiners is made more difficult in these cases, it is in the candidate's interest to make perfectly clear the responsibilities of all the authors of the co-authored papers."

DEDICATION

Ce travail est entièrement dedié
à la memoire de notre frère bien aimé
Mukendi Kabongo Joseph

CHAPTER I

1- INTRODUCTION

The complexity of controlling and preventing parasitic diseases is partly due to constant interaction between humans and parasites and the surrounding environment over time and the establishment of a state of dynamic equilibrium. Thus for many years, researchers have represented the host, the infectious agent (parasite) and the environment as a balanced ecological system known as the epidemiologic triangle (Mausner and Kramer, 1985). In the system, each of the three components must be analysed individually and understood before predictions of possible interactions can be made. Any qualitative and/or quantitative change in any of the components will ultimately shift the existing equilibrium of the triangle.

At the time this system concept was developed, the focus of epidemiology was mainly on bacterial diseases. Infectious organisms were separated from other environmental factors and identified as agents, and health outcomes were related to single isolated factors or to the agent. However, recent epidemiologic concepts (MacMahon and Pugh, 1970; Friedman, 1980), simple variations of the old epidemiologic triangle, maintain that health outcomes never depend on a single isolated factor, but rather on a chain of factors linked to each other. Some of these factors are characteristics of the host, i.e., innate and acquired immunity, age, gender etc. Others are intrinsic to the agent, i.e., pathogenicity or virulence. Finally, certain factors are characterized by the environment in which both the host and parasite dwell, i.e., lack of sanitation and condition imposed by seasonality. These factors are linked with each other both within and between the components. Within the complexity of these combinations exist possible explanations to a variety of as yet unanswered questions. Why do similar insults have different health outcomes? Why do malnourished children resist malaria when well-nourished children do not? Why is Ascaris lumbricoides still prevalent in the tropics despite available effective treatment? While speculative answers to these questions exist, perhaps the simplest one is that interaction of the factors within the epidemiologic triangle can dramatically alter the equilibrium at any given time by enhancing or reducing disease outcomes.

What epidemiologists seek in parasite control programs is how to manipulate the epidemiologic triangle in a way that will be favorable to the human and unfavorable to the parasite. Whatever type of manipulation is used for this purpose, a shift of the system from a higher equilibrium point (i.e., pre-control infection level) to a lower equilibrium point (i.e., post-control infection level) is the usual goal. Depending on resource availability, field workers can choose to manipulate the host component (i.e., vaccination), the parasite component (i.e., chemotherapy), the environment component (i.e., improvement of sanitation) or combinations therein.

As a first step in designing a control strategy, factors that could be manipulated should be identified in each component of the system, their relationships to each other investigated as well as their relative contribution to the outcome of interest. This is a critical point as the extent to which the system may respond to manipulation will most certainly depend on the contribution of selected individual factors to the outcome and the amount of variability of the outcome that such factors may explain as a group. That is to say, if multivariate analyses are used to explore potential predictors of an outcome, individual factors with the highest contribution to such an outcome should be altered to achieve desirable changes in the epidemiologic triangle. Such predictors may differ between different areas of the same community. However, if they are of the same nature, manipulative efforts may be applied on them as a group rather than individually. For instance, the number of persons per bedroom, the number of persons per toilet, the frequency of open defecation in an house yard are all variables of structural nature and relate to crowding or sanitation. If each has been confirmed as a predictor of a given health outcome in at least one area of a community, manipulation of crowding or sanitation in general may have the same modulatory effect on the health outcome just as if each of those variables was manipulated individually.

2- THE PROBLEM

There is a population explosion in some Third World cities today. Formerly, this explosion was attributable to freedom of movement and settlement acquired by local people after independence of their countries, and the need for better jobs among rural dwellers. Today, the situation is maintained by factors such as political disruption, war, improvement in the transportation network and sometimes by natural disasters such as drought (Prothero, 1977). Most cities are incapable of coping with the resulting proliferation of dwellings. Thus expanded urban services are not being provided to new comers, sanitary facilities are non existent and food availability is very limited. For instance a study conducted in Zaire (Franklin et al.,1984a) showed that, between 1978 and 1979, the proportion of malnourished children increased every month in most communities in Kinshasa. In Lubumbashi, the second largest city in Zaire after Kinshasa, such data are not available, but since its last urban planned structures were completed in the late fifties no other planned structures have been built in the city. Yet its population has grown from less than 50,000 inhabitants in 1950 to 565,000 inhabitants in 1991 (Anon, 1991).

Such population growth, however, cannot occur without causing alterations in environmental and living conditions as the city was built to contain one twelfth of the actual population. The effect of such alterations on host-parasite relationships within the city and on the health status of the population is not known.

In 1991, we started the Urban Development and Parasitic Diseases Project in order to address these questions and advise local authorities on feasible parasitic disease control measures. The International Development Research Centre provided funding for the project which started in the summer of the same year. When we arrived in Lubumbashi, two types of neighborhoods existed; those where anyone could settle and those reserved for senior government and company officials. In the first type, also known as lower socio-economic (LSES) neighborhoods, roads and sanitation infrastructures were in disrepair, basic urban services were non-existent, and dwellings were substandard due to aging, negligence and lack of basic utilities. In contrast, the second type or higher socio-economic (HSES) neighborhoods were comparable with those seen in the best European or North American suburbs. Talks with local administrative and health authorities prior to the beginning of field-work revealed that malaria, gastrointestinal infections, diarrheal diseases and malnutrition were major health problems in the city. A search for published data supporting these claims was unsuccessful. The most recent literature on parasitic infections in the region was on hookworms and was dated to 1969 (Ripert and Carteret, 1969). Data on malnutrition, diarrheal diseases or other health outcomes were not available. The only current literature on Lubumbashi was the 1991 census results (Anon, 1991), hence, parasitic infections and clinical conditions directly associated with the current living conditions of this city were unknown, yet information was urgently needed.

3- GENERAL OBJECTIVE

The objective of the study was to determine the relationships between current environmental and living conditions of Lubumbashi, parasitic infections and collective health problems in order to effectively alter disease-promoting factors and promote health and well-being in Lubumbashi and in other cities with similar problems. Three steps were taken to address this objective.

In Chapter III, environmental and living conditions that are usually considered as risk factors for infection are identified and then related to parasitic infections. In Chapter IV, indicators of nutritional deficiency are identified and their relationships with the socio-economic status and parasitic infections are assessed. In Chapter V, clinical conditions reflecting the general health status of individuals are identified and their association with the socio-economic status and parasitic infections are investigated. In Chapter VI links between Chapters III, IV and V are examined in the context of the epidemiological triangle. Also presented in Chapter VI are limitations and advantages of this type of study, our conclusions and recommendations to the Zairean and other third-world country policy makers and finally my contribution to original knowledge.

4- EXPECTATIONS

Intervention studies have shown that poor environmental and living conditions such as those seen in some neighborhoods of Lubumbashi are associated with high levels of parasitic infections (Mata, 1982) and that these infections are in turn associated with nutritional deficiency (Stephenson et al.,1985; 1989; Gupta, 1990) and/or other debilitating health outcomes (Wolfe, 1978; Rooth and Björkman, 1992; Adedeji and Ogumba, 1986). Given this information together with what we have just presented on Lubumbashi, we fully anticipated that: (i) infection with intestinal helminths and Plasmodium would be higher in the LSES compared with the HSES neighborhoods; (ii) The level of childhood protein energy malnutrition would be associated with the average level of infection with intestinal helminths and Plasmodium in each neighborhood; (iii) similarly the level of diarrhea, anemia, abdominal pain or other health outcomes would also be directly related to the level of infection.

To address these questions, we had the choice among three types of observational studies, the cohort, the case control and the cross-sectional study. Given the limitations of our budget and time-frame, only the last two types of study were appropriate. Case control studies compared with cross-sectional studies however, have the disadvantage of not being able to address multiple outcomes. Therefore we chose to use the cross-sectional approach as it was the only time and cost-convenient approach that can investigate relationships involving multiple exposures and outcomes given our budget and time-frame.

CHAPTER II

LITERATURE REVIEW

I- URBANIZATION AND COMMUNITY HEALTH

Although urbanization is sometimes related to modernization or industrialization, it is a process related to social aggregation or urban living (Williams, 1990). In an effort to define what is urban or what is a city, the United Nations has recognized settlements of over 20,000 people as "Urban", of more than 100,000 people as "Cities", and of more than 5,000,000 people as "Big Cities" (Drakakis-Smith, 1987). WHO's report on urbanization and health in developing countries revealed that the level of urbanization, as a proportion of the total national population, in the Third World, is expected to increase from 33.9% in 1990 to 39.5% by the end of the century and to 56% by the year 2025 (Harpham and Stephens, 1991). The level of urbanization is much higher in developed countries where 3/4 of the population live in urban areas (Drakakis-Smith, 1987).

Why are we so concerned with urbanization in the Third World when the population is three times more urbanized in the West? The answer to this question lies not in the level of urbanization but in the rate of urban population growth. This has now reached 2-8%/year in the Third World compared to less than 1%/year in developed countries (Drakakis-Smith, 1987). This is aggravated by the fact that newcomers usually settle on the least desirable urban sites jeopardizing their own health and that of others around them.

Factors responsible for ill-health in urban areas are numerous. Some encompass the direct impacts of urbanization and some are by-products of modernization and industrialization (Philips, 1990). Health impacts are not the simple consequence of isolated conditions such as housing, income. nutrition etc. but rather the result of their interactive effects. Thus, gains in one sector can be clouded by losses in another sector; for instance, morbidity or mortality prevented by improving sanitation (i.e., low level of nematodes) may be clouded by morbidity or mortality caused by poor nutrition (i.e., higher level of protein energy malnutrition). Such inter-dependencies demonstrate why inter-sectorial actions for improved health should be adopted, rather than efforts aimed at individual problems. This is especially important in endemic areas where determinants of ill-health are so diversified (Buck et al, 1978a; Chac-Tai, 1989), and include human mobility or movement (Watts, 1986; 1987), physical, social, cultural and environmental factors (Philips, 1993).

1- URBAN HEALTH DETERMINANTS

A- MOBILITY AND URBAN HEALTH

An intensive rural-urban migration has been incriminated in the demographic explosion in Africa (Preston, 1990). In the past, such migration was mainly due to the freedom of movement and settlement acquired after independence, and the need for better jobs among rural dwellers. Now, the situation is maintained by factors such as political disruption, war, improvement in the transportation network and sometimes by natural disasters such as droughts (Prothero, 1977).

Once in the city, newcomers usually settle illegally on the least desirable urban sites, shanty town or slums, known to be foci of high transmission of infections (Eldson-Dew, 1953; Sadun, 1955; Bundy et al.,1988; Chac-Tai, 1989; Victora et al.,1988; Henry, 1988; Kan et al.,1989; Harpham and Stephen, 1991; Esrey et al.,1991). Even though residents of such neighborhoods are said to be socially "marginalized" from other city residents, the fact that they work hand-in-hand with people in industries and elsewhere in the city indicates that in reality they are not completely marginalized (Harpham and Stephens, 1991). Therefore, it is difficult to believe that infections prevailing in such poor urban populations are confined within the same communities. Mansell Prothero (1977) described three transmission patterns linked to human mobility: (i) transmission of disease by those who move into new communities (active transmitters); (ii) exposure of those who move to diseases in the course of their movement and at their final destination (passive acquirers); (iii) the possibility of some individuals being both active transmitters and passive acquirers. There is evidence that even a single individual's movement may a have dramatic influence in active transmission; i.e., the cholera epidemic in West Africa in the 1970s was initiated by one single person from Russia (Prothero, 1989). Recognition of this variety of movements is particularly important in assessing the impact of mobility upon vector-borne diseases. Each element/pathogen, vector, and host has its individual ecology, and each element and its ecology may be affected by movement. Pathogen and vector may be directly transported. Through movement, people may be brought into ecological conditions which expose them to vectors to which they were not exposed before, or people may modify ecological conditions so that they become favorable for vector invasion and breeding. A typology of mobility by Prothero (1977) gives a comprehensive description of the mechanisms by which infections are introduced and maintained in some areas. This approach has been used to investigate indirectly transmitted parasites (Watts, 1987), but to date it has not been used for directly transmitted parasites such as gastrointestinal nematodes, and quantitative data are lacking, perhaps because movement is technically difficult to measure. However there are speculations that human mobility is involved in geohelminth transmission (Goldsmid, 1968; Chac-Tai, 1989). In Macao city, 22% of children were infected with geohelminths (Chac-Tai, 1989). Given the urban and socio-economic development of the city, this type and level of infection was not anticipated. Ascaris lumbricoides and Trichuris trichiura infections were found to be related to vegetables imported from neighboring China, where the use of night soil was very frequent (Chac-Tai, 1989). While the study is a good example of rural-urban nematode transmission, it also raises questions about the extent to which such transmission may be occurring between different urban communities.

B- PHYSICAL DETERMINANTS OF URBAN HEALTH

All essential epidemiological parameters of urban health, whether entomological or parasitic, clinical or therapeutic, are likely to be affected by the ecological and physical changes which come with the urban population explosion. In endemic areas, many cities can barely provide basic services for their citizens especially for poor neighborhoods. Facilities such as sewage, waste-disposal, safe water, effective transportation and affordable shelter, known as urban health determinants (Philips, 1993), are usually deficient or absent. Industrial pollution is also often uncontrolled and most human activities only help create breeding sites for disease vectors such as mosquitoes. Thus seasonal transmission patterns of some parasitic infections have become perennial, as is the case for "man-made-malaria" in some urban areas of Sub-Saharan Africa (Bruce-Chwatt, 1980). Indeed, Trape and Zoulani (1987a) observed considerable differences in anopheline density in different districts of the same city. The number of infective bites varied from 100 per person per year in new neighborhoods, where there was intensive environmental or ecological degradation, to less than one per person every three years in older more stable neighborhoods. Such significant differences in the distribution of the vector have important implications in the epidemiology of parasites, given the close proximity of dwellings in urban areas. The changing distribution and epidemiology of parasitic diseases in urban and peri-urban areas caused by the development or urbanization process has been reviewed by Mott et al. (1990); many of the points raised in their work can only be influenced by cultural practices and lead to greater risks of disease.

C- SOCIO-CULTURAL DETERMINANTS OF URBAN HEALTH

Significant socio-cultural development plays an important role in the control of parasitic diseases (Mata, 1980). Evidence from field work has shown that different ethnic groups living in the same city have different levels of nematode infection (Bundy et al.,1988) and that children with educated mothers are less infected than those with non-educated mothers (Carrera et al., 1984). These results suggest that different attitudes and behaviors place certain individuals at different levels of risk of infection even though that they all live in the same neighborhood.

Outdoor activity after dark, squatting, ablution, etc. are other socio-cultural determinants of parasitic infection in Third World urban areas (Mata, 1982) and should also be considered if control of infection is sought. For example, successful control of malaria has been attained in the past with little regard for socio-cultural factors, but rather reliance on insecticides, treatment and chemoprophylaxis. However, the development of insecticide resistance in vectors, of drug resistance in Plasmodium and of an increase in extra-domiciliary habits of the human host, has made control more difficult and set back eradication of malaria in many parts of the world (Barnes, 1968). Suitable control strategies therefore need to address all possible determinants of infection in those communities.

D- ECONOMIC DETERMINANTS OF URBAN HEALTH

Communities within many Third World cities are clearly divided into areas of higher (HSES) and lower (LSES) socio-economic status. Features of the HSES stratum resemble those of modern western cities, whereas LSES neighborhoods often are referred to as shanty towns or slums (Drakakis-Smith, 1987). The actual number of people living in shanty towns is estimated to be 1/3 of the total urban population in the Third World (Harpham and Stephens, 1991). Their living conditions reflect poverty, hardship and limited education (Mata, 1982), and have been long associated with high levels of infection, morbidity and mortality (Eldson-Dew, 1953; Sadun, 1955; Bundy et al.,1988; Chac-Tai, 1989; Victora et al.,1988; Henry, 1988; Kan et al.,1989; Harpham and Stephen, 1991; Esrey et al.,1991). However, given the interaction between communities, it is difficult to believe that health determinants in the LSES strata do not influence the health of those living in the HSES strata.

Quantitative data are lacking on the precise distribution of health outcomes and provision of basic urban services among different sub-groups of cities. Although this lack of data makes it difficult to know whether the needs of the urban poor impact on the health of the rest of the population, there are reports of comparable levels of infections between individuals with better living conditions and individuals without (Feachem et al.,1983). This indicates that poorer urban communities may be a source of contamination of the wealthier communities. While levels of infections may be comparable, resulting morbidity may equate with the socio-economic status of individuals (Cerf et al.,1981), because individuals of higher socio-economic status are likely to have better nutrition (Franklin et al.,1984b), and easier access to health care than individuals of lower socio-economic status (Cerf et al.,1981). However, there are examples where the level of health outcomes did not differ between lower and higher socio-economic groups (Trape et al., 1987), which may suggest that wealth does not necessarily equate with better health.

Urbanization seems to affect the health of all residents. Therefore efforts to improve urban health should be directed toward the whole city rather than toward individuals or subgroups. For instance, the most significant increase in life expectancy recorded in England and Wales this century was during the two decades between World War I and II. The fact that such an improvement was associated with public effort rather than personal income (Sen, 1993) strongly corroborates Owen's (1927) view that "The individual happiness of a man can be increased and extended only in proportion as he actively endeavors to increase and extend the happiness of all around him". This perspective is particularly important as it touches crucial issues of poverty and inequality and how unmet needs of the urban poor impact on the health of the wealthier inhabitants.

2- STRATEGIES TO CONTROL ILLEGAL MIGRATIONS

Numerous strategies have been used to control the urban population explosion due to illegal migrations. Most are variations of the South African pass system (Hutt, 1971), designed to prohibit urban residence to those without official permission and/or work permits. China has reduced urban unemployment by issuing ration tickets for food and clothing that are redeemable only at certain locations (Reynalds, 1975). To reinforce similar regulations, the government of Kenya set fire to migrant settlements, the Tanzanian government periodically rounded up unemployed migrants and sent them back to their respective rural areas, and other governments redirected migrants away from large cities to other reception areas, where land was available for development (Drakakis-Smith, 1987). Such draconian policies, however, have never been successful; illegal migrants usually find their way back into the city and live with relatives or friends. Some find jobs in the informal sector and some are employed even in industries with the blessing of their employers. After all, the urban industrial expansion depends on cheap labour from illegal migrants (Peattie, 1975).

Indirect control strategies based on narrowing the gap between rural and urban incomes potentially seem promising (Blecher, 1990), but decisions on wage increase/decrease depend on employers rather than governments. The implementation of this strategy cannot be easy; the fact that migrants are increasingly likely to be working in the informal sector can only make it more difficult. Even if such programs are undertaken in a joint effort between government and industries, thy are long-term and financially demanding. Most Third World countries prefer cheaper, short-term measures based on direct control of population movement into the city, but the use of force and draconian measures in order to reinforce such laws (Drakakis-Smith, 1987) violates the Human Rights Act and therefore makes them less attractive. If prior to taking such measures, governments could educate migrants on the economical, social and health consequences associated with their settling in shanty towns or slums, vis à vis their own welfare and that of their children, migrants will be able to understand why they are deported to rural areas. However, such control measures do not imply that rural residents can no longer move into cities. That is not the case; rural migrants are very welcome in cities, assuming that they settle legally where they will be able to use existing urban services in order to keep health outcomes under control. To be effective, the adoption of urbanization control strategies as a way of improving environmental and living conditions in order to control infections or health outcomes, needs parallel and sustainable control of major tropical health problems such as malaria and gastrointestinal infections (WHO, 1991a, 1991b), and childhood protein energy malnutrition (Onis et al.,1993).

II- THE PARASITE

1- NEMATODES

Of all human nematodes Ascaris lumbricoides, Trichuris trichiura and hookworms (Necator americanus and Ancylostoma duodenale) are the most common in the sub- and tropical regions.

A- DESCRIPTIVE STATISTICS

The World Health Statistics Annual Report (WHO, 1991b) indicates that one billion people in the world are infected with Ascaris, 900 million with hookworm and 500 million with Trichuris. From published data (Brown and Cort, 1927; WHO, 1964; Anderson and May, 1991), the actual world population of adult Ascaris may be estimated to be close to six billion. This provides sufficient grounds to justify the pressing need to control nematode infections, especially in endemic areas where polyparasitism is frequent and children are often heavily infected (Kan, 1985; Bundy et al.,1987a). Fortunately, the extent of environmental contamination with eggs is regulated by factors such as the standard of sanitation and hygiene (WHO, 1981; 1987), behavior and culture (Schad et al.,1983; Kan, 1985; Akogun, 1989). Indeed, these factors are related to the level of development of communities, which in most cases is negatively associated with the level of infection. For instance in Zambia where 46.2-52.2% of the population has access to safe water and sanitation (WHO, 1991b), the prevalence of Ascaris infection is estimated at 6.4% (Crompton et al.,1989). Yet in neighboring Zaire, where only 9.3-32.1% of the population enjoys safe water and sanitation (WHO, 1991b), 57.3% of the population is estimated to be infected with Ascaris (Crompton et al.,1989). Similar trends exist between other countries, suggesting that communities of the HSES are less infected than those of LSES (Henry, 1981; Chiwuzie, 1986; Holland et al.,1988). However results in the literature are contradictory. Cases have been reported where communities of HSES or communities with safe water and sanitation had infection levels comparable to those of LSES communities (Gatti et al.,1969; Bidinger et al.,1981; Gryseels and Gigase, 1985).

B- BIOLOGY AND PUBLIC HEALTH IMPLICATIONS

Two separate populations and habitats of intestinal nematodes exist in the world: (i) the adult worms that parasitize the human host and (ii) the free-living infective stages (egg or mobile larvae) that contaminate the environment. Sexually-mature female worms release eggs into the external environment at the following rates per day: Ascaris 240,000 (Brown and Cort, 1927; WHO, 1964; Pawlowski, 1982); hookworms, 3000-20,000 (Anderson and May, 1991); Trichuris, 3000-5000 (Anderson and May, 1991).

In the case of A. lumbricoides and T. trichiura, once the egg is released on the soil, it goes through four juvenile stages, known as larval stage number one (L1), two (L2), three (L3) and four (L4) and the preadult stage before becoming an adult worm in the small intestine of the host. Crompton and Pawlowski (1985) reported that the development to L1 and L2 took place within the eggs in the external environment while the rest of the developmental process continued in the host body.

On the other hand, Blood et al. (1983) stated that not only the L1 and L2 but also the L3 stage developed within the eggs in the external environment before infecting the host. Regardless, the important point is that the egg embryonates in the external environment and becomes infective. The time taken to reach that infective stage depends on the ambient temperature. Crompton and Pawlowski (1985) estimated that about 10 days are needed for the L1 embryonation to be completed in the case of Ascaris. Once on the ground, hookworm eggs hatch and develop through the L1 and L2 stages to L3 stage which is the infective, freely mobile larva (Gilman, 1982).

The extent to which the environment is contaminated with nematode eggs and larvae depends on the level of safe sanitation (Henry, 1981), and on behavioral and/or cultural characteristics (Schad et al.,1983) of each community. Physical factors such as heavy rains, altitude, soil structure, moisture, ultra-violet irradiation, high temperature and desiccation also regulate nematode egg populations (Beaver, 1975; Wharton, 1979; Clarke and Perry, 1980). Thus, eggs of A. lumbricoides have a life expectancy of up to 6 years (Crompton and Pawlowski,1985) in temperate climates, or as little as hours in some tropical conditions (Lysek and Bacovski, 1979). Krasnosos (1978) reported that, in Samarkand, USSR, Ascaris eggs were still alive after 14 years in the external environment. However Anderson and May (1991) indicated that the average life expectancy of A. lumbricoides eggs was between 28 and 84 days.

Pica, soil contaminated hands and food or water are the major means of Ascaris and Trichuris transmission, whereas hookworms enter the host body by skin perforation. A. duodenale, unlike N. americanus, can penetrate the host orally as well as by skin perforation and is capable of arrested development in the host tissue and of transmammary transmission from mother to offspring (Brown and Girardeau, 1977).

Once in the human body, hookworm larvae start the heart-lung migration, but orally ingested larvae of A. duodenale may develop in the gut without migration (Gilman, 1982). Once ingested, Ascaris and Trichuris eggs are immediately exposed to a temperature and a pH different from the external environment and are subjected to the effects of bile and other digestive enzymes. This stimulates the hatching process which takes place a few hours after the eggs have been ingested. After hatching in the intestine, Trichuris larvae migrate into the large intestine and colon where development leading to pre-adult worms takes place. Ascaris larvae move into the intestinal mucosa to start the heart-lung migration. This takes them to the liver via portal vessels, then to the right heart and lungs. Both Ascaris and hookworm larvae leave the lungs via the bronchi, trachea and oesophagus. They reach the gut as mature larvae. Contradictory reports are found in the literature on specific times of moulting (Crompton and Pawlowski,1985; Blood et al.,1983). Estimates of prepatent period have been reported as two months for A. lumbricoides (Crompton and Pawlowski, 1985), two to three months for T. trichiura, seven weeks for N. americanus (WHO, 1987) and five weeks to nine months for A. duodenale (WHO, 1987).

Not all the ova/larvae invading the host become mature worms. When Andersen and colleagues (1973) inoculated high numbers of Ascaris suum larvae into pigs, they collected very few adult worms, but when the number of inoculated larvae was decreased, a higher proportion developed into adult worms. These results supported experimental work done in humans in 1934 (Kendrick, 1934) and confirmed the existence of control mechanisms acting on the recruitment of adult worms at the individual level (Anderson and May, 1991).

Adult Ascaris live free in the lumen of the jejunum, as opposed to Trichuris, which live attached to the wall of caecum and the proximal part of the colon, but both have a life expectancy of 1-2 years (Anderson and May, 1991). Hookworms, which live longer (5 years or more) (Anderson and May, 1991), settle in the small intestine of the host.

Health outcomes caused by nematodes are multiple. In 1985, WHO reported that Ascaris infection alone was responsible for respiratory symptoms and signs such as pneumonia, asthma and, during its intestinal phase, it was one of the most common causes of abdominal surgical emergency in children in many countries. Thein-Hlaing (1987) reported that, at the Rangun Children Hospital, 3% of the hospital admissions were due to Ascaris and, of the total Ascaris cases, 61.6% were treated in the surgical wards. Nokes et al. (1991) found that school children with low academic performance had a higher intensity of Ascaris than those with higher academic performance. The impairment of children's mental development was also related to Trichuris dysentery syndrome (Callender et al.,1992).

Atopic disorders including asthma are commonly linked to helminthiasis due to the higher level of IgE found in the blood in both conditions (Johansson et al., 1968). However, work still needs to be done in this field as Godfrey (1975) failed to find any cases of asthma among healthy infected rural and urban school children, although a number of asthmatics were seen in hospitals.

Morbidity due to Ascaris is mostly associated with the intensity of infection, when worms remain in their normal site of infection (small intestine). Unfortunately, adult worms have a predilection of migrating into narrow orifices and other body cavities when disturbed. Thus, cases of ectopic foci of adult worms are numerous in the medical literature (Ramos et al., 1980; Bambira et al.,1985; Goldberg and Doman, 1987), and pathologies attributed to such displacements are multiple. Adedeji and Ogumba (1986) incriminated A. lumbricoides as responsible for pyrexia of unknown origin due to other pathogens that they carry with them in their migrations through the host body. A. lumbricoides have been found to be responsible for abdominal cavity tumor formation (Ramos et al., 1980; Bambira et al.,1985). Hepatobilliary and pancreatic ascariasis are common cases in hospitals in endemic areas (Khuroo et al., 1990; Karim, 1991). In animals, Ascaris has been reported to depress growth, reduce food intake , decrease utilization of nitrogen and fat and the ability to digest lactose during the intestinal phase of the infection. Also, studies with children incriminated A. lumbricoides as a cause of growth retardation (Stephenson et al.,1980b; 1989), the intestinal malabsorption of nutrients (WHO, 1985), intestinal obstruction (Ochoa, 1991) and the gastrointestinal bleeding (Jacob et al., 1983), similar to the bleeding of the large and small intestines caused by Trichuris (Bundy and Cooper, 1989) and hookworm (Lintermans, 1976), respectively anemia was associated with Trichuris and hookworms. Ankylostome duodenale and N. americanus, attached to the intestinal wall, suck blood (Gilles, 1985) at the respective rates of 0.14-0.26 ml and 0.02-0.07 ml per worm per day (WHO, 1987), while Trichuris is known to cause rectal prolapse (Kamath, 1973), abdominal pain, diarrhea, headache, nausea and vomiting (Wolfe, 1978). Hookworms and Trichuris have been also associated with stunting and wasting (Stephenson et al.,1989). Given that poly-infection is very common in endemic areas, and that most nematodes and other pathogens have been linked with intestinal malabsorption, their pathogenicity can only be aggravated. Indeed the heavy mortality recorded among Puerto Ricans during the Spanish American war was due to the fact that N. americanus infection occurred in combination with tropical sprue (Crosby, 1987).

C- FACTORS AFFECTING THE TRANSMISSION OF NEMATODES IN ENDEMIC REGIONS

Host-parasite population dynamics are characterized by continual immigration and death of parasites in the host population (Anderson and May, 1991). Anderson and May (1982) identified five factors affecting this relationship: (i) the parasite life expectancy which reflects the average time-scale of the host-parasite association, as the parasite lives for a much shorter time than the host (Kendrick, 1934; Anderson and May, 1991), (ii) the severity of the host's control mechanisms on parasite recruitment, fecundity and survival, (iii) the degree of parasite aggregation in the host population, (iv) the mating probability for gastrointestinal nematodes, (v) the basic reproductive rate (R_o), defined as the average number of female offspring produced throughout the lifetime of a mature female parasite which themselves achieved reproductive maturity in the absence of density dependence. Thus R_o constitutes a measure of the transmission dynamics, a value equal to 1 indicates that each female worm at best produces only one other adult female within its lifetime (Pawlowski, 1984). The second measure of the dynamics of transmission is the re-infection rate which depends on the rapidity with which the community re-acquires the infection. Indeed, R_o and the re-infection rate are used for planning mass chemotherapy programs and to monitor the impact of sanitation programs in different communities. This is because factors affecting the transmission of nematodes fluctuate from one place to another and are modulated by variables such as climate, microgeography, host predisposition, behavior, living conditions and nutritional status.

a- CLIMATE AND SEASONALITY

Temperature, moisture, oxygen pressure and ultra-violet radiation from sunlight are important physical or ecological factors regulating the population of nematode eggs outside the human host (WHO, 1981; Ali-Shtayeh et al.,1989). Significant differences in the level of infection between equatorial and tropical parts of a country have been reported (Ratard et al.,1991). The periodic fluctuation of factors unfavorable to nematode eggs may be regarded as the principal modulator of seasonal breaks in nematode transmission (Beaver, 1953; Schad et al., 1973; Ali-Shtayeh et al.,1989). When Tedla et al.(1988) studied the epidemiological pattern of Ascaris in Ethiopian school children, infection was characterized by two peak periods, one between March and May, and the other between August and October, corresponding respectively to the light and heavy rainy seasons. Although there was no intervention, results showed that the transmission rate, increased in the rainy season and decreased and/or stopped in the dry season because of dessication of the free-living infective stages (Beaver, 1953). These observations have been supported by other studies (Nawalinski et al.,1978; Knight and Merrett, 1981; Undosi, 1983; Ali-Shtayeh et al.,1989).

Inhibition of transmission in hookworm infection has been associated with hypobiosis of migrating larvae within the host (Schad et al., 1973), but this process is itself modulated by seasonal variations (Nawalinski et al.,1978). Thus A. duodenale larvae acquired in one rainy season delay their development until the next rainy season (Schad et al., 1973). Studies conducted in West Bengal (Schad et al.,1973; Nawalinski et al.,1978) demonstrated hypobiosis of migratory larvae in the normal life cycle of A. duodenale in association with the monsoon period. This study identified a difference between the epidemiology of A. duodenale and N. americanus. While the former undergoes a period of dormancy in its life-cycle, the latter does not. Studies conducted in Kenya somewhat support the latter postulate (Griffin, 1981). No seasonal pattern was found in hookworm infection possibly because N. americanus was the only hookworm species infecting Kenyans in Mombasa and Machakos (Griffin, 1981). However, unsuitable physical factors which occur in the dry season in Africa (Undosi, 1983) would have been expected to severely reduce the life expectancy of infective N. americanus larvae on the soil surface (Anderson and May, 1991) and to lead to a seasonal pattern (Beaver, 1953) comparable to that reported for A. duodenale and other nematodes (Schad et al.,1973; Knight and Merrett, 1981; Tedla et al.,1988).

b- SPATIAL DISTRIBUTION OF NEMATODES

The spatial and temporal dynamics of soil contamination with geohelminth eggs are a function of factors such as the nature of the soil (Beaver, 1952), the degree of shade (Schad et al., 1983), sanitation, host environmental and living conditions and crowding (Henry, 1988; Holland et al.,1988), and host cultural and behavioral variables (Singhi et al.,1981; Schad, 1983). In the absence of continuing soil contamination, physical factors such as those prevailing in the tropics may contribute to the eradication of the egg population on the soil surface (Schad et al., 1983; Wong and Bundy, 1990). On the other hand, clean soil may become polluted with nematode eggs simply through the action of physical factors such as rain. However, alternation of wetting and drying of soil as occurs in the tropics accelerates the death of nematode infective stages (Beaver, 1953).

Thus due to variability in physical factors, socio-economic, demographic parameters etc., the distribution of nematode eggs in each community is overdispersed (Hominick et al.,1987; Wong and Bundy, 1990). Hominick et al.(1987) found that the overdispersion of nematode infective stages was remarkable even within socially recognized defecation grounds where the area was heavily polluted with feces. These observations were partially supported by Wong and Bundy (1990) when they did a quantitative assessment of contamination of soil by eggs of Ascaris in two children's homes in Jamaica. The distribution of eggs in soil was overdispersed in one home but underdispersed in the other, suggesting that the spatial distribution of eggs is not always aggregated, especially in locations with low densities of eggs (Wong and Bundy, 1990). The outstanding finding in their work was the relationship between the degree of soil contamination in each institution and the level of infection among residents. Residents of the home with the higher level of soil contamination had the highest level of infection. This corroborates research done in animal models showing a linear relationship between the number of parasites that established in a single host and the density of infective stages to which the host was exposed (Anderson and May, 1991). Hominick et al. (1987) also found that people who defecated at sites positive for larvae tended to have higher mean fecal egg counts than those who defecated at negative sites. Moreover, in 1979, May and Anderson stated that the rate of recruitment of adult parasites in the host was proportional to the number of contacts between the host and the parasite infective stage. The number of contacts does not include only those at the host residential place or neighborhood however, but also includes contacts made at the work place, school, market, relatives' neighborhood, etc. Therefore, while it is accepted that the level of infection in the community is a function of the number of infective stages in the soil, the infection level in a host population likely relates also to the level of infection in places other than the home and the degree to which the host moves within and/or between these places (Wessen, 1971; Watts, 1986; 1987).

Soil contamination may virtually be absent in a community but food stuffs may be heavily contaminated. Such a distribution pattern occurs mainly when food stuffs are imported from contaminated farms. Twenty two percent of school children living in Macao City, China were infected with Ascaris and Trichuris (Chac-Tai, 1988). Yet, in that city, most families lived in multi-story buildings provided with tap water and a private aqua privy, and where all roads were cemented. Therefore, geohelminth infection was unlikely to have originated locally (Chac-Tai, 1988). The author hypothesized that infective ova were brought into the city through fresh vegetables from China where night soil is extensively used (Sadighian et al.,1976). An investigation conducted in Nigeria reported similar findings, as 6%-25.6% of food stuffs were contaminated with Ascaris ova (Ogumba and Adedeji, 1988). Ascaris ova have even been found on paper money (Gonzalez, 1951). This complexity in the exposure pattern to nematode infections is amenable to speculation that infection in some cities is maintained by contact with shanty towns and rural areas since such communities have been long identified as foci of high transmission (Elsdon-Dew, 1953), due to crowding and poor sanitation (Henry, 1988; Victora et al., 1988), lack of safe water (Victora et al., 1988; Esrey et al.,1991) and absence of maternal technology (Mata, 1982). Maternal technology is the wealth of mothers' know-how in the handling and storage of water and food, their attitude toward primary health care, disposal of excreta, waste, etc. (Mata, 1979). However regardless of people's exposure level to infections, nematodes have been found to be aggregated in almost every community (Croll, 1983; Bundy et al.,1985; 1988).

c- FREQUENCY DISTRIBUTION OF NUMBER OF WORMS PER HOST

Most people in endemic areas harbor few worms and the majority of worms are carried by only a few individuals (Croll and Ghadirian, 1981; Croll, 1983; Bundy et al.,1985; 1988). Studies conducted in two Iranian villages (Croll and Ghadirian, 1981) showed that out of 80 individuals in a village, 2 carried 30% of the total A. duodenale count and 4 persons carried 38% of the total N. americanus. Out of 111 persons in another village, 5 carried 16% of the total A. lumbricoides count. The authors (Croll and Ghadirian, 1981) used the term "wormy persons" to describe those individuals with the highest worm burdens. This was to highlight that these individuals were likely to disseminate a disproportionate number of infective stages into the community (Croll and Ghadirian, 1981). The number of worms carried by wormy persons varies with communities. In some localities wormy persons may carry 40 A. lumbricoides while elsewhere, they may carry 400, etc. Despite such variations, the relative worm burden of "wormy persons" is consistently excessive compared with that of their neighbors in a predictable and constant numerical relationship. In other words, the frequency distribution of worms per host is clumped, aggregated or overdispersed rather than random. The degree of that aggregation is best described by the negative binomial coefficient or k (Crofton, 1971); the greater the aggregation in a community, the smaller is the value of k. Values of k for A. lumbricoides in different communit.:s were reported to vary from 0.36 to 0.81 (Guyatt et al.,1990). In children between 2-4 years, k was found to be 0.85 (Elkins et al.,1986), and in those between 10-14 years of age it was 1.73 (Elkins et al.,1986). Bundy et al (1987b) reported similar value of k in these age groups; the lowest k for A. lumbricoides was among the 2-4 years old children and the highest among children below 2 years of age. Different factors have been suggested to cause aggregation. Croll and Ghadirian (1981) stated that aggregation was caused by increased susceptibility to infection, by behavioral or occupational risks or by super-imposition of several random dispersions. These factors, however, are similar to those said to predispose some hosts to heavy and others to light infections: heterogeneity in genetic susceptibility to infection (Wakelin, 1986), heterogeneity in exposure to infection (Bundy and Cooper, 1988; Wong and Bundy, 1991), heterogeneity in socio-economic and living conditions (Chiwuzie, 1986; Holland et al.,1988), or the combinations of these factors.

d- HOST PREDISPOSITION AND IMMUNITY TO NEMATODE INFECTIONS

It is known that some individuals and/or groups of people are predisposed to heavy or light infection (Anderson and Medley, 1985; Kan, 1985; Schad and Anderson, 1985; Bundy et al.,1987a; Bundy and Cooper, 1988; Forrester et al.,1988; Chandiwana et al.,1989; Bradley and Chandiwana, 1990), not by chance but by as yet undefined parameters (Schad and Anderson, 1985). In addition to those noted above, in 1934, Kendrick treated 30 prisoners, counted expelled worms then experimentally re-infected the prisoners with 200 hookworm larvae, at Madras Penitentiary, India. On day 12 post infection, larvae were isolated from the sputa of infected persons. Several weeks later adults worms were expelled and counted. Amazingly, infection failed to establish in the person from whom considerable numbers of larvae were recovered. On the other hand, the largest number of worms was recovered from those participants who had been heavily infected prior to experimental infection. These observations have three possible interpretations: (i) the existence of some control mechanism at the individual level, exemplified by the person from whom larvae were found in the sputa but who did not have adult parasites; (ii) previous infection does not confer immunity to the host but control mechanisms at the individual level do exist, (iii) predisposition to heavy or light infection exists, as those who had heavy infection before the experiment regained heavier worm loads than those who did not. Field studies on predisposition have been very conclusive. Correlations between the pre- and post-control intensity of infection were consistently reported regardless of whether the infections were estimated directly or indirectly (Bundy et al.,1987a). It should be noted that some other studies have failed to reveal any evidence of predisposition to infection (Bundy et al.,1985; Bundy and Cooper, 1988). Intensity of infection had a convex relationship with host age, peaking at pre-school or school age children (Kan, 1985) and declining in adulthood (Anderson and Medley, 1985; Bundy, 1986; Bundy et al.,1987c), suggesting that the rate of recruitment of adult worms is age-dependent (Bundy et al.,1987c). Children re-acquired a higher infection than did adults as a consequence of their behavior (Kan, 1985; Akogun, 1989), but even when data were standardized for age, those with heavy (light) infections still re-acquired the same level of infection, implying that predisposition to heavy or light infection was independent of the host age (Bundy et al.,1987c).

Heavily infected individuals were found together in the same household (Forrester et al.,1988) and ethnic groups re-acquired infection at different rates despite the fact that participants were all exposed to essentially the same environmental and living conditions (Bundy et al.,1988). These distribution patterns have been attributed to genetic resemblance (Wakelin, 1986), and to similarity in behavior and/or cultural background among different group members (Schad et al., 1983; Bundy et al.,1988; Forrester et al.,1988; Scott et al.,1989). Predisposition to infection has also been associated with sex (Pugh and Gilles, 1978), occupation (Croll et al.,1982; Chandiwana et al.,1989; Bradley and Chandiwana, 1990). Such complexity of causative factors of predisposition to infection are suggestive of a multifactorial modulation (Beisel, 1982a,b; Bundy and Cooper, 1988). Thus contrasting results between different studies may be attributable to heterogeneity of such modulatory factors, particularly nutritional status (Beisel, 1982a; Bundy and Golden, 1987; Michael and Bundy, 1988; 1991), which may have a profound influence on an individual's immune response to nematode infection (Beisel, 1982b). How protective that response is and how it operates, is not well established. It is known that nematodes stimulate the host immune response (WHO, 1981; Chandra, 1982), and that control mechanisms at the individual level act on parasite recruitment, development and fecundity (Kendrick, 1934; Croll et al 1982; Anderson and May, 1982; Solomons and Scott, 1994).

e- HOST NUTRITIONAL STATUS

Morbidity caused by nematodiasis in endemic areas is likely to be greater in communities compromised by malnutrition, and concurrent infections caused by the resulting immunodeficiency (Beisel, 1982a; 1982b). Bundy and Golden (1987) pointed out that infection enhanced malnutrition, and that, inversely, host malnutrition potentiated parasite transmission. However both malnutrition and infection were reported to operate synergistically or antagonistically in the host, depending on the degree or stage of each of them (Beisel, 1982a; Bundy and Golden, 1987). Extreme malnutrition is prejudicial to nematode recruitment and establishment in the host gut, due to the absence of physio-chemical triggers for hatching or development such as gastric acidity, mucus secretion, intestinal mobility, bile constituents, enzymatic activities and/or deficiency in trace elements such as zinc (Golden and Golden, 1981; Mayrhofer, 1984; Bundy and Golden, 1987).

In moderate malnutrition, such as that which occurs in endemic areas, immunosuppressive changes are more frequent than the intestinal pathophysiology in severe malnutrition. Thus, individuals in endemic areas are likely to harbor heavy worm burdens (Bundy and Golden, 1987; Bundy et al.,1987c). Nutritional immunosuppression is multifactorial and primarily induced by a depletion of trace elements and protein. For instance, zinc deficiency suppresses T cells function and copper deficiency suppresses the B cell immune response (Beisel, 1982b).

An experimental study with CBA/Ca mice has shown that Trichuris muris number decayed faster in mice fed a higher protein diet than in those fed a lower protein diet (Michael and Bundy, 1988; 1991). This observation is suggestive of a lower immune response in mice fed the low protein diet. Furthermore, calculations made from experimental work revealed that children infected with an average of 26 adult Ascaris, lost approximately 4 g of protein per day while they were on a daily diet of 35-50 g of protein, due to their worm burden (WHO, 1967) or the subsequent malabsorption (WHO, 1985). Such children were also reported to excrete low amounts of vitamin C and A (WHO, 1967).

Nematode infection and the subsequent malabsorption causes growth retardation in children (WHO, 1985). Epidemiological evidence supporting this is multiple (Henry, 1981; Thein-Hlaing et al.,1991a). Significant increases of height-for-age and weight-for-age were revealed when infected children were treated for nematode infection as compared to non-treated control children (Henry, 1981; Stephenson et al.,1989; Thein-Hlaing et al.,1991a). However, a study conducted in Bangladesh by Greenberg et al. (1981) failed to show significant anthropometric improvement after treatment of infected children. Instead, the intervention group tended to exhibit even lower growth rates than the placebo group. Similar results were obtained by Gupta and Urrutia (1982), who prospectively studied a group of children from whom growth rate did not change after treatment for Ascaris infection. These workers did not find growth improvement in those children likely because only 4.4% of children were malnourished at the beginning of the study. Also, after treatment, the infection level in the children was brought down only from 60% to 33%.

The complexity of the relationship between nematode infection and malnutrition is also reflected in the host behavioral profile. In endemic areas pica is commonly observed in children living on a deficient diet and/or heavily infected with nematodes (WHO, 1967; Singhi et al.,1981).

f- CULTURAL AND BEHAVIORAL ASPECTS

In epidemiological studies, it is important to comprehend the behavioral and cultural repertoire of a community and its contribution to disease transmission before designing intervention programs (WHO, 1967; Croll, 1983), because, while some behaviors and cultures promote health, others potentiate ill heath (Schad et al.,1983). May and Anderson (1979) stated that the rate of recruitment of adult parasites in the host was a function of the number of contacts between host and parasite infective stages. Contacts are linked to specific host behaviors. For example, farm workers working barefoot were predisposed to heavier hookworm infection (Chandiwana et al.,1989), and geophagic behavior or pica was related to higher nematode infection and malnutrition (Wong et al., 1991; WHO, 1967). Pica is also the consequence of deficiency of trace elements such as iron, zinc, copper etc. (Crosby, 1971; McDonald and Marshall, 1964; WHO, 1967; Beisel, 1982b). Stress and psychological deprivation, which in fact are most predominant in socio-economically compromised communities such as those in developing countries, are amongst major causes of pica (Singhi et al.,1981). Psychosocial stress in children is generated by lack of maternal care, when mothers are pregnant, working or if they die (Singhi et al.,1981). Results indicate that the mean proportion of silica in stool orphaned or abandoned children exceeded the level attributable to dietary sources (Wong and Bundy, 1988) and their worm load correlated with the amount of silica or soil that they ingested (Wong et al., 1991). However pica is not limited to children alone. Pregnant women reportedly consumed clay in Turkey, Iran and the southern USA (Crosby, 1971), perhaps due their physiological condition.

Most epidemiological studies on predisposition to infection have analysed the data according to the host age group (Nawalinski et al.,1978; Bundy et al., 1987a; Bundy et al.,1988; Scott et al.,1989), because behaviors are more similar within age groups. Preschool children were found to be the age group most predisposed to Ascaris (Kan, 1985) due to their playing and/or defecation behavior. Akogun (1989) reported that, in some Nigerian communities, children's feces were regarded as "pure" and therefore children were allowed to defecate anywhere around the house or the playground. Amazingly these children were reported to use fecally contaminated soil and garbage as toys (Akogun, 1989). Ill-health-promoting behavior was also reported among adult agricultural workers. Not only did workers indiscriminately defecate in the fields (Schad et al.,1983), but they also used night soil in fields, where in most cases they worked without shoes (Croll et al.,1982; Croll, 1983; Chandiwana et al.,1989; Bradley and Chandiwana, 1990). Thus in Zimbabwe where only 0.05-1.6% of the population is infected with nematodes (Taylor and Makura, 1985), 80% of adult farm workers were infected with hookworm due to such working behavior (Bradley and Chandiwana, 1990). Environmental contamination resulting from such behaviors does not present a risk to farm workers alone; it is a risk to consumers, even to those living some distance from those farms (Chac-Tai, 1988). Consumption of farm products contaminated with nematode ova likely has an impact in families with deficiency in maternal technology (Mata, 1979). Unfortunately, deficiency in maternal technology is most encountered in families belonging to the low SES, living in already contaminated environmental conditions (Mata, 1979; 1982; Holland et al.,1988) g- ENVIRONMENTAL AND LIVING CONDITIONS

In the context of nematode infections, the relation between host and parasite is modulated by the extent to which infective stages are available in the environment (Hominick et al.,1987; Wong and Bundy, 1990). The availability of infective stages is a function of variables such as living conditions, and the socio-economic status of people in the community (Ilardi et al.,1987; Holland et al.,1988). Studies conducted in Panama among school children established a strong association between the SES of children and infection with Ascaris, Trichuris and hookworms (Holland et al.,1988). The prevalence of single or multiple infections was significantly higher in children living in housing made of wood or bamboo than in those living in housing made of concrete blocks (Holland et al.,1988). These findings have strong support from other studies (Henry, 1981; Mata et al.,1982; Chiwuzie, 1986;.Wong and Bundy, 1990; Wong et al.,1991).

Quantitative evidence relating aspects of the SES and living conditions to nematode infections are becoming available; studies conducted in two children's homes in Jamaica related the degree of soil contamination in each institution to the level of infection among residents. Higher level of infection occurred in the home with higher soil contamination and lower standard of sanitation (Wong and Bundy, 1990; Wong et al.,1991). The United Nations Center for Human Settlements (UNCHS, 1990) revealed that the prevalence of worm infection correlated well with poor environmental and living conditions. These conclusions corroborated observations made by Mata in 1982 when he reported that poverty, high demographic density or crowding, ruralism, and deficient maternal technology, were determinants of parasitic infections. In fact the deficiency in maternal technology explains the attitude of some mothers toward children's feces as described by Akogun (1989) and indeed it is an indicator of poverty, lack of education, and low SES (Mata, 1979; WHO, 1981).

The WHO (1981) recognized that illiteracy, poor sanitation and high density of human populations were the main factors that promoted the transmission of nematode infective stages to humans, and that the rate of reduction in infection levels was associated with the rate of improvement of indoor facilities and environmental and living conditions (Schliessmann, 1958; Victora et al.,1988). For instance, in the USA the prevalence of Ascaris among all age groups was 71% lower in people with private aqua privy sanitary system and indoor plumbing, compared with a group that had lavatories but no well water (Schliessmann, 1958). In the West Indies there was a 30-50% drop in Ascaris and Trichuris infection after water supply and sanitation were improved (Henry, 1981). On the contrary, studies conducted in Zaire (Gryseels and Gigase, 1985) and Zambia (Feachem et al.,1983) failed to show similar improvements; there was no significant difference in the level of infections between groups with improved living conditions (better housing, safe water, improved sanitation, better jobs) and those without. These results suggest that, in endemic areas, the distribution of nematode between different groups is not function of the socio-economic status of such groups, possibly due to interactions between these groups; more realistic control strategies are therefore needed in endemic areas.

D- CONTROL STRATEGIES

Attempts to control helminth infection have been put into question due to multiple failures and continual re-infection in endemic areas (Warren, 1981; Croll et al.,1982). In reality, such failures do not imply failures to control infection at the individual level, since effective and safe anthelminthic treatment is available (WHO, 1967; Stephenson et al., 1989; Bundy et al.,1990; Asaolu et al.,1991; Thein-Hlaing et al.,1991b). Indeed, the unresolved question to date is how to use these drugs for the benefit of the community. The best answer to this question is to be found within communities where there is need for such control (WHO, 1967), since control programs designed and implemented by members of the same community are likely to be more realistic.

Environmental improvement has had a great impact in the control of geohelminth infection (WHO, 1967; Moridhita and Yokogawa, 1973; Henry, 1981; Croll et al.,1982), but behavioral and cultural factors which permit the contact between the host and infective stages still is the hinge in the host-parasite relationship (Crosby, 1971; Wessen, 1971; May and Anderson, 1979; Singhi et al.,1981; Mata, 1982; Arfaa, 1984; Akogun, 1989). Therefore, any control program targeted at people with ill-health-promoting behaviors will reduce infections, if the program results in a change to health-promoting behaviors (Croll et al.,1982; Mata.,1982; Thein-Hlaing et al.,1991b). Unfortunately, it is difficult for people to abandon behaviors that have been acquired over years. Such a goal in cultural societies like those in Africa cannot be achieved without incorporating community leaders not only in the implementation of health educational programs (WHO, 1967), but also in the conception and elaboration of these control strategies.

Short-term control programs which have combined environmental intervention with health education and chemotherapy have brought positive results (WHO, 1967; Arfaa et al.,1977; Arfaa, 1984; Bundy et al.,1990; Asaolu et al.,1991). Approaches used for drug delivery were mass, selective, and targeted chemotherapy or combinations of these methods. Results indicate that significant reduction in nematode egg counts were recorded in whole communities by targeting treatment only at children 2-12 years of age (Anderson and May, 1982, Croll et al.,1982; Asaolu et al.,1991; Bundy et al.,1990; Thein-Hlaing et al.,1991b).

A selective approach to deliver drugs only to those heavily infected individuals could reduce both the morbidity and the transmission (Anderson and Medley, 1985), but this approach has been shown to be time consuming, costly and not suitable for communities with limited resources (Stephenson et al.,1980a; Anderson and Medley, 1985; Asaolu et al.,1991). Asaolu et al.(1991) even reported that, when they used selective chemotherapy in Nigeria, villagers were concerned why certain individuals were treated while others were excluded. Yet when they used an age-targeted approach, no such reaction occurred, because adults were able to understand that their children were at risk and needed treatment (Asaolu et al.,1991). However such concern can be eliminated if the selective chemotherapy is combined with an initial mass treatment.

In countries where the population is nutritionally compromised such as those in endemic areas (Beisel, 1982a; 1982b; Bundy and Golden, 1987), the efficacy of anthelminthic drugs can be altered (either enhanced or reduced) in the malnourished individual. The rate of uptake of drugs, their distribution through the body, their rate of metabolism into active and inactive compounds, their mode of action, and their rate of excretion all depend on physiological and biochemical activities of the host body (Solomons and Scott, 1994).

Mathematical models have been used to estimate the proportion of people to be treated (g) in different communities per unit of time with eradication as the goal (Anderson and May, 1982, Croll et al.,1982), given g as a function of the efficacy (h) of the drug to be used in the field and the R_0 basic reproductive rate of the parasite. These variables must each be defined within specific communities (Croll et al.,1982; Thein-Hlaing et al.,1991b). If the proportion treated is greater than

$\{1-\exp[(1-R_0)/A]\}/h$ (Anderson and May, 1982, Croll et al.,1982),

such control should bring R_0 below unity. In this case, each mature female worm is incapable of even replacing itself. For eradication, the control program should be kept in place for a period of not less than the maximum life span of the longest-living stage in the parasite life-cycle (Anderson and May, 1991), assuming that infection is not brought in through exogenous sources such as immigrants (Goldsmid, 1968; Anderson and May, 1991). Immigration is a principal component of the urbanization process in the third world, and it commands major consideration in parasite control strategies (Wessen, 1971; Watts, 1987; Mott et al.,1990).

2- MALARIA PARASITE

Malaria is caused by haemosporidian protozoa of the genus Plasmodium. Nearly 100 different species of Plasmodium in the world infect birds, reptiles, monkeys and higher apes. Only four Plasmodium species are known to infect humans (Bruce-Chwatt, 1980), namely Plasmodium vivax, the causal agent of benign tertian malaria; Plasmodium ovale, which causes oval tertian malaria; Plasmodium malaria, responsible for quartan malaria and Plasmodium falciparum, the causal agent of malignant tertian or sub-tertian malaria. The last is the most common and pathogenic type of malaria in the tropics and sub-tropics. A number of non-human Plasmodium have been transmitted naturally or experimentally to man (Acha and Szyfres, 1987) and speculations are that Plasmodium rodhani described in chimpanzees (Acha and Szyfres, 1987), is the human P. malaria (Collins and Aikawa, 1977). If these speculations are true, then chimpanzees are potential reservoirs of quartan malaria (Bruce-Chwatt, 1980).

A- DESCRIPTIVE STATISTICS

About 280 million people in the world carry malaria parasites (WHO, 1991a). Of these, almost 110 million are estimated to suffer each year from clinical malaria. In Africa south of the Sahara alone, 249 million people supposedly are carriers (WHO, 1989) and 88-90 million cases of clinical malaria (WHO, 1989; 1991a) are reported each year. WHO (1993) recognized malaria as the leading cause of morbidity and mortality in endemic areas.

Although there are indications that, in some areas of Africa, malaria specific mortality may be declining (WHO, 1989), these reports are not very convincing. WHO statistics on the world malaria situation (WHO, 1989; 1991a) are based on reports from national surveillance programs from its regional offices in member states but many of the reports are based on clinical diagnosis without microscopic confirmation (WHO, 1991a; Bassett et al.,1991), and thus may not be reliable. For instance, in 1992, Rooth and Björkman investigated the ability of medical doctors to differentiate malarial episodes from other febrile illnesses without laboratory examination. Although fever was present in 98% of malarial cases, the experienced local physicians correctly identified only half of the febrile episodes not related to malaria before microscopic examination. A similar study (Bassett et al.,1991) done in Zimbabwe indicated that symptoms reported by patients with positive malaria slides did not differ from symptoms reported by patients with a negative test. In addition, most cases of Plasmodium infection in endemic areas are asymptomatic (Schwetz, 1948; Swellengrebel, 1950; Trape et al.,1987), thus putting into question data on malaria morbidity/mortality reported to WHO. Such morbidity/mortality may relate to infectious diseases other than malaria, given that people in endemic areas are often multiply infected (Buck et al.,1978b; Ashford et al.,1992) with other infections that are difficult to differentiate clinically from malaria without proper expertise. Currently, the best reports on malaria morbidity and mortality are those in which data on malaria and all concurrent infections are presented, so that proper adjustment can be made for estimates of malaria specific morbidity/mortality.

B- BIOLOGY AND PUBLIC HEALTH IMPLICATIONS

Falciparum malaria infection of man is initiated by the bite of a female anopheline mosquito and the inoculation of its saliva containing sporozoites. In the host's blood stream, fewer than 100 sporozoites are sufficient to infect a susceptible host (Nussenzweig and Nussenzweig, 1985). Transmission may also occur accidentally via contaminated needles or through blood transfusion (Ungureanu et al., 1976; Carosi et al.,1986; Carme et al.,1993). Following inoculation of sporozoites, the blood becomes infective for about half an hour before sporozoites are cleared from the blood. Many sporozoites are destroyed by phagocytes, whereas others enter the liver parenchymal cells where they undergo schizogony or asexual multiplication. The pre-erythrocytic schizogony leads to the formation of merozoites, of which some are phagocytised and some successfully invade red blood cells present in the liver. Once merozoites are released from the tissue schizonts they invade the erythrocytes and become ring form trophozoites.

After successful schizogony, mature schizonts rupture and release merozoites which will then invade fresh erythrocytes to initiate a new generation of parasites. The erythrocytic schizogony will continue repeatedly, leading to a progressive increase of parasitaemia until the process is slowed down by the immune response of the host or successfully treated. The ring forms and older trophozoites usually disappear from the peripheral circulation after 24 hours and become sequestered in the capillaries of the internal organs, such as the brain, heart, placenta, intestine or bone marrow, where their future development takes place. Most fatal cases of falciparum malaria are due to the occlusion of capillaries by clumps of infected red blood cells. Anemia often develops; in about 20% of patients with acute malaria, their hematocrit is below cut-off for anemia (Bruce-Chwatt, 1980). The periodic rupture of mature schizonts every 10 hours and the discharge of merozoites into the blood stream is reflected clinically by a febrile response known as malaria paroxysm (Bruce-Chwatt, 1980). A typical malaria paroxysm comprises three successive stage: (i) the cold stage shivering (rigor) or feeling of intense cold; (ii) the hot stage characterized by a distressing heat and temperatures reaching 41°C or more (Trape et al., 1985; Rooth and Björkman, 1992) and associated headache, nausea, vomiting; (iii) the sweating stage dominated by profuse sweating and a rapid fall of temperature, often below the normal level. If this stage is not treated there may be progression to (i) cerebral malaria, coma or other neurological symptoms such as intoxication and heat stroke, (ii) algid malaria, resembling surgical shock, or (iii) gastro intestinal malaria causing watery diarrhea, dysentery, abdominal pain, renal failure, pulmonary edema and death.

Interestingly, in malaria holoendemic and hyperendemic areas where almost everyone is infected (Schwetz, 1948; Sellengerebel, 1950; Trape et al.,1987), the above conditions are seen only in a few people. The majority of the population is asymptomatic and healthy (Schwetz, 1948; Swellengrebel, 1950; Trape et al.,1987; Musonda, 1993) supposedly due to a lower level of parasitaemia (Swellengrebel, 1950; McGregor, 1964; Trape et al.,1985). Parasitaemia below 400 parasites/µl of blood or a total of 400 parasites in about 400 oil immersion fields (Rooth and Björkman, 1992) or a parasite/leucocyte ratio below 2 (Trape et al., 1985) are known as cutoffs for clinical malaria. P. falciparum can reach densities of 500,000/ul of blood (Bruce-Chwatt, 1980), indicating that the low parasite densities seen in endemic areas (Swellengrebel, 1950; McGregor, 1964; Trape et al., 1985) are caused by host-modulatory factors such as acquired immunity.

After generations of merozoite production in the peripheral blood, some merozoites give rise to sexually differentiated forms or gametocytes. These are ingested by a female Anopheles mosquito when it takes a blood meal. Once in the mosquito host, gametocytes undergo sexual development leading to the formation of thousands of sporozoites in the midgut. These migrate to the salivary glands at which time the female mosquito becomes infective. The prevalence of infection within the vector population is generally very low i.e., 1.87% (Krafsur, 1977).

C- FACTORS AFFECTING THE DISTRIBUTION OF MALARIA

Development of the malaria parasites in human and mosquito hosts as well as its transmission dynamics are regulated by various factors.

a- CLIMATE AND SEASONALITY

Climatic and seasonal variations have a great impact on the life of mosquitoes and the development of malarial parasites. Anopheles mosquitoes are most frequently encounter in tropical or sub-tropical regions, although they are also found in temperate and even in arctic regions during the summer (Bruce-Chwatt, 1980). Malarial parasites however cease to develop in the mosquito when the temperature falls below 16°C; thus optimal conditions for the development and transmission of Plasmodium are within the temperature range of 20-30°C and a mean relative humidity of at least 60%. Temperatures above 35°C and humidities below 50% drastically reduce the longevity of female Anophela which, under favorable climatic conditions, is over 3-4 weeks (Bruce-Chwatt, 1980; Anderson and May, 1991).

In the cold season, male mosquitoes are killed off while females hibernate until the next warm season. When the season becomes too hot and dry, the female Anophela remain in a cool damp place until the dry spell is over (aestivation). In most tropical countries there are two types of season: (i) the rainy season characterized by an increase in mosquito breeding activities and higher oocyst rate (the proportion of infected mosquito) and sporozoite rate (proportion of infective mosquitoes); (ii) the dry season when mosquito activities and malaria incidence supposedly reach their lowest levels (Delacollette et al.,1990). Unfortunately the emergence of "Man-made malaria" where man's activities lead to the formation of suitable breeding places for malaria-carrying mosquitoes has tremendously changed seasonal patterns of malaria in many areas with bimodal seasons. Reports of intense and year long malaria transmission in such areas are many (Ngimbi et., 1982; Trape and Zoulani, 1987b; Mulumba et al.,1990). Ngimbi and co-workers (1982) studied 2,267 Zairean individuals and found no difference between parasite rates recorded during the rainy and dry seasons, indicating that malaria was stable in Zaire. Although Delacollette et al. (1990) reported an unstable and higher transmission during the rainy compared to the dry season in Eastern Zaire, they recognized that transmission continued throughout the year. Mulumba and co-workers

(1990) reported that, in Zaire, such transmission was promoted by a condition of disrepair of the streets and the absence of basic urban services.

b- ALTITUDE AND VEGETATION

Bruce-Chwatt (1980) pointed out that Anopheles are not found at altitudes above 2000-2500 metres. The same author, however, indicated that indigenous malaria has been recorded around the Dead Sea at 400 metres below sea level and at 2600-2800 metres above sea level in Argentina, suggesting that the effect of altitude varies with the type of mosquito. Four types of Anopheles are found in Zaire: A. gambiae, A. funestus, A. nili, and A. marshalli; all are very rare at altitudes between 1600-1700 m and completely disappear at 1800 m (Schwetz, 1948).

In Africa, south of the Sahara, malaria is holoendemic in forest and savanna regions with altitudes up to 1000 m and rainfall over 2000 mm/year. Above altitudes of 1500 m and rainfall below 1000 mm/year, endemicity decreases and the potential for outbreaks increases (WHO 1989).

c- IMMUNE RESPONSE TO MALARIA

Malarial innate immunity is a refractory state due to a resistance of the host cells to support the parasite independently of the host immune mechanisms. Such resistance may be derived from resistance of the liver cells to invading sporozoites or from resistance of the red blood cells to merozoite invasion, intra-erythrocytic growth or release of merozoites (Yuthavong et al.,1990; Nagel, 1990). A typical example of malarial innate immunity is given by sickle cell hemoglobin or hemoglobin S (HbS); a condition found in many parts of the world (WHO, 1982) but frequently among Africans in malaria holoendemic regions. It is lethal in its homozygous expression (SS) but relatively harmless in its heterozygous form (AS). The latter variant has been associated with 90% protection against severe malaria in West Africa. Though there are many other genetic variants of sickle cell hemoglobin i.e., HbC, HbF(fetal), thalassaemia or HbE, it is not clear whether all confer protection against malaria. In Liberia, beta thalassaemia was found to be protective for both clinical and malarial infection (Willcox et al.,1983), but in Thailand, results were not conclusive (Kruatrachue et al.,1969; Brown et al., 1990). Recently it was found that only persons with Hb E who consumed fava beans were protected against malaria, whereas Hb E carriers with no such diet were not protected (Kitayaporn et al.,1992). Interestingly, people with the Hb AS genotype were all resistant to malaria (Kitayaporn et al.,1992), thus leaving no question as to the protective effect of Hb AS genotype against malaria.

In areas where transmission of malaria is very high, infants under 6 months of age rarely suffer from clinical malaria mainly due to antibodies acquired transplancentally from immune mothers (Bruce-Chwatt, 1980). This type of immunity declines after the age of 6 months, and children start experiencing severe symptoms of malaria (Greenwood et al.,1987) as serum gamma-globulin decreases. Such a decrease, however, is not permanent if children continue to be exposed to malaria. Gilles and McGregor (1959) studied the changes in the serum gamma-globulin fraction in protected and unprotected groups of African children living in the same hyperendemic environment from birth to 6 years. The higher concentration seen at birth declined reaching the lowest level between 3-6 months of age, but thereafter began to rise, an indication of a change between passively acquired gamma-globulin and actively synthesized protein. Children are therefore most vulnerable to malaria between the exhaustion of maternal malarial antibodies around 3-6 months of age (McGregor et al.,1956; Walter and McGregor, 1960), and the time when an active humoral antibody response is fully established around 3-6 years of age (McGregor et al.,1956; Gilles and McGregor, 1959; Walter and McGregor, 1960).

To detect how long malarial acquired immunity could last, two groups of apparently immune African adults were studied (Gilles and McGregor, 1961). Members of one group received regular anti-malaria chemoprophylaxis whereas members of the other group were untreated. Gamma-globulin concentration in the protected group dropped steadily and after 24 months of treatment reached proportions similar to those observed in 3 year old children who never experienced erythrocytic malaria. In contrast, in the unprotected group, gamma-globulin concentration remained unchanged and was significantly higher compared with 3 year old children over the study period. These results indicate that the protective effect of gamma-globulin against malaria is related to the level of exposure to malaria and that a progressive loss of protection occurred when exposure to Plasmodium infection stopped (Schwetz, 1948; Gilles and McGregor, 1961).

d- NUTRITIONAL DEFICIENCY AND RESISTANCE TO MALARIA

Solomons and Scott (1994) made it clear that in addition to impairment of the host immune system, other physiological, biochemical, and behavioral changes in malnourished hosts play a significant role in the relationship between malnutrition and infection, by affecting either exposure to parasite infective stages or establishment/development of the parasite within the host. For instance children suffering from extreme malnutrition usually are very weak and do not bother brushing away biting insects. Although such children are more exposed to vector-borne parasites such as malaria, the future of such parasites within the malnourished host has two possible pathways. Malnutrition may lower host resistance to the parasite and aggravate the infection as in the case where folic acid and Vitamin B12 deficiency increase the severity of Plasmodium knowlesi infection in monkeys. Such an interaction is referred to as synergistic (Scrimshaw et al., 1968; Solomons and Scott, 1994). Alternatively, malnutrition may discourage the multiplication of the parasite, making the combined effect less than would have been expected. Such an interaction is seen with deficiency in pantothenic acid and infection with P. gallinaceum in chickens (Scrimshaw et al., 1968) and with deficiency in methionine or vitamin C and infection with P. knowlesi in monkeys (Scrimshaw et al., 1968). These are referred to as antagonistic interactions between malnutrition and infection (Scrimshaw et al., 1968; Solomons and Scott, 1994). Both synergistic and antagonistic associations have been reproduced between protein deficiency and malaria. Plasmodium lophurae produced more severe and prolonged parasitaemia in chicks put on low protein diets compared to those fed high protein diets (Scrimshaw et al., 1968), whereas P. berghei produced more severe infections in rats when their diet was high in protein (Scrimshaw et al., 1963).

These laboratory findings have also been supported by work conducted in human hosts. During the Sahelian drought in Eastern Niger, 41% of patients admitted to the hospital for reasons other than malaria and their healthy accompanying relatives suffered a malarial attack five days later. It was suggested that the early hyperferraemia, apparently related to re-feeding in the hospital, led to rapid multiplication of the parasites and malaria attack (Murray et al.,1975). In a similar situation, the same workers (Murray et al.,1978) randomly assigned to two groups 137 iron-deficient Somali nomads, 67 of whom were treated with placebo and 70 with iron. Seven episodes of infection occurred in the placebo group and 36 in the group treated with iron. The 36 episodes included activation of pre-existing malaria, brucellosis and tuberculosis. These results are indicative that the host defense mechanism against these infections was much better during iron deficiency than during iron repletion (Murray et al.,1978) and corroborate evidence from Nigeria that well-nourished children were more susceptible to cerebral malaria than malnourished children (Edington, 1967). Given that malnutrition is always associated with poverty and low socio-economic status (Bertrand et al.,1988; Sive et al.,1993), it is obvious that malaria distribution in endemic areas is also affected by the socio-economic status.

e- SOCIO-ECONOMIC STATUS AND MALARIA

Although malnutrition has been said to be protective of malaria and poverty is associated with malnutrition, speculating that low socio-economic status may be protective to malaria is not justified. Studies, in fact, show that low socio-economic status is associated with a high risk of infection (Carme et al.,1994). Mata (1982) pointed out that the incidence of parasitic infections was decreasing in many areas that have improved their social and economic situation, a good example that higher living standards lead to lower level of infection.

Seven urban communities with different socio-economic levels were compared in Kinshasa, Zaire. Results indicated that the higher the socio-economic status, the lower the parasite rate (Ngimbi, 1982). More recently, Carme et al. (1994) studied the socio-economic risk factors of cerebral malaria in Brazzaville, Congo. Their findings strongly support what was reported in Zaire (Ngimbi, 1982). Households with a child who had been hospitalized for cerebral malaria were compared with households where such an event had not occurred; the group in which at least one child had been hospitalized for cerebral malaria had a lower socio-economic standard than the control group (Carme et al.,1994). The authors noted no significant differences between the groups with regard to ownership of mosquito nets or use of insecticides or repellents (Carme et al.,1994).

Poor housing, the presence of swamps and pools of rain/sewage water caused by the lack of proper drainage systems and sewers are important determinants of malaria in urban areas. Such conditions predominate poorer neighborhoods (Hedberg et al.,1993) and the mosquito population is believed to vary with the socio-economic status. Trape and Zoulani (1987a) reported significant differences in anopheline density and in the number of infective bites in different subdivisions of the same city. A transmission rate of up to 100 infective bites per person per year was recorded in the peripheral part of the city where basic urban services were absent compared with less than one infective bite per person every three years in the central part of the city where most urban services were provided (Trape and Zoulani, 1987a). Such patterns have important implications both in malarial clinical medicine and for designing malarial control strategies.

D- CONTROL STRATEGIES

Few parasitic infections have received as much attention as malaria. Strategies for malaria control are many and seemingly all look simple, straight-forward and very promising to the point that one cannot comprehend why almost four decades after the adoption of the principle of malaria eradication by the World Health Assembly (Bruce-Chwatt, 1980) and lately by the declaration of the Ministerial Conference on Malaria in Amsterdam (WHO, 1993), malaria still remains a threat to the world. Malaria is a curable disease and application of available control strategies has successfully eliminated the parasite from many parts of Europe and North America. So why is malaria still a problem today? The social, political, economic changes and population movements such as those occurring in Africa have been incriminated for the failure to control malaria (WHO, 1993). The development of insecticide resistance in vectors (Bruce-Chwatt, 1980) and of drug resistance in Plasmodium

(Bruce-Chwatt, 1980; Ngimbi et al., 1985; Afari et al.,1992), compounded with an increase in environmental deterioration (Coene, 1991) and changes in human behavior (Mata, 1982) are major factors that have hindered malaria control and have set back eradication programs in the tropics and subtropics. Given these complicating factors, some workers have expressed the need for aggressive research into new control strategies and greater understanding of the disease among the affected population (Barnes, 1968). In endemic countries, the goal of control programs is the prevention of malaria mortality, and the reduction of morbidity and socio-economic losses related to the disease. Perhaps a careful application of current control strategies or their combination can lead to eventual eradication, but success depends on political support from the highest level and on the suitability of the approach taken for control. Interestingly, current guidelines for malaria prevention are still those provided 4 decades ago (Russell, 1952): (i) prevent mosquitoes from feeding on man, (ii) eliminate or reduce mosquito breeding by altering the environment, (iii) destroy mosquito larvae, (iv) destroy adult mosquitoes, and (v) eliminate Plasmodium in the human host.

a- PREVENT MOSQUITOES FROM FEEDING ON MAN

The level of malaria in communities is obviously a function of the man-vector contacts (Anderson and May, 1991), thus there is no question that prevention measures seeking to decrease the level of such contact will equally decrease the level of malaria. Given the indoor late night biting behavior of A. gambiae (Zoulani et al.,1994), the major Plasmodium vector in Africa, the use of insecticide impregnated bednets is likely the best strategy for reducing man-vector contact. Zoulani et al (1994) studied the effect of bednets impregnated with deltamethrin on the biting behavior of A gambiae in Djoumouna, Congo and found that impregnated bednets reduced by 50% the biting rate of A. gambiae on humans. Coene (1991) even said that the use of bednets is the only realistic means at this moment for malaria prevention. However, the final outcome of a large scale implementation of malaria control based on impregnated bednets will depend on health education, on the availability of bednets at low cost, on the creation of the appropriate structures for the re-impregnation and distribution of the nets and finally on the sustainability of the whole effort. The success of other repellents, such as those applied to the skin or clothing, depends on the same factors. Field trials are needed to evaluate the short- and long-term effects on malaria transmission and on its clinical expression, as well as on the build-up of natural immunity.

b- ELIMINATE OR REDUCE MOSQUITO BREEDING SITES BY ALTERING THE ENVIRONMENT

Many human activities such as gardening, construction projects, squatting, create breeding places for malaria-carrying mosquitoes and raise the incidence of the disease. Several methods have been suggested for mosquito control in such situations: the filling of unnecessary depressions in which water collects, the regulation of natural water sources, drainage activities, weed control, intermittent drying, etc. (Bruce-Chwatt, 1980). Although these tasks are relatively cheap and require neither skilled personnel nor expensive equipment, the presence of shallow water remains a threat in most malarious countries (Ngimbi et al.,1982; Trape and Zoulani, 1987a, Mulumba et al.,1990), possibly due to economic or socio-cultural reasons.

c- DESTROY MOSQUITO LARVAE

Larvae of A. gambiae are commonly found in pools usually exposed in sun, and are more common in temporary pools than long standing ones (Bruce-Chwatt, 1980). Although insecticides continue to be the mainstay of mosquito-borne disease control, concern about environmental contamination and petroleum price increases have renewed interest in biological control (WHO, 1976; 1980). Some researchers believe that use of larvivorous fish is a single and cost effective measure (Wickramasinghe and Costa, 1986) to control mosquito larvae. For example, the introduction of Gambusia affinis in Afghanistan to control the main malaria vector had a significant impact on breeding and biting densities. The fish operations cost only US $ 0.02 per person protected compared to US $ 0.50 per person, for residual spraying of DDT 75% water dispensable powder (Wickramasinghe and Costa, 1986). Unfortunately aquatic vegetation impedes predation of mosquito larvae by larvivorous fish. Therefore, the joint use of herbivorous and larvivorous fishes is possibly the most efficient biological means to control mosquito larvae. If nutritional habits or food shortages in some communities result in humans consuming such fish, the use of biological agents such Bacillus sphaericus can be preferable. Karch et al. (1992) evaluated the control of A. gambiae and other mosquito larvae with a granular formulation of Bacillus sphaericus (Vectolex) in rice fields and swamps. Although treatment reduced larval populations of A. gambiae by 98% after 48 h, and A. gambiae human biting by 13.6% during the post-treatment period, indications were that the efficacy of B. sphaericus was limited and that repetitive applications were required every 15 days. Thus B. sphaericus has a low potential for A. gambiae control and the use of larvivorous fish remains the best biological control measure for mosquito larvae.

d- DESTROY ADULT MOSQUITOES

Anopheles gambiae and malaria have been eradicated from some parts of the world (Bruce-Chwatt, 1980) mainly through outdoor spraying of chemicals such as chlorinated hydrocarbons (DDT, HCH, dieldrin etc.). Seemingly, malaria can be eradicated from a community by keeping mosquitoes out of the area until every infected individual is properly treated. After such a program, whether or not the mosquitoes population bounces back to its previous level, the success of the control program will depend on rigor of malaria surveillance in the community. This perception of mosquito control seems to be more appropriate for savanna or tropical forest regions. The absence of roads in those regions however, renders control programs very difficult as insecticide spraying in some areas could only be possible by aeroplane pulverization. Yet such a strategy is expensive to sustain and obviously not very attractive for most third world countries.

The price of petroleum products alone is reportedly causing more and more concern about the cost-effectiveness of outdoor insecticide use (Wickramasinghe and Costa, 1986). Concerns are even greater about environmental contamination created by insecticide use (WHO, 1976) and about the fact that mosquitoes are becoming resistant to some insecticides (Bruce-Chwatt, 1980).

e- ELIMINATE PLASMODIUM IN THE HUMAN HOST

This is commonly achieved by the use of suppressant drugs such as chloroquine, but the use of chemoprophylaxis in infants and young children is controversial, given that it delays or blocks the development of acquired immunity and increases the incidence of serious forms of malaria in groups normally spared (Greenwood, 1984).

The most serious problem related to malaria chemoprophylaxis, however, is the development of resistance to chloroquine, first seen in Colombia and Brazil, then in Asia and lately in Sub-Saharan Africa (Bruce-Chwatt, 1980; Ngimbi et al., 1985; Afari et al.,1992). Of particular interest is the study conducted in 3 different ecological zones of Ghana (Afari et al., 1992) which incriminate the frequent use of chloroquine as a determinant in the distribution pattern of P. falciparum resistance. The pattern of reduction in the resistance of P. falciparum to chloroquine from the coast to the forest zone and from the urban to the rural sub-zone indicates that the sensitivity of P. falciparum to chloroquine varies with accessibility to health care system, with the frequency of chloroquine use and with the level of malaria endemicity and acquired immunity. The fact that chloroquine resistance was lower in forests where people were more immune lends support to results from Kinshasa, Zaire (Ngimbi et al.,1985) where cases of resistance to chloroquine were found only among children of less than 4 years of age, the least immune subjects in the community. However despite reports of resistance to chloroquine, most clinical trials conducted in Africa still favor chloroquine as the drug of choice (Ngimbi et al.,1985; Turaman et al.,1992; Afari et al.,1992) for malaria treatment.

While the means to achieve malaria control/eradication in the tropics and sub-tropics remains a puzzle, new hopes are focussed on possible vaccines. Indeed intensive research on sub-unit vaccines has shown some candidate vaccines (Jones and Hoffman, 1994) and the most recent field trials of SPf66 have brought promising results (Alonso et al.,1994; Aldhous, 1994)

3- POLYPARASITISM

Polyparasitism is the common designation for infection in which more than one species of parasite is involved. Infection may vary from simple combinations such as those involving only soil-transmitted helminths (Robertson et al.,1989), to complex combinations involving gastrointestinal, blood, lymphatic and tissue helminths and protozoa (Buck et al.,1978a; 1978b; Ashford et al.,1992). The actual extent of polyparasitism in the world is unknown; therefore its clinical and pathological consequences within individuals and communities remain unassessed. This lack of information is particularly marked for infections that do not present pathognomonic signs or that are clinically unapparent such as a number of intestinal helminth infections (Keusch and Migasena, 1982). Seemingly, the distribution of multiply infected individuals throughout the world is related to the distribution of the most prevalent parasites.

A- DESCRIPTIVE STATISTICS

WHO (1991a; 1991b) estimates that one billion people in the world are infected with A. lumbricoides, 900 million with hookworms, 500 million with T. trichiura, and 280 million with malaria parasites. These estimates, however, do not consider how many people are infected with more than one single type of parasite (Buck et al.,1978a; Kan, 1985; Bundy et al.,1987b; Adeyeba and Dipeolo, 1984; Meunier et al.,1984). They are compiled from reports sent to WHO by regional offices where the focus is more on single infections rather than on polyparasitism. Although field workers usually record the frequencies of different types of parasite in communities, very few investigate the extent to which parasites are found together in individual hosts. In an effort to alleviate this problem, estimates of polyparasitism have been generated through mathematical modelling using published data on single infections (Bundy et al.,1991). In Africa 36 million people are estimated to harbor both Schistosoma and geohelminths and 15.6 million are estimated to harbor Schistosoma, geohelminths and Onchocerca. In Brazil, between 2.9 and 4.3 million people are estimated to have multiple infections. These estimates, however, may be far from the reality, since the relative frequency of different types of parasite combinations within an individual or community host varies not only with the number of co-endemic parasites but also with many other factors (Buck et al.,1978b; Keusch and Migasena, 1982).

B- FACTORS AFFECTING POLYPARASITISM

Factors affecting polyparasitism are complex, but basically they fall under two main headings: (i) those involving direct interactions between the parasite and specific characteristics of the host and (ii) those involving interactions among parasites themselves. The latter has to do with how different parasites associate with each other, and will be discussed separately in the next section.

Some host specific characteristics may predispose (Kan, 1985) or protect (Mason et al.,1977) the host against certain types of parasites. For instance, in a community endemic for A. lumbricoides and P. vivax, the number of individuals with combined A. lumbricoides-P. vivax infection will depend on the number of individuals predisposed to A. lumbricoides who also are positive for the duffy genotype. One of the requirements for blood stage infectivity with malaria parasite is the presence of specific red blood cell receptors for merozoite attachment (Butcher et al.,1973). In the case of P. vivax this receptor is related to duffy blood group determinant (Mason et al.,1977). Thus while the duffy positive genotype predisposes the host to P. vivax infection, the duffy negative genotype predominantly seen among people of Bantu origin in Sub Saharan Africa (Miller et al.,1976; Welch et al.,1977) is protective to P. vivax infection (Mason et al.,1977). Other host physio-pathological characteristics that may play a role in the distribution of polyparasitism are sickle cell hemoglobin (HbS and HbE), iron deficiency etc.

Parasites have different levels of immunogenecity. Africans living in malaria holo/hyperendemic areas have higher concentrations of serum gamma-globulin (Bruce-Chwatt, 1980; Ngimbi et al.,1982;

Musonda, 1993), and the density of parasites in such individuals has been reported to be below the cut-off for clinical malaria (Trape et al.,1985); yet individuals heavily infected with A. lumbricoides usually return to their previous infection level after a treatment program has been removed suggesting that acquired immunity in A. lumbricoides infection is not as effective as in malaria infection. Croll et al. (1982) believed that acquired immunity was not a significant feature of Ascaris infection due to constancy of the intensity of infection throughout adult age classes. But the convex relationship described between A. lumbricoides intensity and age (Kan, 1985; Bundy et al.,1988) is suggestive of some type of immunity against Ascaris. How protective is that immunity and how it operates, are not known.

Though it is known that parasites depend on the host for nutritional sustenance, nutritional demands of most parasites are still not understood, primarily because of difficulty of maintaining gut helminths in vitro (Franke and Weinstein, 1984). Failure to satisfy the nutritional requirements of the parasite, for example in malnourished children, is likely to have profound negative effects on parasite survival and/or reproductive function (Keusch and Migasena, 1982; Bundy and Golden, 1987; Solomons and Scott, 1994). These speculations suggest that the extent of polyparasitism can only be estimated with certainty from direct field observations, as various factors affect the distribution of each parasite in many different ways.

C- ASSOCIATION AMONG PARASITES

Few parasitological surveys have investigated the extent to which parasites associate with each other within individual host. However, those who have attempted to investigate this question have repeatedly reported two types of associations among parasites. Positive associations have been reported when correlation coefficients (Ashford et al.,1992), odd ratios (Ashford et al.,1992) or other measures of relationships between parasite species were significant and positive (Annan et al., 1986; Haswell-Elkins, 1987; Robertson et al.,1989; Karumba et al., 1991). These indicate that parasite species occur together and develop in the same habitat, without interference on each one's development. This type of association is also known as synergistic, as the additive effect of the combined infection is presumably detrimental to the host (Buck et al.,1978a; Keusch and Migasena, 1982). When measures of relationships among parasites are significantly negative, the association is referred to as negative or antagonistic (Beisel, 1982a), and can be due to interspecific competition leading to mutual exclusion between parasites. Such parasites are less likely to develop together in the same habitat and therefore the relationship is seen as beneficial to the host (Murray et al.,1978; Beisel, 1982a; Keusch and Migasena, 1982; Scrimshaw, 1991). At the community level, Buck et al.(1978b) explained that a negative association between two infections could result from differences in the age patterns, when one infection has its highest prevalence in early childhood i.e., hyperendemic malaria (Schwetz, 1948; Bruce-Chwatt, 1980), and the other has its highest prevalence in early adulthood i.e., hookworm (Bradley and Chandiwana, 1990).

However, whether synergistic or antagonistic, to date, it still unclear whether associations between parasites are due to ecological or biological processes, especially for parasites with striking similarity in their life cycles and frequency distribution such A. lumbricoides and T. trichiura. Robertson and co-workers, (1989) investigated 661 schoolchildren in 4 different schools of Cocle province, Panama. The prevalence and intensity of different intestinal helminths were determined and associations between parasites were assessed. Chi-squared statistics using prevalence data were estimated as a qualitative measure of association; the Kendall's coefficient on intensity data was estimated as a quantitative measure of association. The following significant positive associations were found: between A. lumbricoides and hookworm in schools 2 and 3 but not in schools 1 and 4; between A. lumbricoides and T. trichiura in schools 1, 2 and 3 but not in school 4; between hookworm and T. trichiura in all four schools. A significant positive correlation was found between A. lumbricoides and T. trichiura intensities using only children infected with both parasites in the fourth school. Though the authors speculated that the observed results may have been due to environmental factors, they did not specifically elaborate why parasites positively associated in one school were not associated in other schools. It was clear that the discrepancy was due to ecological differences between the schools. It is unfortunate that the authors did not estimate rank correlations for each school as they did with qualitative measures of association. If they did and found the same association patterns as in their qualitative analysis, that would have implied that the associations were ecological and not biological.

The concept of ecological and biological associations among parasites is not clearly described in the literature. However, from published data (Buck et al., 1978a; Croll and Ghadirian, 1981; Haswell-Elkins et al.,1987; Robertson et al.,1989; Bundy et al.,1991; Anderson and May, 1991; Ashford et al.,1992), perhaps an association between two parasites may be perceived as biological when it remains consistent whenever or wherever the two parasites dwell in the same ecosystem. When such an association changes in magnitude or direction from one ecosystem to another, the association may be defined as ecological. This is to say that, given a suitable sample size, the same biological association should be detected in every ecological stratum analysed. If a stratified analysis indicates differences between such strata this may be attributable to ecological heterogeneity within stratification factors (i.e., community) and not to biological characteristics such as the life cycle of the parasite. This distinction between ecological and biological associations may alleviate confusion from conflicting reports about associations among parasites. For instance Croll and Ghadirian (1981) did a direct estimation of the intensity of intestinal helminths through worm counts in three different villages of Iran. Their results contrasted with those of Robertson et al. (1989) and others (Haswell-Elkins et al.,1987) as "wormy persons" could only be identified for one parasite. In other words, individuals who carried excessive burdens of one helminth were not necessarily prone to concurrent higher infection by other helminths. This was so even when the biology of the helminths was very similar as in A. duodenale and N. americanus or A. lumbricoides and T. trichiura. These results are supported by others (Bundy et al., 1987) and imply that similarity in life cycles of parasites is not a sufficient condition for those parasites to be biologically associated. Ashford et al.(1992) found strong associations between parasites when the entire sample was measured but when the analysis was done by groups of individuals matched for village and age, most associations were eliminated and those that remained were reduced in magnitude. The disappearance of the associations in some strata suggest the associations were indeed ecological.

D- IMPLICATIONS OF POLYPARASITISM

Polyparasitism has important implications in clinical and laboratory medicine, as well as in the cost-effectiveness of control programs.

a- CLINICAL AND LABORATORY MEDICINE IMPLICATIONS

Polyparasitism poses serious problems in clinical and laboratory medicine in endemic areas. In the majority of cases it is impossible to assign a single cause to a child's health condition or death (Schwetz, 1948), because often children are battling several conditions. Often the diagnostic label given is arbitrary and in most cases will reflect the area of specialization or preconceived ideas of the investigator. After several years of medical practice in Africa, Jelliffe (1978) recommended that all the conditions present be listed in the cause of admission to hospital or death in the tropics with a tentative assessment of primary and secondary cause. The diagnostic problems are further enhanced by mimicry of the clinical picture of even the advanced stages of certain chronic parasitic diseases. Abdominal pain, diarrhea, weight loss, anemia, fatigue, headache, fever, splenomegaly, hepatomegaly etc. are clinical features that are associated with all of the following parasites: A.

lumbricoides, hookworm, T. trichiura, P. falciparum and possibly with many other tropical parasites (Wolfe, 1978; Banwell and Schad, 1978; Bruce-Chwatt, 1980; Gilles, 1985; WHO, 1985; Stephenson, 1989). With such a wide symptomatic similarity it is difficult to diagnose these infections in developing countries where basic laboratory equipment such as microscopes are not usually available and most diagnoses are based on clinical features (Greenberg et al.,1989). Cases of misdiagnosis are numerous. Possibly this is why Greenberg et al.(1989) observed that 62.2% of all pediatric deaths from malaria in a Kinshasa hospital occurred in the emergency ward. Often parents brought their children to hospitals when they became moribund and medical attention in their neighborhood clinics, where diagnosis had been made clinically, was unsuccessful.

Malaria (Bruce-Chwatt, 1980; Jelliffe, 1966) and schistosomiasis (Buck et al.,1978a) are both associated with splenomegaly and hepatomegaly. To investigate speculation that combined infection increased the severity of hepatosplenomegaly, Buck et al.(1978a) investigated four villages with different combinations of schistosomiasis and malaria. Of those, two had hyperendemic infection with S. haematobium and malaria, one had S. mansoni and malaria and one had malaria only. Their results were consistent with the hypothesis that joint occurrence of malaria and S. mansoni produces more hepatosplenomegaly and larger livers in the community than either malaria alone or in combination with S. haematobium infection. A similar observation was made for splenomegaly, indicating that co-endemic infections with malaria and S. mansoni are more detrimental to the host than single infections with either parasite.

b- ECONOMICAL AND EPIDEMIOLOGICAL IMPLICATIONS

The availability of safe and effective drugs has made it feasible to control the risk of morbidity by reducing the intensity of infection. The use of chemotherapy as a control tool, however, is constrained by the limited financial resources in developing countries. Maximizing the available resources by integrating the control of several parasitic diseases or using a single community program to deliver multiple treatments against several parasitic infections is an attractive operational strategy (Keymer and Bundy, 1989), as the cost of delivery is often the major proportion (75-90%) of the control budget (Bundy et al.,1991). But such an approach has to be justified epidemiologicaly. A multiple treatment approach can only be justified in situations where the distribution of combined infections is high. For relatively rare parasites, the combined treatment approach cannot be recommended; instead appropriate control strategies should be sought at specific foci where such infections are prevalent (Bundy et al.,1991).

In terms of multiple infections, it has been revealed that some villages or communities were wormy (Croll and Ghadirian, 1981). The authors suggested that identification of such villages or communities was possible by examination of a small sample size and concentration of control effort in such groups would likely achieve maximum benefit at minimum cost and perhaps prevent the development of drug resistance (Croll and Ghadirian, 1981). This is because the rate of development of drug resistance in some infections can be retarded by selectively treating those with high parasitaemia (Anderson and May, 1991).

In a study conducted in Kinshasa, Zaire, 575 individuals with different gastrointestinal helminths were investigated to assess the efficacy of albendazole in comparison with pyrantel (Mbedi et al.,1985). One hundred percent efficacy rate was recorded for albendazole when individuals were singly infected with A. lumbricoides, T. trichiura, A. duodenale, Strongyloides stercoralis or Taenia. The efficacy rate was slightly lower in double infections with the same parasites with the lowest rate being 90.9% in A. lumbricoides-A. duodenale combination. The efficacy rate decreased further in triple infections with the lowest rate being 75% in A. lumbricoides-T. trichiura-S. stercoralis combination. The efficacy of pyrantel was significantly lower than that of albendazole in single as well as in combined infections. The authors did not elaborate on these interesting patterns possibly because it was not the aim of their study, even though these results obviously suggested that the efficacy of both albendazole and pyrantel dropped as the number of parasites co-occurring in the same host increased. This is possibly an indication that the greater the diversity of parasites found together, the less responsive each is to treatment.

III- HOST NUTRITION

Nutritional status is an important feature of host health. Although vitamin and/or mineral deficiencies are responsible for morbidity and mortality (Latham, 1984), protein and energy deficiency, commonly known as protein energy malnutrition (PEM), is the most important nutritional problem in the world today. It is the main type of malnutrition that the World Food Program Committee is trying to correct (WHO, 1983), because it is the cause of most morbidity and mortality in the developing world and often has long-term consequences on children's health. For instance children affected by marked growth retardation usually have limited biological and intellectual abilities in adulthood (Hutchinson, 1952; Pollitt, 1990). Stunted children frequently experience social disadvantages detrimental to their development, stunted women have increased obstetric risks (Calloway, 1982). Deficiencies of vitamins, mineral or protein and calories also have important modulatory effects on host defense mechanisms, influencing susceptibility to infectious agents. Growth assessment is probably the single measurement that best defines the nutritional as well as the general health status of children and/or communities. This is because nutritional disturbances, regardless of their etiology, invariably affect children's growth.

1- ASSESSMENT OF THE HOST NUTRITIONAL STATUS

Several methods to assess PEM exist, but WHO recognizes anthropometry as the most useful tool to provide a comprehensive description of children's growth status. Standard anthropometric measurements were defined by the USA National Centre for Health Statistic (NCHS) and WHO Joint Commission in 1983. Basic data were collected from American children on age, sex, weight, and height. Anthropometric indices of weight-for-height, height-for-age and weight-for-age of those children were estimated and used to form an international reference/standard. For statistical reasons, it was recommended that measurements from other studies be compared to that of the US NCHS (WHO, 1983) reference group by their standard deviation scores or Z-scores. Children falling above + 2 standard deviations (SDs) of the median child of the reference group for any anthropometric index are considered as having problems of overweight. Those falling below -2 SDs of the median child of the reference group for height-for-age are classified as stunted, those falling below -2 SDs for weight-for-height are referred to as wasted, and those falling below -2 SDs for weight-for-age are said to be underweight.

Anthropometric indicators (wasting, stunting and underweight) are useful in the biological and epidemiological interpretation of nutritional data. For instance, wasting indicates a deficiency in tissue and fat mass from a child compared with the amount expected in a child of the same height. It reflects situations where food supplies are limited and food intake of children is low. Given that wasting can develop very rapidly under unfavorable conditions but that weight is restored quickly under favorable conditions (Ashworth, 1969), wasting is a form of acute PEM and its presence at one point in time is considered as a reasonable indicator of the incidence of the process that is causing it (WHO, 1986). The prevalence of wasting is greatest between 12-24 months of age, when dietary deficiencies are common and when diarrheal diseases are most frequent (WHO, 1986).

Stunting, or chronic PEM, reflects a slowing in the skeletal growth due to early childhood insults and represents accumulated consequences of retarded growth (WHO, 1986). It is commonly associated with poor overall economic conditions, mild to moderate chronic or repeated infections, as well as inadequate nutrient intake. Stunting is more prevalent between 36-60 months of age.

It has been shown that weight-for-height and height-for-age together account for more than 95% of the variance in weight-for-age (WHO, 1986) meaning that weight-for-age incorporates the information given by the other two indices. Therefore weight-for-height and height-for-age and their indicators, wasting and stunting, are enough to describe the nutritional status of a population.

Kwashiorkor is another form of PEM. It is characterized primarily by edema, enlargement of the liver, with preservation of the subcutaneous fat (McLaren, 1981). Kwashiorkor and wasting are known as the most severe forms of PEM, but the prognosis for wasted children is better than for those with kwashiorkor (Beisel, 1977). Identification of cases of kwashiorkor is not easy using the US/NCHS reference group. In a study conducted in Kinshasa, Zaire (Franklin et al., 1984b), only 4.1% of children with kwashiorkor were found to be both acutely wasted and edematous, and 71.7% of the children with edema were not wasted. Therefore if calculation of the proportion of children with acute PEM had been based only on estimation from the US/NCHS reference group for weight-for-height, 71.7% of children with kwashiorkor would not have been considered to be acutely malnourished. Fortunately, natives and medical personnel in regions where kwashiorkor is common have a sound knowledge of this condition and have no difficulty in diagnosing it (Konotey-Ahulu, 1994).

A further difficulty associated with the use of the US/NHSC reference group in developing countries is that growth potential may differ among children with different racial/ethnical backgrounds (Golstein and Tanner, 1980). In communities characterized by low growth potential, the magnitude of nutritional problems may be over-estimated if the US/NCHS population is used as the reference group. Studies conducted in Trinidad and Tobago (Gueri et al.,1980), for example, indicated that children of African origin were significantly heavier than those of East Indian origin. However because similar differences were not detected in Jamaica or Barbados, the authors concluded that the growth potential was the same in all ethnic groups. They attributed the difference between African and Indian children in Trinidad to differences in socio-economic conditions between these groups (Gueri et al.,1980). To alleviate concerns that reference groups derived from industrialized countries are not appropriate for use in the developing world (Golstein and Tanner, 1980), Graitcer and Gentry (1981) collected anthropometric data from 2366 children aged 6-59 months in Egypt, Togo and Haiti. The children were chosen from private day care centers, pediatricians' offices and families of military and government officials, in other words from the privileged group. These data were compared with the US/NCHS reference population. The distributions of weight-for-height and height-for-age for the privileged group and the reference population were nearly identical. These findings suggest that the use of the US/NCHS reference population in developing countries is well justified (Graitcer and Gentry, 1981), and that children's growth rates are independent of their race or ethnicity (Habicht et al.,1974). The relevance of the US/NCHS international reference is that nutritional data can be compared throughout the world and the magnitude of problems compared.

2- DESCRIPTIVE STATISTICS

Five hundred million children in the world (0-6 years old) suffer from PEM (Latham, 1984); of these, 1 million have clinical cases of kwashiorkor and wasting (Latham, 1984). These estimates however are gross and do not express the real magnitude of all forms of PEM in different countries. Recognizing the magnitude of the problem is a critical first step to mobilizing the human and financial resources required to overcome nutritional problems in the world.

Using WHO's global database on child growth, Onis and co-workers (1993) described the distribution of PEM among under-five year old children from 79 developing countries, using the following categories. Prevalence of underweight and stunting was classified as low (<20%), moderate (20-29%), high (30-39%) or very high (≥40%). The prevalence of wasting was defined as low (<4%), high (4-7%) or very high (≥8%). Given these categories, wasting, stunting, and underweight were found to be low to moderate in Latin America, with only 5% of children affected. In contrast, the prevalence of PEM indicators varied from high to very high in Asia, with 80% of children affected, mainly in southern part of the continent. In Africa there was a combination of moderate, high and very high prevalences of PEM indicators, (15% of children affected). The western and eastern parts of the continent were the most affected. In central Africa, available data were insufficient to allow regional generalization.

3- CORRELATES OF MALNUTRITION

Nutritional problems during childhood are the result of a wide range of factors, most of which occur particularly in underprivileged populations and relate to severe and repeated infections (Stephenson et al.,1985; Stephenson, 1987; Stephenson et al.,1989), diarrhea (Sepulveda et al.,1988), poverty (Ighogboja, 1992; Sive et al.,1993) or poor food availability (Branca et al.,1993). The effects of these factors are influenced by seasonality (Branca et al.,1993), age and sex (Mbago and Namfua, 1992).

A- INFECTION AND DIARRHEA

Interactions between malnutrition and infection have been partly reviewed in previous sections; in this section only critical points are discussed. While the negative nature of the association existing between infection and growth cannot be put into question (Stephenson et al.,1989), the magnitude of effect is dependent upon many factors (Cerf et al.,1981).

Cerf and co-workers investigated relationship between infection and children's growth in three hamlets of a Balinese village in 1981. The three communities were similar in environmental and living conditions as well as in various socio-economic and cultural aspects but significantly differed in their access to health care and in food availability. A significant negative association between A. lumbricoides and children's growth was found only among children living in the two most underprivileged hamlets located in the periphery of the village. No such association existed in the centrally located hamlet where children apparently enjoyed easy access to health care and had adequate food intake. While these results suggest that easy access to adequate food and to health care influence A. lumbricoides-PEM relationships, they also explain why the causal role of A. lumbricoides in the development of PEM cannot be proven in some studies (Shah et al.,1975; Gupta and Urrutia, 1982). However there is speculation that some types of PEM may decrease A. lumbricoides infection through anorexia, thus reducing exposure to A. lumbricoides infective stages in food (Solomons and Scott, 1994). Interestingly infection has been described to affect growth using the same pathway (anorexia). In studies conducted in the Gambia (McGregor et al.,1956) children who did not receive weekly chloroquine and suffered repeated malarial attacks reportedly gained less weight than age-matched children receiving chloroquine; the weight-for-age profile showed that the group not receiving chloroquine repeatedly lost and regained weight more frequently than the chloroquine treated group. Seemingly, decrease in weight-for-age in non-treated children related to decreased food intake during malarial attacks, and the increase in weight-for-age was related to increased food intake during the recovery period. These results indicate that infection-PEM interaction is a bi-directional relationship. Perhaps this is why, in endemic areas infection and PEM usually go hand-in-hand, as infection predisposes to malnutrition (Stephenson, 1987; Stephenson et al.,1989) and malnutrition predisposes children to infection (WHO, 1972) and diarrheal diseases (Gordon et al.,1964; Tomkins, 1981; Sepulveda et al.,1988).

Studies conducted in Guatemala (Gordon et al.,1964) provided evidence that the number of cases and the severity of diarrhea increased with the degree of malnutrition. In Nigeria, Tomkins (1981) found that the frequency of diarrhea was significantly higher in wasted compared with underweight or stunted children. While these studies provide evidence that malnutrition predisposed children to diarrhea, they both have limitations as to whether or not those associations were confounded by other variables such as parasitic infections or socio-economic status. More recently, Sepulveda et al. (1988) investigated associations between nutritional status and diarrhea in Mexican children and used multinomial logistic analysis to control for potential confounding factors. Weight-for-age and age were the strongest predictors of subsequent diarrhea, thus lending support to the relationship between diarrhea and PEM.

B- SOCIO-ECONOMIC STATUS

Association between children's socio-economic status and PEM is well documented (Franklin et al., 1984b; Sive et al.,1993; Mbago and Namfua, 1992). Franklin et al. (1984b) studied 27,000 thousand children in three different subdivisions of Kinshasa, Zaire. From the standpoint of income, environmental sanitation, socio-economic status, and duration of residence in the city, the first subdivision ranked highest, the second ranked medium and the third ranked lowest. The third subdivision was found to have the highest prevalence of stunting and wasting while the lowest level of PEM indicators were in the first subdivision (Franklin et al.,1984b). While these results are consistent with a relationship between the socio-economic status and PEM, they say nothing as to whether the residential zone was actually the determinant or just a confounder in that relationship. In an effort to search for causations of malnutrition in an urban area, Bertrand et al. (1988) measured the nutritional status, morbidity, socio-economic and behavioral variables of children. Potential predictors of PEM were explored using multivariate analyses. Wasting was mainly predicted by morbidity, whereas stunting was predicted by the zone or subdivision of residence of the children. This was very compatible with the WHO (1986) statement that the prevalence of stunting was a measure of social deprivation in a community.

C- SEASONALITY

PEM has been linked to food production/availability (Branca et al.,1993; Pastore et al.,1993). Since food production/availability in the tropics varies with the season, it is obvious that PEM in endemic areas will be more severe in seasons when food production is low. To investigate the impact of seasonality on nutritional status, Branca et al. (1993) studied 203 Ethiopian rural families for 13 months. Bi-monthly questionnaires on consumption and availability of food and other characteristics were administered to the families and anthropometry was performed on children. Results showed seasonal changes in weight-for-height Z-scores and in the height growth velocity pattern. Values of the height growth velocity were closed to normal in July to December, a period characterized by better food availability, and lower in January to June, when there are heavy rains and poor food availability. Height-for-age Z-scores did not display any seasonal pattern but rather a continuous deterioration. The absence of seasonal catch-up in height-for-age, also described by Billewicz (1982), is very compatible with the fact that stunting is the result of remote childhood insults (Keller and Fillmore, 1983) and thus does not reflect any current process. The sensitivity of wasting and growth velocity to seasonal food availability is consistent with reports that these variables are affected by current processes (Ashworth, 1969; WHO, 1986). Nevertheless the fact that Branca et al. (1993) obtained the lowest values in the height growth velocity during the heavy rains season, a period when infections peak in the tropics (Jelliffe and Jelliffe, 1992) and when families have problems storing their food, may lead to hypotheses that infections and/or mold also contribute the seasonal pattern of PEM in endemic areas.

Although parasite, bacterial and viral infections may account for the seasonal pattern of various form of PEM, mold contamination of foodstuff during the rainy season has been specifically implicated in the seasonality of kwashiorkor (Jelliffe and Jelliffe, 1992). The aflatoxin Aspergillus flavus are suggested as the causal agent of kwashiorkor. Aspergillus flavus group of fungi occur worldwide, but their optimal conditions for toxin production are a mean temperature of ±27°C and a relative humidity of ≥85% (Goldblast, 1969). In Africa, where environmental conditions tend to favor toxin production, staple food stuffs, such as maize, cassava and peanuts are often heavily contaminated with aflatoxin. Hendrickse (1991) reviewed clinical and epidemiological data on kwashiorkor and found that the concentration of aflatoxin in the sera of kwashiorkor children was significantly higher than in marasmic (wasted) or healthy children. These findings together with the fact that the distribution of kwashiorkor is mostly in tropical and sub-tropical regions (Jelliffe and Jelliffe, 1992), seems to support the view that aflatoxin is one of the major etiological agents (Hendrickse, 1991; Jelliffe and Jelliffe, 1992) of kwashiorkor and thus responsible for its seasonal pattern. But given the similarity in dietary patterns of kwashiorkor and wasted children (Gopalan, 1970), it is difficult to validate this hypothesis, without knowledge of why and/or how some children become wasted (Branca et al.,1993) whereas others living in the same community develop kwashiorkor (Trowell et al.,1954).

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CONNECTING STATEMENT 1

As the overall objective of this thesis was to study relationships between current environmental and living conditions of Lubumbashi, parasitic infections and health outcomes, the first step was to measure qualitative and/or quantitative aspects of environmental, living conditions and socio-cultural variables that are possible modulatory factors of parasitic infection in the area. The lack of previous work on any of these aspects in this city made it difficult, as we had no insight into the socio-cultural aspect of the community. Thus, every information and observation that we made was collected and quantified if possible (appendix 1-5).

What follows as Chapter III is the first of a three step study to identify environmental, living conditions, socio-economic and cultural variables that are possible risk factor of parasitic infections in Lubumbashi and their relationship with A. lumbricoides infection (used as an index of other parasites that were identified in the city).

Three communities were randomly selected and 42 households were identified in each of them. Mother or care-giver were interviewed in each household, the interviewer also made observations of the home and surrounding area and major characteristics were recorded. Single stool samples from each participant were examined and associations between infection and exposure variables were assessed.

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CHAPTER III

ASCARIS LUMBRICOIDES INFECTION AND ENVIRONMENTAL RISK FACTORS IN AN URBAN AFRICAN SETTING

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ABSTRACT

Identification of appropriate strategies for controlling gastrointestinal nematodes in communities depends, in part, on an understanding of the conditions that increase risk of exposure to infective stages. This study was conducted in Lubumbashi, Zaire. The objectives were to identify features of the environment and living conditions that were significant predictors of *Ascaris lumbricoides* infection, and to determine whether the same predictors were important in populations living in subdivisions of lower (LSES) and higher (HSES) socio-economic status. Forty-two households from each of three subdivisions (2 LSES and 1 HSES) were selected at random. Mothers were interviewed, observations on the environment around the home were recorded, and single stool samples collected from all children and mothers were examined for nematode eggs. Maternal education was a significant predictor of *A. lumbricoides* intensity in both LSES and HSES subdivisions. Factors related to poor sanitation (open defecation and high number of people using the same toilet) were important in the LSES subdivisions but not in the HSES subdivision. In contrast, the ratio of relatives to direct family members per household was a significant predictor of high intensity of infection in the HSES subdivision, but not in the LSES subdivisions, indicating that relatives and live-in visitors contribute to *Ascaris* transmission in the HSES population.

INTRODUCTION

The prevalence and intensity of gastrointestinal nematodes varies widely not only among communities (Higgins *et al.*, 1984; Kan *et al.*, 1989; Ratard *et al.*, 1991), but also among individuals within the same community (Bundy *et al.*, 1988; Forrester *et al.*, 1990). Review articles cite a wide range of environmental and living conditions as important determinants of infection intensity (WHO, 1981; Mata, 1982; Schad *et al.*, 1983; Sanjur, 1989), but the importance of such factors varies from one study to another. For example, Henry (1988) studied the association between reinfection rates with *Ascaris lumbricoides* in St. Lucia and crowding, income, water use, family size, availability of latrine, maternal education, and garbage disposal. He found significant associations only with sanitation and crowding. Similarly, Holland *et al.* (1988) reported that poor sanitation and crowding were associated with higher levels of infection with *A. lumbricoides*, *Trichuris trichiura* and hookworm in Panama, but they also detected associations with type of housing, level of maternal education and socio-economic status. In contrast, Feachem *et al.* (1983) suggested that the type of sanitary facility did not necessarily affect nematode infection levels in cross-sectional studies in Botswana, Ghana, and Zambia.

In planning control programs for gastrointestinal nematode infections, three approaches are usually considered: (1) chemotherapy as a short-term solution; (2) education; and (3) improved standards of housing, sanitation, hygiene and access to safe water, as approaches with longer-term implications. Given the need for a long-term commitment to the latter approaches, it is important to identify those aspects of the environment and living conditions that are the most important determinants of infection level, and therefore that deserve priority attention.

We undertook a cross-sectional study in Lubumbashi, Zaire, with the intent of defining the interrelationships between intensity of gastrointestinal nematodes and living conditions in the area. Initial interviews with local administrative and health authorities prior to commencement of field work revealed that worm infections were among the major health problems in Lubumbashi, and that poor sanitation and hygiene associated with deteriorated living conditions were common, particularly in subdivisions of lower socio-economic status. Our objectives were (1) to compare the level of *A. lumbricoides* infection between families living in higher and lower socio-economic subdivisions; and (2) to determine the important predictors of intensity of *A. lumbricoides* infection in households and whether they were similar for both strata.

METHODS

Study Sites

Lubumbashi was founded in 1909 as a mining camp in Shaba Province, southeastern Zaire; its most recent urban-planned structures were completed in the late fifties when its population was less than 50,000 inhabitants. Today Lubumbashi covers an area of 747 km^2 and has an estimated 565,000 inhabitants (Anon, 1991) with an average annual per capita income of US $170. The dry season extends from May to mid September with average temperatures of 17-22° C. During the rainy season (October through April) temperatures average 21-25° C. The total annual rainfall is 1,100-1,300 mm (World Weather Records, 1967).

The city is divided into seven administrative subdivisions. The two subdivisions that had been restricted to Belgian colonizers before independence in 1960 are now the residential areas for the higher socio-economic class (HSES subdivisions). They are characterized by modern dwellings with electricity, access to safe water and sanitation, and paved roads. The remaining five subdivisions were for laborers of the copper mine, railway, breweries and other companies in the colonial era. Today they are occupied by the lower income class (LSES subdivisions). Sanitary systems and roads are in disrepair, and permanent dwellings have become substandard through aging, negligence, and lack of basic utilities. These subdivisions are typical of slum communities as defined by Drakakis-Smith (1990).

Study Design and Methodology

Three subdivisions were randomly selected, two of LSES: Zone Kamalondo (Subdivision "I") and Zone Kenya (Subdivision "II"); and one of HSES: Zone Lubumbashi (Subdivision "III"). In Subdivisions I and II, census data from the city were supplemented by our own census to include squatters not listed in the city registers. A total of 1904, 2662 and 2100 households were respectively identified in Subdivisions I, II and III. For the purpose of this study, household is defined as the group of persons (related by blood or not) that dwell together. Using systematic sampling from registers compiled from all census information, 42 households in each subdivision were selected and written or oral informed consent was requested. Two households in Subdivision I, 3 in Subdivision II and 5 in Subdivision III chose not to participate, and they were replaced to give a total of 126 households. The study was conducted between June and August, 1991, with approval from a McGill University Ethics Committee and the Zairean Ministry of Health.

A face-to-face interview was conducted with the mother or care-giver in each household. In households with more than one mother, the senior, more respected mother was interviewed. Demographic information on all members of the household was taken. Direct family members were defined to include the immediate family, parents and their children as conceived in the Zairean culture as "famille restreinte". Other members of the household were identified as indirect family members/relatives or "famille élargie" as in the Zairean context. An extended family index, calculated as the ratio of indirect to direct family members, was used to estimate the contact between direct and indirect family members. The interviewer also made observations of the home and surrounding area. Information on housing and crowding, sanitation, access to safe water and food, access to health care system, maternal education and occupation, and socio-cultural life were collected. Comparisons of environmental and living conditions among subdivisions were done using Chi-Squared Analysis or Binomial Confidence Intervals for Percentages (Sokal and Rohlf, 1981).

At the time of the interview, participants (children aged 4 months to 16 years and their mothers) were asked to bring a stool sample in the allocated marked container to the laboratory the following day. Stool samples were received from 1100 participants, and examined in duplicate using the modified Kato technique (Forrester and Scott, 1990) to obtain an estimate of intensity of *A. lumbricoides*, reported as eggs per gram of stool (epg). Participants returned to the laboratory two days later, and all infected individuals were provided with mebendazole (100 mg twice a day for three days; Vermox, Janssen Pharmaceutica, Belgium) by the staff physician. Prevalence and intensity of infection of all participants were compared among subdivisions using Binomial Confidence Intervals for Percentages and One Way Analysis of Variance on log-transformed data, respectively.

A single index child (direct family member, aged 4 months to 16 years) was randomly selected from each household for analyses of significant predictors of intensity of nematode infections, in order to meet assumptions of independence of data. Associations between infection and exposure variables were assessed by univariate and multivariate regression procedures (Altman, 1992) for each subdivision independently. Exposure variables with $P \leq 0.70$ were analysed using a backward stepwise regression procedure (Altman, 1992; Armitage and Berry, 1994). We present the models that explain the highest proportion of variability in nematode egg counts, and include those exposure variables with $P < 0.05$. Redundancy and multicollinearity of covariates were checked after each computation.

Data were analysed using Excel (Redmond, Washington, USA), Statworks TM, Cricket Software, (Philadelphia, PA, USA) and Systat (Evanston, IL, USA) on a Macintosh LC Computer at the Institute of Parasitology and the School of Dietetics and Human Nutrition at McGill University, Montreal, Canada.

RESULTS

Characteristics of Subdivisions

The demography of the sampled households in the three subdivisions was similar. On average, households consisted of 12.5 ± 0.5 individuals (mean ± SEM), and 86% of participants were 16 years of age or younger (44% girls and 42% boys). Of these, 40% were below 6 years of age. A total of 87% of participants were classified as direct family members. Of the 13% indirect family members, 26% were less than 6 years old. Many households had more than one mother (average of 1.2 ± 0.5); polygamy is not uncommon in Zaire. Of the mothers, 58% had less than grade 8 school education. All selected families had lived at the same address for more than two years.

Certain features of the home and environment were similar among all three subdivisions. Approximately 94% of houses were constructed of brick, and all houses had tap water. Evidence of rats and/or cockroaches was present in approximately 91% of homes. Children in 72% of the households played in the yard or neighboring roads. All participating families were Christian and none claimed to visit witch doctors.

Differences among subdivisions were detected, however, in most features considered to be indicative of risk of exposure to nematode infections (Table 1). In general, the two LSES subdivisions (I and II) differed from the HSES (III) but were similar to each other (Table 1), supporting the existing stratification used in Lubumbashi. Of particular note were the higher crowding, the poorer sanitation and access to health care in the lower socio-economic strata, along with a lower proportion of mothers with college education or with jobs outside the home.

Prevalence and Intensity of Infection

Ascaris lumbricoides was common in all three subdivisions, with a prevalence ranging from 59% to 76% (Table 2). We had hypothesized that infection levels would be higher in the two subdivisions of LSES than in the HSES subdivision. Prevalence and mean epg of *A. lumbricoides* were significantly higher in LSES Subdivision II when compared with HSES Subdivision III. However, infection levels were similar between LSES Subdivision I and HSES Subdivision III (Table 2).

Predictors of Ascaris Infection

Regression analyses, using *A. lumbricoides* (log epg+1) of index children as the dependent variable, considered 30 exposure variables that differed among subdivisions; seven of these were excluded from further analysis ($P > 0.7$): number of bedrooms, cement floor, children that play away from home, functional sewer, eat on the floor, pests present, and mothers per family. The remaining 23 variables were used in backwards stepwise regression models. Of those, only six remained in the final models: non-educated mother, extended family index, open defecation, persons per bedroom, persons per toilet and gender (Table 3). The presence of an uneducated mother was the most consistent predictor of *A. lumbricoides* epg as it entered all three models with the highest beta value (explanatory power). In the two subdivisions of LSES (I and II), poor sanitary conditions (open defecation) and crowding (persons per toilet, persons per bedroom) were also significant predictors of *A. lumbricoides* intensity. These variables were not significant predictors in Subdivision III. In contrast, extended family index was a significant risk factor in Subdivision III, indicating a positive relationship between *A. lumbricoides* epg in direct family members and the ratio of relatives and live-in visitors to direct family members in the home. Finally, male index children were more at risk of infection than females in Subdivision II.

DISCUSSION

In the present study, environmental and living condition variables were assessed in households from three different subdivisions of Lubumbashi and their relationship with intensity of *Ascaris lumbricoides* infection was analysed. Perhaps the most interesting finding from our study is that high proportions of indirect family members are a significant risk factor for *A. lumbricoides* infection, but only in households in the subdivision of higher socio-economic status. The important role of maternal education as a risk factor in all subdivisions regardless of socio-economic status, and of crowding and poor sanitation in subdivisions of lower socio-economic status supports results found in other studies. Our other interesting finding was that the prevalence and intensity of *A. lumbricoides* at the subdivision level was not associated with the socio-economic status of the subdivision in a consistent manner. This was surprising, especially given the clear differences between HSES and LSES subdivisions in conditions that others have reported to be important determinants of infection.

To our knowledge, no previous studies have considered that a family's level of socialization, or interaction with others, may be a predictor of nematode infection. To investigate this type of association, we designed the extended family index which estimated the level of contact between direct family members and others living in the same household. This variable was identified as a positive predictor of *A. lumbricoides* epg in Subdivision III, but was not a predictor in Subdivisions I or II. The lack of predictive power of this variable in the subdivisions of lower socio-economic status may reflect different transmission patterns between lower and higher socio-economic strata. The high number of indirect family members in Subdivision III is very consistent with the local cultural requirement that "a successful family" foster needy members of the extended family. Often, children whose parents are poor and live in nearby slums or rural areas are fostered by families living in Subdivision III. These children, who spend weekends and holidays with their parents in poorer areas of the city or in rural areas, may provide a continuing source of infection to their foster households in Subdivision III. Based on these observations, we consider it possible that the surprisingly high levels of infection in Subdivision III may, in part, relate to transmission between communities. We believe that this concept should be investigated further, and that information on other types of interaction between communities should also be examined in light of nematode transmission.

The major importance of maternal education as a risk factor for *A. lumbricoides* infection is evident as it is the only risk factor that appeared in all three models (Table 3). The concept of maternal technology, defined by Mata (1982) to include mothers' knowledge of primary health care, and appropriate procedures for storage of food and water, and handling of children's faeces, is presumably a reflection of maternal education. The importance of maternal education in the prevention and control of geohelminth infections has been well documented. For example, two separate studies in Panama have reported that mothers of *A. lumbricoides*-infected children have significantly fewer years of schooling than mothers of uninfected children living in the same contaminated area (Carrera *et al.*, 1984; Holland *et al.*, 1988). These results are in line with ours, where maternal education was a significant predictor of *A. lumbricoides* intensity in all three subdivisions (Table 3). In our study, we classified mothers as educated if they had received at least 8 years of schooling. Most mothers with less than grade eight school education did not read or write French or Swahili and therefore were functionally illiterate.

Indices of poor sanitation were important predictors of *A. lumbricoides* intensity in both of the lower socio-economic subdivisions, but not in the model for the higher socio-economic subdivision. This may be explained by the generally good sanitary conditions in Subdivision III, where 90% of households had indoor toilets (in comparison with only 5-10% in Subdivisions I and II). In the two subdivisions of lower socio-economic status, open defecation was important in Subdivision II and number of persons/toilet was a significant predictor in Subdivision I. Reports of associations between open defecation and nematode infection are found in the literature (Croll *et al.*, 1982; Schad *et al.*, 1983; Akogum, 1989; Chandiwana *et al.*, 1989; Bradley and Chandiwana, 1990). Wong and Bundy (1990) and Wong *et al.* (1991) looked directly at soil contamination in two orphanages in Jamaica, and found that residents of the home with the higher numbers of eggs in soil samples had higher levels of infection with *A. lumbricoides* and *T. trichiura*. Our model for Subdivision II supports a link between open defecation and intensity of *A. lumbricoides*. Although households in Subdivision I had a comparable level of open defecation to those in Subdivision II, we assume that the lack of predictive power of this variable was due to the collinearity with persons per toilet in the Subdivision I sub-model. An association between these two variables was reported by Songsore and McGranahan (1993) who found that children often practiced open defecation when they could not use their toilet, and that more outdoor defecations were observed in groups with less access to a toilet. Our data showed the same pattern. Families who regularly defecated in the open had 27.0±1.9 mean persons per toilet whereas those who did not had 18.6±1.4 mean persons per toilet.

Persons per toilet can be interpreted either as an index of sanitation or as an index of crowding. In order to address crowding in the Zairean context, we measured the size of families and five other variables that reflect the concentration of people in the living space, with respect to access to sanitary facilities and to use of the house by stock animals. Persons per toilet was important in the Subdivision I model, as discussed above, and persons per bedroom showed borderline significance in the Subdivision II model. These results suggest that, in Lubumbashi, access to proper sanitary facilities may be a more important factor in nematode infection than crowding per se.

Our model for Subdivision II indicated that male children were more at risk of *A. lumbricoides* infection than female children. Differences between boys and girls are occasionally reported (Crompton, 1994), but more often the prevalence of infection is similar in both sexes (Martin, 1983; Bundy *et al.*, 1987; Tedla *et al.*, 1988). Interestingly, Higgins *et al.* (1984) reported a higher infection level in girls compared with boys, a pattern opposite in direction to that observed in Subdivision II. We have no explanation for why, in our study, boys were more at risk of *A. lumbricoides* infection than girls, or for why this difference was only detected in Subdivision II.

While our results are consistent with other studies undertaken around the world, showing that sanitary conditions and maternal education are important predictors of *A. lumbricoides* infection, to our knowledge, this is the first report that indirect family members may be a risk factor to households. We believe that the high proportion of indirect members in households of HSES Subdivision III may explain why infection levels in that population were comparable to those in LSES Subdivision I. This variable or others reflecting social interaction among communities warrants further study.

The community ecosystem presents a complex, multifactorial set of interactions between social, cultural, behavioral, economic, structural (ie housing, latrines) and physical (ie soil conditions) features of the environment (Sanjur, 1991), all of which are expected to influence intensity of nematode infection. Yet investigations of a comprehensive set of variables in given communities that control for the complex interactions among these variables are lacking. We have shown that some of the key determinants of infection intensity vary among communities despite similar levels of infection. Aside from maternal education which was important in all populations, key determinants were mainly of a structural nature in the LSES subdivisions, whereas in the HSES subdivision they were more related to the socio-cultural aspect of the community.

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Table 1. Profile of environmental and living conditions in three subdivisions of Lubumbashi, Zaire. Two are of lower socio economic status (LSES) and one of higher socio economic status (HSES)

VARIABLES	Subdivision I (LSES) (N = 42)	Subdivision II (LSES) (N = 42)	Subdivision III (HSES) (N = 42)	Total (N = 126)
HOUSING AND CROWDING				
Brick house (%)	88.0	93.0	100.0	94.0
Pests present (%)	91.0	97.0	82.0	91.0
Person per household (X±SE)	11.5±0.7	13.8±0.9	12.1±1.1	12.5±0.5
Number of bedrooms (X±SE)[1]	3.1±0.3[ab]	3.1±0.2[a]	3.9±0.2[b]	3.3±0.1
Persons per bedroom (X±SE)	4.4±0.4[ab]	5.2±0.5[a]	3.8±0.3[b]	4.5±0.2
Cement floor (%)	86.0[ab]	79.0[a]	100.0[b]	88.0
Persons per toilet (X±SE)	26.8±2.3[a]	25.0±1.6[a]	13.5±1.5[b]	22±1.2
Share toilet with others (%)	66.7[a]	66.7[a]	5.0[b]	46.0
Share house with animals (%)	45.0[a]	36.0[a]	12.0[b]	31.0

1: Different letters reflect significant differences among subdivisions ($P<0.05$).
2: Ratio of relatives or indirect family members to direct family members per household.

...continued...

Table 1. (continued)

VARIABLES	Subdivision I (LSES) (N = 42)	Subdivision II (LSES) (N = 42)	Subdivision III (HSES) (N = 42)	Total (N = 126)
SANITATION				
Indoor toilet (%)	5.0^{a}	10.0^{a}	90.0^{b}	34.0
Non functional latrine (%)	40.5^{a}	52.4^{a}	0.0^{b}	31.0
Open defecation (%)	50.0^{a}	57.0^{a}	7.0^{b}	38.0
Adjacent road paved (%)	2.3^{a}	9.5^{a}	88.0^{b}	32.5
Sewage in the yard (%)	93.0^{a}	95.0^{a}	14.0^{b}	67.5
Functional sewers (%)	2.4^{a}	0.0^{a}	86.0^{b}	29.4
ACCESS TO SAFE WATER AND FOOD				
Food is cooked indoors (%)	59.5^{a}	71.4^{ab}	90.5^{b}	73.8
Eat on the floor (%)	79.0^{a}	69.0^{a}	14.3^{b}	54.0
Eat street food (%)	98.0^{a}	88.0^{ab}	64.3^{b}	83.3

1: Different letters reflect significant differences among subdivisions ($P<0.05$).

2: Ratio of relatives or indirect family members to direct family members per household.

...continued...

Table 1. (continued)

VARIABLES	Subdivision I (LSES) (N = 42)	Subdivision II (LSES) (N = 42)	Subdivision III (HSES) (N = 42)	Total (N = 126)
ACCESS TO HEALTH CARE SYSTEM				
Have medicare (%)	50.0	26.0	52.0	43
Never able to see a doctor (%)	14.3[a]	7.0[ab]	0.0[b]	7.0
Always able to buy drugs (%)	9.5[a]	7.0[a]	28.6[b]	15.0
MOTHERS' EDUCATION AND OCCUPATION				
Mothers per family (X±SE)	1.2±0.1	1.3±0.1	1.2±0.1	1.2±0.1
Mother with college education (%)	0.0[a]	2.4[a]	10.0[b]	4.0
Mother in formal job (%)	16.7[a]	9.5[a]	38.0[b]	21.4
SOCIO-CULTURAL INDICES				
Play away from home (%)	35.0	31.0	18.0	28.0
Extended family index (X±SE)[2]	0.1±0.02[a]	0.1±0.03[a]	0.8±0.2[b]	0.3±0.1
Indirect family member (X±SE)	0.7±0.2[a]	0.8±0.2[a]	2.1±0.3[b]	1.2±0.1

1: Different letters reflect significant differences among subdivisions ($P<0.05$).

2: Ratio of relatives or indirect family members to direct family members per household.

Table 2. The prevalence and intensity (eggs per gram) of *Ascaris lumbricoides* in participants and index children in three subdivisions (SDV) of Lubumbashi, Zaire.

	All participants[1]				Index children[2]			
	N	Age (Y) (X±SE)	Prevalence[3] (%)	Intensity[3] epg (X±SE)	N	Age (Y) (X±SE)	Prevalence (%)	Intensity epg (X±SE)
SDV I (LSES)	363	12.5±0.6	64.0[ab]	19125±2016[a]	42	5.5±0.3	67.0	40948±9453
SDV II (LSES)	410	10.5±0.5	76.0[a]	31153±2202[b]	42	5.0±0.3	73.8	51618±9539
SDV III (HSES)	327	11.9±0.6	59.0[b]	14105±1783[a]	42	5.7±0.4	62.0	26454±6408
Total	1100	11.6±0.3	67.0	22116±1201	126	5.4±0.2	67.0	39886±5042

1: Participants included everybody who entered the study.
2: One index child, between 4 months and 16 years of age, was randomly selected from each participating family; only direct family members were included.
3: Different letters reflect significant differences among subdivisions ($P<0.05$).

Table 3. Multiple regression analysis of *Ascaris lumbricoides* intensity (epg) on environmental and living condition variables of index children from three subdivisions of Lubumbashi, Zaire.

Dependent variable: A lumbricoides log (epg+1)

	Subdivision I (LSES)		Subdivision II (LSES)		Subdivision III (HSES)	
Covariates	Beta	Coeff (SE)	Beta	Coeff (SE)	Beta	Coeff (SE)
Non-educated mother						
(Yes=2, No=1)	0.31	1.33†(0.58)	0.41	1.77††(0.59)	0.39	1.68†(0.60)
Extended family index[1]	-	-	-	-	0.29	0.44†(0.21)
Open defecation						
(Yes=2, No=1)	-	-	0.41	1.73††(0.58)	-	-
Persons per toilet	0.45	0.07††(0.02)	-	-	-	-
Persons per bedroom	-	-	0.22	0.15¥(0.09)	-	-
Gender						
(Female=2, Male=1)	-	-	-0.32	-1.35†(0.57)	-	-
Constant (A)		-0.98		-1.07		-0.37
F for the equation		8.25††		4.66††		8.18††
R square		0.30		0.34		0.30
N		42		42		42

1:Ratio of relatives or indirect family members to direct family members per household.
† $P<0.05$; ††$P<0.01$; ¥borderline significance $P=0.056$; - did not fit in the model.

CONNECTING STATEMENT 2

In the last Chapter (Chapter III), environmental, living conditions, socio-economic and cultural factors were identified and related to Ascaris infections. How the infections and socio-economic variables impacted on the nutritional status of the community was unknown. We were aware that in Kinshasa, the largest city in Zaire, nutritional deficiency was very common especially among those living in lower socio-economic neighborhoods, but such data were not available for Lubumbashi.

Therefore, what follows as Chapter IV is the second step of the study. It assesses the nutritional status of three communities in Lubumbashi and investigates their relationships with parasitic infections and the socio-economic status of each community.

Five hundred and fifty eight children aged 4 months to 10 years, met the requirements to enter the study. A clinical examination was conducted on all of them, standard procedures were used to obtain their weight, height and date of birth. Single stool samples from each child were examined as well as both thick and thin blood smears. Associations between infection, the socio-economic status and indicator of protein energy malnutrition were assessed.

The manuscript of the study has been submitted to the Journal of Tropical Pediatrics. It is presented here as submitted to the journal.

CHAPTER IV

EPIDEMIOLOGY OF PROTEIN ENERGY MALNUTRITION IN AN URBAN AFRICAN SETTING: RELATIONSHIPS WITH PARASITIC INFECTIONS AND THE SOCIO-ECONOMIC STATUS

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ABSTRACT

A clear understanding of protein energy malnutrition (PEM), infection and their interactions are essential in formulating health and development policies. The prevalence of PEM indicators and the prevalence and/or intensity of infection were compared among 558 Zairian children aged 4 months to 10 years from different socio-economic communities. Multivariate analyses were used to estimate relationships between PEM indicators, infection and other risk factors.

Stunting was found in 40.3% of children, wasting in 4.9% and kwashiorkor in 5.1%. A higher proportion of stunted children were found in the lower SES communities, however, parasite burden (except Plasmodium) was comparable across communities. The risk of stunting was higher in children with A. lumbricoides that of wasting was higher in children with A. lumbricoides or T. trichiura whereas the risk of kwashiorkor was high with T. trichiura but very reduced in those with A. lumbricoides. These relationships highlight important interactions (both synergistic and antagonistic) between nutrition and parasites.

Key words: protein-energy, malnutrition, stunting, wasting, kwashiorkor, parasites, A. lumbricoides, T. trichiura, Plasmodium, hookworm.

INTRODUCTION

Protein energy malnutrition (PEM) is the most important nutritional problem in the world today. Anthropometric assessment of height and weight in children provides a comprehensive description of children's growth status. In some regions of Africa, kwashiorkor, a severe form of PEM, can be readily diagnosed clinically by local people very familiar with this disease (1). An attempt to provide a global overview of PEM among children was made by the World Health Organization (WHO)(2) in 1983 and more recently an updated document using nutritional data from many countries in the world has been released (3). The prevalence of wasting, stunting and underweight are low in Latin America, high in Asia and variable in Africa. Unfortunately, however, data are lacking for many African countries.

A high prevalence of PEM is often found in areas with higher levels of parasite infections because both are associated with poor environmental and living conditions (4). Two types of associations between PEM and parasite infections have been described: (i) an association wherein poor nutritional status is associated with a greater parasite burden (5-7) and (ii) an association wherein malnutrition in the host is associated with a lower parasite burden, presumably because the host no longer provides a suitable environment for the parasite (8,9). A comprehensive description of the major types of malnutrition and parasite infections in an urban African setting, and an understanding of associations between PEM indicators and parasite infections are crucial in planning and formulating health and development policies in those areas. For these reasons, we conducted a cross-sectional survey of nutritional status and parasite burden in Lubumbashi, Zaire.

The aims of the study were to: (i) to estimate the prevalence of wasting, stunting, and kwashiorkor among children aged 4 months-10 years and the association of these indicators with the socio-economic status of the children; (ii) and to investigate associations between these indicators of PEM and parasite infections (gastrointestinal nematodes and Plasmodium) while controlling for the effects of the socio-economic status.

MATERIAL AND METHODS

Study site

The study was conducted in Lubumbashi, the capital city of Shaba province located in the Southeastern part of Zaire. The city covers an area of 747 km^2 and has an estimated 565,000 inhabitants. The dry season extends from May to mid September with average annual temperatures of 17-22°C. During the rainy season (October through April) temperatures average 21-25°C. The total annual rainfall is 110-130 cm (10). The city is divided into seven administrative entities or subdivisions locally known as Zones, two of which were restricted to Belgian colonizers before independence in 1960. Now both subdivisions are the residential areas for the higher socio-economic class; they have modern dwellings, paved roads, electricity and access to safe water and sanitary facilities. Five subdivisions, used in the colonial era by laborers of the copper mine, railway, breweries and other companies, are today occupied by lower income groups and have sanitary systems and roads that are in disrepair. The environmental and living conditions in Lubumbashi are further described by Tshikuka et al. (11).

Design and methodology

To obtain a representative sample of the entire urban population, two of the five subdivisions of lower socio-economic status (LSES) were randomly selected: Subdivision I, Zone Kamalondo; Subdivision II, Zone Kenya. One subdivision of higher socio-economic status (HSES) was chosen: Subdivision III, Zone Lubumbashi. In Subdivisions I and II, census data from the city were supplemented by a census specific to this study in order to include squatters dwelling in the subdivisions. Using systematic sampling of households (sampling interval 50), based on registers from the city and/or our own census lists, 42 households in each subdivision were identified and visited. Informed consent was obtained from all but 7% of selected households who refused to participate. These were replaced by choosing a neighbor to give a total of 126 households with 625 children aged 4 months to 10 years. All subjects were of Zairean nationality.

A face-to-face interview was conducted with the mother in each household and the interviewer recoraed observations of the home and surrounding area. A clinical examination was conducted on all children by a local physician with the assistance of a local nurse.
Kwashiorkor was diagnosed when a child had pitting edema and a combination of the following characteristics: light colored hair, skin changes and potbelly. Standard procedures (12) were used to obtain weight, height and date of birth. Weight was measured to the nearest 100 grams, using a bathroom balance calibrated daily. Height was measured using the Zerfa insertion tape. The date of birth was obtained from parents' identity papers, the child's school report cards or birth certificates. All children were measured, but date of birth could not be obtained for 67 leaving a total of 558 (290 girls and 268 boys) for whom a complete set of data was available.

Mothers received a marked container for each child and were asked to bring stool samples to our laboratory the next day. Finger prick blood was collected when participants reported to our laboratory. Both thick and thin blood smears were made and the presence of Plasmodium was recorded. Samples of malaria smears were taken to the McGill Centre for Tropical Diseases (Canada), for speciation of Plasmodium; 95% of positive slides contained P.falciparum. Stool samples were examined for the prevalence and intensity of Ascaris lumbricoides, Trichuris trichiura and hookworms using procedures described elsewhere (11). No attempt was made for speciation of hookworm; however, previous studies have indicated the predominance of Necator americanus in the region (13). The consistency of stool and presence of blood in the stool were checked according to Cheesborough's recommendations (14). Children with an unformed or fluid stool sample and/or a history of more than 3 loose defecations in the 24 hours preceding the clinical examination were classified as having diarrhea (15). All stool examinations were done without any knowledge of the anthropometric measurements.

Participants returned to our research centre two days after examination. Those with nematode infections were treated with mebendazole at a dose of 100 g by mouth twice a day for three days (Vermox®, Janssen Pharmaceutica, Belgium). Those with Plasmodium infection and clinical malaria as defined by Trape et al. (16) and by Rooth and Björkman (17) were given a standard chloroquine dose totaling 25 mg/kg over 3 days (18), while those with asymptomatic malaria were asked to report to our clinic for treatment if symptoms occurred.

The study was approved by the McGill University Ethics Committee. Permission to conduct the study in Lubumbashi was granted by the Zairean Ministry of Health.

Data processing and analysis

For each child, the Z scores for height-for-age (HAZ), and weight-for-height (WHZ), were calculated according to NCHS/WHO (2) using Anthro Software (Centers for Disease Control, Atlanta, GA, USA). Children more than 2 standard deviations below the median child of the NCHS international standard for height-for-age were classified as stunted; those falling more than 2 standard deviations below weight-for-height were classified as wasted. The prevalence (%) of children with wasting, stunting, and kwashiorkor by age group and subdivision were estimated. The mean Z-scores (±SD) for height-for-age, and weight-for-height were estimated for all children and for each nutritional status group. Comparisons among age groups and subdivisions were made using Chi-Squared Analysis, and the Binomial Confidence Intervals for Percentages (19). Parasite intensity (epg) was compared among age groups using one way analysis of variance on log transformed intensity data. The prevalence of parasites and diarrhea were calculated for each nutritional status group.

For each of the three nutritional indicators, multiple logistic regression (20) was used to compute odds ratios and their 95% confidence intervals as an approximation of relative risk. The following potential predictors were investigated in those models: presence/absence of A. lumbricoides, T. trichiura, hookworms, Plasmodium, diarrhea, age, gender and the socio-economic status of the children, as indicated by subdivision. Also investigated as potential predictors were the intensity of A. lumbricoides, T. trichiura and hookworms. Multiple regression (21) of log A. lumbricoides epg was done using Z-scores for weight-for-height and height-for-age, kwashiorkor, wasting, stunting, age and socio-economic status as independent variables.

Redundancy and multicollinearity of covariates were checked after each computation. All variables significant in the main effects models as well as those suspected to have different relationship with outcome variables depending on the third factor were investigated in a series of interaction terms. We present here the models that explain the highest proportion of variability of the outcome variables. Software used in data analysis were Excel (Redmond, Washington, USA), Cricket Software, (Philadelphia, PA, USA) and the Logit Module of Systat (Evanston, IL, USA).

RESULTS

Prevalence of PEM

A total of 50.2% of the children studied had no indication of PEM, 40.3% were stunted, 3.4% were wasted, 4.7% had kwashiorkor and stunting, 1.1% were stunted and wasted, and 0.4% had evidence of kwashiorkor, stunting and wasting. The frequency distribution of different PEM indicators by age groups is shown in Table 1. Stunting was more prevalent in the groups older than two years and the percentage of stunted children remained stable after this age. Wasting was most prevalent in the 0-2 year age group.

The frequency distribution of different PEM indicators per subdivision is shown in Table 2; the percentage of children with no indication of PEM was highest in the higher SES subdivision and that of stunted children was lowest in the same subdivision. Differences in the prevalence of kwashiorkor and wasting (or their combinations) by subdivision were not statistically significant, but were lowest in the higher SES subdivision.

For all subsequent analyses, all the children with kwashiorkor, regardless of stunting or wasting are classified as having kwashiorkor. Those who were wasted are classified as wasted even if also stunted. The stunted group represents those who were stunted but had none of the other nutritional problems. All the children without any PEM indicator are classified as normal. In Table 3, the mean height-for-age Z-scores and weight-for-height Z-scores for these nutritional classifications are presented. The overall mean Z-score for height-for-age was -1.79±0.08, and weight-for-height was 1.11±0.06.

Prevalence and intensity of infection

Profiles of parasite infection by age group are presented in Table 4. A. lumbricoides was the most prevalent nematode infection in every age group, followed by T. trichiura and hookworm. A. lumbricoides reached a peak prevalence and intensity in children aged 2-4 years and remained at that level. No other important age effect on prevalence was observed. Infection with Plasmodium was elevated in all age groups. There were no striking differences in the prevalence and intensity of nematode infection between the high (Subdivisions III) and low SES Subdivisions (I and II), however, Plasmodium infection was significantly ($P<0.05$) lower in the higher SES subdivision III (Table 5). Of those with Plasmodium infection, 15% had clinical malaria and 85% were asymptomatic.

Association between infection and PEM

The prevalence of parasite infection in each of the protein-energy malnutrition indicator groups is shown in Table 6. A final column indicating the prevalence of diarrhea is presented as this is a potential confounder in any nutrition-parasite association (22). Those with acute malnutrition, either kwashiorkor or wasting, had a high prevalence of diarrhea, yet the parasite profiles of these two groups of children were very different. The prevalence of A. lumbricoides was very low in the children with kwashiorkor; 10.7% of the children were infected compared with [illegible] in wasted children and 63.2% in normal children (p< 0.05). None of the children with kwashiorkor had hookworm infection but this effect was not statistically significant.

In a multivariate analysis, we examined the association of parasite burden and other co-factors with each of the nutritional status indicators (Table 7). The stunted children were more likely to be infected with A. lumbricoides, to be older, and to be of lower socio-economic status. Comparing wasted to non-wasted children, the former were also more likely to be infected with A. lumbricoides, and possibly with T. trichiura (P=0.07), they were very likely to have diarrhea and were younger. There was no association of wasting with the socio-economic status once the above variables were controlled. Children diagnosed as having kwashiorkor presented a very different portrait. Virtually all children with this diagnosis had diarrhea and there was a strong negative association of kwashiorkor with A. lumbricoides. Only two children with kwashiorkor had A. lumbricoides. In contrast the risk of T. trichiura was elevated among those with kwashiorkor. Kwashiorkor was also more prevalent in those with lower SES. Age was not a significant predictor of kwashiorkor once the above variables were controlled.

The above analyses were based on the assumption that parasitic infection was a potential risk factor for malnutrition. However, it is also possible that malnutrition predisposes children to infection (23). In order to examine the relationship of the intensity of A. lumbricoides and the nutritional indicators we examined the data using log A. lumbricoides, epg(s), as the outcome variable in a multiple regression analysis (Table 8). Wasting, stunting and kwashiorkor, age and socio-economic status were included as independent variables as well as Z-scores for hight for age and Z-scores for weight for hight. The analysis indicated very low epg in those with kwashiorkor ($p<0.01$), higher epg(s) in children with a lower Z score for height-for-age and higher epg(s) in older children. In this analysis, weight-for-height was not significantly associated with epg once these other indicators were controlled.

DISCUSSION

This cross sectional survey provides new data on the nutritional status of children in Zaire and describes relationships between parasite infection and growth. The different patterns of association of parasitic infection between children with kwashiorkor and wasting, two indicators of the current nutritional deficit, raise many questions about the relationships between nutritional status and infection with different parasites.

With the overall prevalence of 46.4% for stunting, 5% kwashiorkor and 4.8% wasting there is no question that PEM is a serious problem in Lubumbashi. According to the WHO classification of under-nutrition, the prevalence of stunting is very high and the prevalence of wasting is high (3). Our results are similar to research conducted with the Zairean Nutrition Planning Center (4,24,25) in Kinshasa, Zaire in terms of the age distribution of PEM and differences between lower versus higher socio-economic communities.

Wasting and kwashiorkor are considered as the most severe forms of PEM. Although wasted children may look more emaciated and pathetic, the prognosis for such children is better than for those with kwashiorkor (26). There does not appear to be any clear understanding of the differences between severe wasting and the oedematous state of kwashiorkor. Our results indicated that of the 5% children with kwashiorkor only 7% were classified as wasted by anthropometric criteria, indicating that the two conditions reflect very different manifestations (27,28). Although all the children with kwashiorkor in our study were stunted, kwashiorkor needs to be diagnosed by clinical assessment as kwashiorkor and stunting are not differentiated by anthropometric indices.

The association of infection with PEM has been long reported (29-33) and intervention studies (6,7,34) continue to lend support to the positive or synergistic nature of such relationships. Our finding of a positive association between both wasting and stunting and infection equally lend support to those studies. Because stunting is the result of remote/early childhood insults (35) and not an outcome of current exposure factors, it is not surprising that only A. lumbricoides is significantly related to stunting. As this was a cross sectional study, A. lumbricoides infection is probably a proxy for past exposures to parasites or to other poor living conditions. However, since stunting is the result of past insults (36), the data suggest that the children may have been harbouring A. lumbricoides for years. Other studies, however, have proven that in endemic areas children are continuously infected with geohelminths and that even after treatment, they re-acquire their previous worm loads (37-39); if local conditions remain unchanged, return to the previous infection level takes 6-12 months (40-43).

Interestingly, although the level of infection was generally comparable between the lower and higher socio-economic communities, the prevalence of PEM was lower in the higher socio-economic community, suggesting that the socio-economic status on its own was associated with PEM. Franklin and co-workers (25) made the same observation among three communities of different socio-economic status in Kinshasa, Zaire.

Plasmodium infection has been linked with PEM (6). The absence of association between this parasite and PEM indicators in this study is striking. A possible explanation for this is that although Plasmodium was prevalent, the majority of children were asymptomatic; seemingly PEM is more a feature of clinical malaria rather than of the simple presence of Plasmodium. McGregor et al.,(5) supported by Stephenson et al (6) even reported that weight loss in Plasmodium infection was associated with the decrease in food intake during malarial attacks.

The new and very strong finding in our research is the negative or antagonistic association between kwashiorkor and infection with A. lumbricoides. Although research showing antagonistic relationships between malnutrition and infection are found in the literature (8, 29,30,44), none have described an antagonistic relationship between A. lumbricoides and kwashiorkor. Indeed available data are that children with kwashiorkor are heavily infected with A. lumbricoides (31,45) and that relationships between A. lumbricoides and various other PEM indicators are positive (6,31,46-48). It is known that malnutrition and infection can operate synergistically or antagonistically, depending on their relative severity (49,50). In moderate malnutrition for instance, immunosuppressive changes are more frequent and individuals are likely to harbor heavy worm burdens (38,50). Yet extreme malnutrition may be prejudicial to nematode recruitment and/or establishment in the host gut, due to the absence of physio-chemical triggers for hatching or for development (9,50-52) . In fact, in kwashiorkor children the brush border of the small intestine is markedly atrophied and disorganized (53), therefore the activity of many enzymes located in such cells is tremendously reduced (53). While these reports are possible explanations to our findings, the unanswered question is why there is an antagonistic association between A. lumbricoides and kwashiorkor and yet a synergistic effect with wasting. A further is finding that kwashiorkor children had higher levels of T. trichiura. Could it be that a host deficiency in nutrients essential to parasite survival are responsible for these results? Kwashiorkor has been associated with starchy foods such as cassava and yam (25); yet it is not clear that the dietary pattern of children with kwashiorkor differs from children with wasting (54). Gastro-intestinal mobility or diarrhea decreased the number of ascarids and other helminths in some nutritional deficiencies (55), but our data show a comparable level of diarrhea between wasted and kwashiorkor children, although the two groups have opposing associations with A. lumbricoides. Despite the high prevalence of diarrhea, kwashiorkor children had higher levels of T. trichiura. This discrepancy may be explained by the different habitats within the host: A. lumbricoides lives in the small intestine and T. trichiura lives in the colon.

Another possible explanation for the lower levels of A. lumbricoides in the children with kwashiorkor is that the child is unable to support parasitic infections and that those who are infected and those with higher parasite loads die and are thus not included in a cross-sectional survey. On the other hand, the lower level of A. lumbricoides as expressed by egg count in infected kwashiorkor children might have under estimated the true level of infection in kwashiorkor children, due to a deficiency in nutrients essential for their reproductive function; worms might have stopped or decreased their release of eggs (9,50).

Without longitudinal follow-up and/or direct worm count in such population groups it is difficult to understand the direction of the relationships of parasite infection and nutritional deficiencies. It is hoped that findings in this paper will stimulate further detailed research on the association between infection and PEM, particularly in the context of A. lumbricoides and kwashiorkor in developing countries.

In summary, findings in this work were that: (i) the prevalence of PEM was high in Lubumbashi; (ii) although the level of infection was generally comparable between the lower and higher socio-economic communities, the prevalence of PEM was significantly lower in the higher socio-economic community; (iii) while wasting exhibited a synergistic association with parasite infection, kwashiorkor had an antagonistic association with A. lumbricoides, indicating a further difference in these two nutritional indicators; (vi) stunting was associated with A. lumbricoides indicating that the children were likely harbouring the same parasite load for some time before or that their environment was conducive to both conditions.

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Table 1. The frequency distribution (%) of indicators of protein-energy malnutrition by age group*

PEM indicators			Age group (years)					
Stunting	Wasting	Kwashiorkor	0 - 2	2.1 - 4	4.1 - 6	6.1 - 8	8.1 - 10	Total
-	-	-	55.9	37.0	53.6	53.0	52.1	50.2
+	-	-	22.9[a]	47.9[b]	41.8[ab]	43.5[b]	46.9[b]	40.3
-	+	-	14.4[a]	1.7[b]	0.0[b]	0.0[b]	0.0[b]	3.4
+	-	+	5.9	9.2	3.6	2.6	1.0	4.7
+	+	-	0.0	4.2	0.0	0.9	0.0	1.1
+	+	+	0.8	0.0	0.9	0.0	0.0	0.4
Participants (N)			118	119	110	115	96	558

- Absent; + Present; *Different letters within a row reflect significant differences (P<0.05)

Table 2. The frequency distribution (%) of indicators of protein-energy malnutrition by subdivision

PEM indicators			Subdivision (SDV)*			
Stunting	Wasting	kwashiorkor	SDV I (LSES)	SDV II (LSES)	SDV III (HSES)	TOTAL
-	-	-	44.3[a]	40.0[a]	67.6[b]	50.2
+	-	-	42.3[a]	48.9[a]	29.0[b]	40.3
-	+	-	3.6	4.8	1.7	3.4
+	-	+	7.2	5.3	1.1	4.7
+	+	-	2.1	1.1	0	1.1
+	+	+	0.5	0	0.6	0.4
Participants (N)			194	188	176	558

- Absent; + Present; *Different letters within a row reflect significant differences (P<0.05)

Table 3. Mean Z-scores for height for age (HAZ) and weight for height (WHZ) for children by nutritional status groupping

	N	HAZ ±SE	WHZ ±SE
Normal	280	-0.57±0.07	1.14±0.07
Stunting	225	-3.28±0.07	1.54±0.08
Wasting	25	-0.30±0.36	-2.74±0.15
Kwashiorkor	28	-3.48±0.25	0.89±0.31
All children	558	-1.79±0.08	1.11±0.06

Table 4. Prevalence and intensity of parasitic infection among children by age group*

	Age group (years)				
	0 - 2	2.1 - 4	4.1 - 6	6.1 - 8	8.1 - 10
N	118	119	110	115	96
Prevalence (%)					
Ascaris lumbricoides	47.5[a]	73.9[b]	77.3[b]	70.4[b]	70.8[b]
Trichuris trichiura	21.2	30.3	30.0	32.2	30.2
Hookworm	6.0	8.0	6.4	7.0	8.3
Plasmodium	58.5	58.0	58.2	61.7	69.8
Intensity/epg (X±SE)					
A. lumbricoides	13992±2885[a]	43882±5587[b]	39488±4823[b]	32274±4417[b]	28908±229[b]
T. trichiura	443±136[a]	1085±205[b]	904±226[ab]	649±178[ab]	318±132[a]
Hookworm	31±12	30±12	26±11	38±14	37±14

*Different letters within a row reflect significant differences (P<0.05)

Table 5. Prevalence and intensity of parasitic infection among children by subdivision*

	SUBDIVISION (SDV)*			
	SDV I (LSES)	SDV II (LSES)	SDV III (HSES)	TOTAL
N	194	188	176	558
Prevalence (%)				
Ascaris lumbricoides	66.5	72.9	63.6	67.7
Trichuris trichiura	37.6^{a}	20.0^{b}	28.4^{ab}	28.7
Hookworms	6.0	7.4	8.0	7.0
Plasmodium	78.8^{a}	68.1^{a}	33.5^{b}	60.9
Intensity/epg ($\bar{X}\pm$ SE)				
A. lumbricoides	34600 ± 4000^{ab}	38096 ± 3318^{a}	23062 ± 3085^{b}	32139 ± 2046
T. trichiura	673 ± 125^{a}	466 ± 114^{b}	954 ± 181^{ab}	692 ± 82
Hookworms	23 ± 8	32 ± 9	43 ± 12	33 ± 6

*Different letters within a row reflect significant differences ($P<0.05$)

Table 6. Prevalence of infection and diarrhea in normal children and in those with various forms of protein-energy malnutrition

	N	Ascaris	Plasmodium	Trichuris	Hookworms	Diarrhea
Normal (%)	280	63.2[a]	54.6	25.4	7.0	5.7[b]
Stunting (%)	225	79.6[a]	65.8	32.0	8.0	5.0[b]
Wasting (%)	25	76.0[a]	80.0	40.0	8.0	68.0[a]
Kwashiorkor (%)	28	10.7[b]	67.9	25.0	0.0	92.9[a]

*Different letters within a column reflect significant differences ($P<0.05$)

Table 7. Multivariate logistic regression analyses for Stunting, Wasting and Kwashiorkor (N = 558).

Independent variables	B	SE of B	Odds Ratio	C.I of OR
A-Dependent variable: Stunting				
1 *Ascaris lumbricoides* (yes=1; no=2)	0.88	0.20	2.42**	1.63-3.61
2 age (years)	0.14	0.06	1.15*	1.01-1.30
3 †SDV (SDV I=1; SDVII=2; SDV III=3¥)				
SDV I	0.57	0.22	1.76*	1.13-2.75
SDV II	0.76	0.23	2.15**	1.38-3.35
Constant (A)	-1.89			
Log likelihood Ratio (Chi-Squared)	43.09**			

†Subdivision; ¥Reference group; *P<0.05; **P<0.001.

...continued...

Table 7. (continued)

Independent variables	B	SE of B	Odds Ratio	C.I of OR
B-Dependent variable:Wasting				
1 Ascaris lumbricoides	1.29	0.57	3.63*	1.18-11.16
2 Trichuris trichiura(yes=1; no=2)	0.94	0.53	2.56†	0.9-7.34
3 Age(years)	-1.39	0.33	0.25**	0.13-0.48
4 Diarrhea (yes=1; no=2)	2.93	0.51	18.73**	6.80-51.56
Constant (A)	-2.55			
Log likelihood Ratio (Chi-Squared)	82.15**			

†Subdivision; ¥Reference group; *P<0.05; **P<0.001; †borderline significance (P=0.07).

...continued...

Table 7. (continued)

Independent variables	B	SE of B	Odds Ratio	C.I of OR
C-Dependent variable: Kwashiorkor				
1 *Ascaris lumbricoides* (yes=1; no=2)	-4.35	0.97	0.013**	0.002-0.09
2 *Trichuris trichiura* (yes=1; no=2)	2.09	0.89	8.08*	1.41-46.21
3 Diarrhea (yes=1; no=2)	5.50	0.94	244.69**	38.67-1548
4 †SDV (SDV I=1; SDVII=2; SDV III=3¥)				
SDV I	1.98	0.93	7.24*	1.17-44.83
SDV II	1.98	0.98	7.24*	1.07-49.15
Constant (A)	-6.68			
Log likelihood Ratio (Chi-Squared)	146.11**			

†Subdivision; ¥Reference group; *P<0.05; **P<0.001.

Table 8. Multiple regression of *Ascaris lumbricoides* log epg+1 on indicators of protein-energy malnutrition and children's socio-economic status.

VARIABLE	Beta	Coefficient±SE	P(2 tail)
Height for age (Z scores-SD)	-0.18	-0.47±0.11	0.001
Kwashiorkor (yes=2; no=1)	-0.29	-6.35±0.91	0.001
Age (years)	0.09	0.31±0.14	0.03
Constant (A)	-	11.41	-

F for the equation= 23.15 $P < 0.001$ $R^2 = 0.11$ N= 588

CONNECTING STATEMENT 3

In the last Chapter (Chapter IV) the nutritional status was assessed in three communities and nutritional indicators were related to parasitic infections and socio-economic status.

What follows as Chapter V is an investigation of different types of parasite combinations in the study communities and how those combinations impact on clinical outcomes.

One thousand and one hundred participants who entered this study underwent clinical examination in their respective homes. Morbidity that affected their general health status were identified using standard procedure. Single stool samples from each participant were examined as well as both thick and thin blood smears. Associations between infection, the socio-economic status and predominant clinical conditions were assessed.

The study is in press at the Annals of Tropical Medicine and Parasitology. The manuscript is presented here as accepted by the publisher.

CHAPTER V

MULTIPLE INFECTION WITH PLASMODIUM AND HELMINTHS IN COMMUNITIES OF LOWER AND HIGHER SOCIO-ECONOMIC STATUS: RELATION TO MORBIDITY

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ABSTRACT

This study was conducted in the city of Lubumbashi, Zaire. The objectives were (1) to survey parasitic infections and clinical conditions in children and their mothers, (2) to identify combinations of parasites and clinical conditions that commonly occurred together in individuals, (3) and to determine whether single and/or multiple species infections were determinants of the observed clinical conditions. Laboratory analyses of stool and blood samples and a clinical examination were conducted in a sample of 1100 children and mothers from three subdivisions, two of lower socio-economic status (LSES) and one of higher socio-economic status (HSES).

Plasmodium prevalence was higher in the two LSES subdivisions than in the HSES subdivision. Prevalence and intensity of Ascaris lumbricoides infection were low in the HSES subdivision, and one of the two LSES subdivisions. In contrast, prevalence and intensity of Trichuris trichiura and hookworms were similar in all subdivisions. Plasmodium and A. lumbricoides were the most frequently found single-species infections. The combination of A. lumbricoides and Plasmodium was the most frequent double-species infection and that of A. lumbricoides, Plasmodium and T. trichiura was the most frequent triple-species infection. Significant positive associations between parasite species were detected in the HSES subdivision, and in one of the two LSES subdivisions. Because the relationships were not consistently detected, it is hypothesized that the associations are determined by environmental conditions rather than synergy between the parasites in

the host.

The most commonly observed clinical conditions were abdominal pain, diarrhea, fever, and low packed cell volume (PCV). The occurrence of each was significantly lower in the HSES subdivision, than in at least one if not both of the two LSES subdivisions. Abdominal pain and low PCV were most common in individuals presenting with only a single clinical condition, and their combination was the most commonly observed pair of conditions. Abdominal pain, low PCV and diarrhea was the most common combination in individuals with three clinical conditions.

Logistic regression revealed that hookworm infection, T. trichiura infection, young age and residence in a LSES subdivision were determinants of diarrhea. Trichuris trichiura infection, young age and living in a LSES subdivision were determinants of abdominal pain. Plasmodium infection and young age were determinants of fever. LSES was the only predictor of low PCV. A. lumbricoides did not enter any of the models. No significant interactions were detected among parasites, indicating no synergism nor antagonism among parasites in the induced disease.

INTRODUCTION

Most field research in tropical areas is focused on a single species of parasite; in reality, individuals are usually infected with two or more species of parasite concurrently (Buck et al.,1978a; Bundy et al.,1987; 1991). The pattern of distribution of parasite species among hosts is, in part, determined by host genetics (Welch et al.,1977), physiology (Woodruff, 1982), nutrition (Bundy and Golden, 1987) and socio-economic status (Holland et al.,1988), but these factors alone cannot account for the wide variability in polyparasitism among individuals or host populations. Both the number of co-endemic parasite species in the ecosystem and interspecific interactions exerted between parasite species have an influence on the observed profile of polyparasitism.

Hosts concurrently infected with more than one species of parasite are not only at risk of the illnesses associated with each parasite species, but also risk more severe disease due to synergistic interactions among parasite species (Buck et al.,1978a; Beisel, 1982; Woodruff, 1982). For example, Buck et al. (1978a) observed a severe form of hepatosplenomegaly in concurrent Plasmodium falciparum and Schistosoma mansoni infections as compared with mild conditions seen in infections with either parasite alone. Other parasite combinations have been reported to be antagonistic to each other, where the resulting disease is less severe than in single infections (Murray et al., 1978; Beisel, 1982; Scrimshaw, 1991). On Comorro Island, for example, groups of children heavily infected with Ascaris lumbricoides but with a negative blood smear for Plasmodium (and free from clinical malaria) were given either an anthelminthic drug or a placebo. Malarial attacks were reported in 51% of children receiving anthelminthic treatment whereas no malarial attack occurred among those who received the placebo (Murray et al., 1978). Presumably malaria attacks resulted from recrudescence of undetected Plasmodium. Although the design of these studies has been criticized (Stephenson and Latham, 1979), the observations suggest that complex interactions occur between parasite species. Clarification of how concurrent infections alter the severity of disease is crucial in designing parasite control programs (Buck et al., 1978a; Bundy et al., 1991). To date, this has not been attempted in most endemic areas.

The objectives of this study were: (1) to identify the major parasitic infections in individuals living in lower and higher socio-economic subdivisions of Lubumbashi, Zaire; (2) to characterize and compare the profiles of concurrent parasite infections in each subdivision; (3) to document predominant clinical conditions in each subdivision; (4) to characterize the profiles of concurrent clinical conditions in each subdivision and compare them among subdivisions; and (5) to examine associations between each parasite, alone and in combination, and each of the predominant clinical conditions.

SUBJECTS AND METHODS

Study Sites

Lubumbashi is the capital city of Shaba province in the Southeastern part of Zaire. It covers an area of 747 km^2 and has an estimated 565,000 inhabitants. The city is divided into seven administrative subdivisions, two of which form the higher socio-economic stratum (HSES), while the remaining five constitute the lower socio-economic stratum (LSES).

The vegetation of Lubumbashi is that of miombo woodland or savanna. The rainy season extends from October to April with temperatures ranging from 21-24°C and precipitation from 1,100-1,300 mm. During the dry season, temperatures are between 17-22°C and precipitation ranges from 0-4.0 mm. Many streams are found in the city. A lack of proper drainage and sewage systems in many parts of the city (Tshikuka et al.,1995a) has led to the creation of ponds and swamps that form ideal breeding sites for mosquitoes, predominantly Anopheles gambiae (Ngimbi et al.,1982; Trape and Zoulani, 1987). There is no program of insecticide spraying in the city and the use of window screens and bednets is very limited. At the time of this study, anti-malarials and anthelminthics were available although only individuals in the HSES subdivision could afford them (Tshikuka et al.,1995a).

Study Design and Methodology

Two LSES subdivisions were randomly selected: Subdivision I, Zone Kamalondo; Subdivision II, Zone Kenya. One HSES subdivision was chosen: Subdivision III, Zone Lubumbashi. In subdivisions I and II, census data from the city was supplemented by a census specific to this study in order to include squatters dwelling in the subdivisions. Using systematic sampling of households (sampling interval of 50) based on registers from the city and/or our own census lists, 42 households in each subdivision were identified and visited. Written or oral informed consent was obtained from all but 9 (7%) of households. These 9 households were replaced to give a total of 126 households (1100 participants). All selected families had been living at the same address for more than two years and were of Zairean nationality.

A face-to-face interview was conducted with the mother in each household, and the interviewer observed and recorded pertinent characteristics of the home and surrounding area. These data are presented in Tshikuka et al. (1995a). A clinical examination of all participants (children aged 16 or under and all mothers; see Tshikuka et al. 1995a for demographic data) was conducted by a local physician, using diagnostic criteria reported in Table 1.

Each participant received a marked container in which he/she was asked to provide a stool sample which was brought to our pilot centre the next day. The prevalence and intensity (eggs per gram feces, epg) of A. lumbricoides, Trichuris trichiura and hookworms was determined immediately from duplicate stool preparations, using a modified Kato thick smear egg count procedure (Forrester and Scott, 1990). The presence of other helminths and protozoa was also recorded from fresh stool smears.

Duplicate blood samples were collected by finger prick in microcapillary tubes at our laboratory. The packed cell volume (PCV) was processed immediately as described by WHO (1959) and Powers (1989). Thick and thin blood smears were prepared and the presence of Plasmodium was recorded. No attempt was made to estimate the level of haemoglobin (Hb) or density of Plasmodium. Samples of malaria smears were stored at room temperature and species of Plasmodium were identified in collaboration with the McGill Centre for Tropical Diseases, Montreal, Canada.

Participants returned to our pilot center two days later to obtain laboratory results. Those with clinical malaria were given a standard chloroquine dose totaling 25 mg/kg body weight over three days (Turaman et al.,1992). Plasmodium-infected but asymptomatic individuals were not treated but were asked to report to our centre for a free treatment at any time that they became sick. We also followed asymptomatic individuals by weekly visits to their home for 1-10 weeks (depending on when the household was surveyed) to monitor for possible onset of clinical malaria. Those infected with A. lumbricoides, T. trichiura, hookworms, Strongyloides stercoralis or Hymenolepis nana were treated with mebendazole as recommended by the manufacturer (Vermox, Janssen Pharmaceutica, Belgium); those infected with S. mansoni received a single dose of praziquantel (40 mg per kg body weight) (Friis and Byskov, 1989). Ferrous sulfate (200 mg twice daily for six weeks) was provided to each child with a PCV below the cut-off for anaemia (see Table 1); adults with PCVs below cut-off were not treated but were given nutritional counselling.

During the study, environmental, clinical and laboratory data were collected by different teams, but the same people performed the same tasks from beginning to end. The laboratory team had no clinical knowledge of the subjects. The study design was approved by the McGill University Ethics Committee. Permission to conduct the study in Lubumbashi was granted by the Zairean Ministry of Health.

Data Handling and Statistical Analysis

The prevalence of infection by age and subdivision was compared among age groups and subdivisions using the Chi-Square Test or the Binomial Confidence Interval for Percentages (Sokal and Rohlf, 1981). The intensity or the number of eggs per gram of stool (epg) of A. lumbricoides, T. trichiura and hookworms was compared among subdivisions, using One Way ANOVA on log transformed data. Rank correlation coefficients were computed between the two most common nematodes (A. lumbricoides and T. trichiura), using only those participants infected with both parasites.

The frequency of all combinations of single and multiple infections was determined for each subdivision using the technique described by Buck et al. (1978b). Crude measures of associations (odd ratios) between pairs of parasites were computed, with and without adjustment of age and subdivision (Blake, 1985), and Chi-Squared statistics were calculated to determine whether observed associations were significantly different from those expected by chance. Similar procedures were used to determine the frequency of combinations of clinical conditions, and crude measures of associations between pairs of conditions. Associations between clinical conditions were not adjusted for age or subdivision because of the large number of empty cells.

Multinomial logistic analysis (Schlesselman, 1982) was used to determine whether prevalence of Plasmodium, intensity of A. lumbricoides, T. trichiura and hookworm, age and/or subdivision of residence were associated with each of the four predominant clinical conditions. The analysis was redone using only one index child per family (a child aged 4 months- 16 years, randomly selected from each household), in order to examine whether results were biased by using the whole data set. All possible interactions were considered in each model.

Statistical analyses were done using Excel (Redmond, Washington, USA), Statworks TM, Cricket Software, (Philadelphia, PA, USA), Systat and its Logit module (Evanston, IL, USA) on a Macintosh LC Computer. The level of significance was set at 5%.

RESULTS

Characteristics of the Subdivisions

Environmental and living condition variables in the three subdivisions have been described in detail elsewhere (Tshikuka et al., 1995a); in general, Subdivisions I (LSES) and II (LSES) were very similar and both differed significantly from Subdivision III (HSES). Most families (68%) in the lower socio-economic subdivisions shared toilets with neighbors whereas in the higher socio-economic subdivision III, almost every household (95%) had a private toilet. Open defecation was observed in the yard of 50-57% of households in both LSES subdivisions, but in only 7% of yards in the HSES subdivision (Tshikuka et al., 1995a).

Infection Profiles

Seven parasites were detected in our laboratory: P. falciparum, A. lumbricoides, T. trichiura, hookworms, S. stercoralis, S. mansoni and H. nana. The first four parasites were commonly detected, especially in children aged 2-10 years old, whereas the latter three parasites infections were rarely found (Table 2). Ninety five percent of malaria positive slides contained P. falciparum; it was not possible to identify Plasmodium species on the remaining 5% of the slides, possibly due to damage caused during transportation and storage. No attempt was made to identify species of hookworm; however, previous studies have indicated the predominance of Necator americanus in the region (Ripert and Carteret, 1969).

The prevalence and intensity of infections in the three subdivisions are presented in Table 3. The prevalence of Plasmodium was significantly higher in Subdivisions I and II than in Subdivision III, whereas all but one helminth species occurred at similar levels among the three subdivisions. Only with A. lumbricoides were significant differences detected (see Table 3); both prevalence and intensity were highest in Subdivision II, intermediate in Subdivision I and lowest in Subdivision III.

The mean number of parasite species per infected person per subdivision is given in Table 3. The three subdivisions had similar mean numbers of helminth species per infected individual. However, when Plasmodium was included in the calculation, individuals in Subdivisions I and II had significantly higher mean numbers of parasite species than those in Subdivision III.

Of the 128 possible combinations of parasites, only 37 were observed (Fig. 1). Uninfected participants were rare in Subdivisions I and II (9.4% and 7.3%, respectively) and more common in Subdivision III (23.2%). The general patterns of polyparasitism were similar in the three subdivisions. A. lumbricoides and Plasmodium were the most frequently found single species infections. The combination of A. lumbricoides and Plasmodium was the most frequent double species infection and that of A. lumbricoides, Plasmodium and T. trichiura was the most frequent triple species infection. The proportion of individuals with concurrent infection of four parasite species was below 2% and very few individuals were concurrently infected with five parasite species (<0.3%).

Crude estimates of associations between pairs of parasites are shown in Table 4. Odds ratios are measures of the risk of infection with one parasite species in people infected with another, whereas Chi-Squared statistics estimate whether observed associations differ significantly from those expected by chance alone. Significant positive associations were found between the following pairs of parasites: A. lumbricoides and P. falciparum, A. lumbricoides and T. trichiura, A. lumbricoides and hookworms, and hookworms and S. stercoralis. After adjustment had been made for age and subdivision, these associations remained significant in Subdivisions I and III, whereas in Subdivision II they became non significant (Table 5). There were no indications of negative associations between pairs of parasites in either crude or adjusted analyses.

Rank correlation coefficients between A. lumbricoides epg and T. trichiura epg are presented in Table 6. A strong positive correlation between the two parasites was detected in Subdivisions I and III but not in Subdivision II.

Morbidity Profiles

Six clinical conditions were commonly detected in the study population: diarrhea, abdominal pain, low PCV, elevated temperature, splenomegaly and clinical malaria. Of the Plasmodium infected participants, only 9.4% had clinical malaria. A 1-10 week follow-up of asymptomatic participants failed to reveal any case of illness or death due to malaria. Infrequently observed clinical conditions are not reported. Results presented in Table 7 indicate that the prevalence of splenomegaly was very low in all the age groups. The prevalence of clinical conditions was highest in younger children and lower in older age groups. When prevalence of various conditions was compared among subdivisions (Table 8), abdominal pain and low PCV were more common in Subdivisions I and II than in Subdivision III. Elevated body temperature and clinical malaria were more commonly observed in Subdivision II than III. The prevalence of splenomegaly was very low in all three subdivisions (Table 8).

The frequency distributions of conditions, alone and in combination, for each subdivision are shown in Fig 2. On the day of the clinical examination, 70.8% and 71.2% of participants in Subdivision I and II presented with clinical conditions, compared with 38.2% in Subdivision III. Among individuals presenting with only single conditions, abdominal pain and low PCV were most common, and their combination was the most commonly observed pair of conditions. The combination of abdominal pain, low PCV and diarrhea was the most common combination in individuals with three conditions; people with four concurrent clinical conditions were very rare in all subdivisions.

Only positive associations between pairs of conditions were detected (Table 9), even though we expected to see a negative association between low PCV and clinical malaria.

Predictors of Morbidity

The extent to which infection with each parasite species was predictive of each common clinical condition was examined through multivariate analysis (see Table 10), incorporating age and sex of the individual and subdivision of residence (used as a proxy for socio-economic status) as potential confounders. The possibility of synergistic or antagonistic consequences of concurrent infection with more than one parasite species was examined by including interaction terms in the statistical model. For diarrhea, the significant risk factors were infection with hookworms or T. trichiura, young age and residence in a LSES subdivision. Similarly, risk factors for abdominal pain were presence of T. trichiura, young age and residence in a LSES subdivision. In contrast, none of the helminth parasites were risk factors for elevated temperature, but Plasmodium and young age were. The only identified risk factor for low PCV was residence in a LSES subdivision. There were no significant interactions of any type in any of the analyses, indicating that infection with multiple species of parasite did not exert either a synergistic or an antagonistic effect on any of the four clinical conditions examined. Although the models remained similar when we used only index children, some predictors switched to border line/non significance, likely due to reduced sample sizes.

DISCUSSION

This study is the first in the region to relate multiple-species infections with clinical outcomes. Certain combinations of parasite species occurred in individuals more frequently than expected by chance, but their joint occurrence was not associated with either exaggerated or diminished clinical outcomes.

Polyparasitism was examined at two levels. First, we identified the common combinations of parasites. As expected, the most common combinations involved the three most prevalent parasite species, and the patterns were similar in all three subdivisions (Fig. 1). For example, in all three subdivisions, the combination of A. lumbricoides and Plasmodium was the most common two-species infection, and A.lumbricoides, T. trichiura and Plasmodium was the most common 3-species infection. These observations indicate that control programs targeting either a single parasite species, or the range of parasite species, may not need to be customized to different subdivisions. A similar combination of drugs is likely to be useful in all.

Secondly, we investigated in more detail two-species combinations and found only positive associations (Tables 4-6). For example, individuals infected with A. lumbricoides were more likely to be infected with T. trichiura than would have been expected based on the prevalences of the two parasites in the population. No negative associations were detected, implying that treatment for one species of parasite is not likely to increase the risk of infection with a second parasite species.

There are two schools of thought regarding why different parasite species are found within the same individual host more frequently than expected by chance. One school proposes that "biological" associations exist, whereby the presence of one species promotes (or discourages) the establishment and/or survival of the second species, leading to synergy (or antagonism) (Murray et al.,1978; Keusch and Migasena, 1982). The other school proposes that "ecological" associations are generated simply by the concurrence in the environment of factors promoting survival of both species (Buck et al.,1978c; Croll and Ghadirian, 1981; Ashford et al., 1992). For example, A. lumbricoides and Plasmodium may occur together, simply because of poor sanitation and pools of stagnant water near certain homes. In our study we postulate that observed associations between parasite species reflect "ecological" circumstances rather than "biological" synergy, because the associations did not remain consistent in all subdivisions. The underlying ecological condition that led to the associations remains unclear, given that associations seen in LSES subdivision I were not detected in LSES subdivision II, yet both subdivisions were virtually identical in each of the over 30 factors of the environment and living conditions (Tshikuka et al.,1995a).

A second part of our study concerned the clinical profile associated with single or multiple-species infections. In no case did we detect that a combination of parasite species enhanced or diminished the clinical outcomes, compared to single species infections.

A very low prevalence of clinical malaria (9.4%) was reported, despite a high prevalence of Plasmodium (61.2%). Though factors responsible for such a situation are numerous in endemic areas

(Swellengrebel, 1950; McGregor, 1964; Ngimbi et al.,1982; Nagel, 1990; Scrimshaw, 1991; Yuthavong and Wilairat, 1993), we believe that, in Lubumbashi, the parasite density of individuals infected with Plasmodium but not diagnosed with clinical malaria was less than that believed to cause clinical disease (Trape et al.,1985). The fact that no cases of illness or death due to malaria were recorded during our follow-up of Plasmodium-infected but asymptomatic individuals, also suggests that these people were immune to malaria (Hill, 1991).

As previously observed (Wolfe, 1978; Trape et al., 1985), T. trichiura infection was associated with abdominal pain and diarrhea, hookworm infection was associated with diarrhea, and Plasmodium was associated with elevated body temperature. Although none of the clinical conditions were associated with A. lumbricoides infection, we previously reported that A. lumbricoides was the most important risk factor for stunting and wasting among these children in Lubumbashi (Tshikuka et al.,1995b). Strongyloides stercoralis, S. mansoni and H. nana were not associated with any of the clinical conditions, likely because all were rare.

Low PCV values were very common, especially in the LSES subdivisions (Table 9). Anaemia is a common symptom of T. trichiura, hookworm and S. mansoni infection (Wolfe, 1978; Woodruff, 1982; Scrimshaw, 1991), but none of these parasites were identified as risk factors for this condition, possibly because of the low intensities of infection. Anaemia also results from inadequate nutrient intake (Johnson et al.,1982). We suspect that low PCV was related primarily to nutritional deficiencies, especially in the LSES subdivisions where high levels of childhood protein energy malnutrition were found (Tshikuka et al.,1995b).

We also determined whether certain clinical conditions predisposed individuals to, or protected individuals from, other conditions. A variety of significant positive associations were detected, and are all consistent with those reported in the literature (Apley, 1975; Bruce-Chwatt, 1980). In contrast, no negative associations were detected, indicating that none of the common clinical conditions were protective against others. The reported negative association between low PCV (an index of iron deficiency; WHO, 1959) and clinical malaria (Scrimshaw, 1991) was not detected in this study.

Interestingly, subdivision of residence was an important risk factor for three of the common clinical conditions, despite the similar spectrum of parasite species among subdivisions. We believe that subdivision of residence was an appropriate general index of SES in Lubumbashi. Almost every house in Subdivision III belonged to the local companies or the government; only executives and senior officers lived in these houses. In contrast, residents of Subdivisions I and II were generally low paid industrial or unskilled workers, working in the informal sector, or unemployed. Within the Lubumbashi framework, subdivision of residence therefore reflects not only the occupation of the head of the household, his income and educational level, but also a variety of environmental and living condition variables described in Tshikuka et al. (1995a).

It is difficult to pinpoint what feature or combination of features in the LSES subdivisions would elevate risk of diarrhea, abdominal pain, and low PCV, but three possibilities are suggested. (1) Other infectious agents that were not included in our study may have caused these clinical conditions. (2) The generally lower income level in LSES subdivisions influences diet which, in turn, may compromise the host's ability to control the infection (Scrimshaw, 1991; Solomons and Scott, 1994). (3) Access to medical attention is lower in the LSES subdivisions than in the HSES subdivision (Tshikuka et al.,1995a), and this may prolong the duration of diarrhea, for example. Our observation that subdivision of residence contributes to the risk of clinical disease, independently of parasitic infection, was also suggested by Chiwuzie (1986) in a hospital-based study of the relationship between social class and infection.

Implications of polyparasitism examined in this paper are just few of the many that reflect the third world scenario where a variety of infections and health outcomes co-occur in the same individuals. Such phenomena are not only of academic interest, but they are a priority that should be addressed in order to increase the effectiveness of health care programmes in the tropics.

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Table 1. Definitions and diagnostic criteria of clinical conditions investigated

Condition	Definitions and diagnostic criteria	Reference
Elevated body T°	Axillary temperatures of ≥38 °C.	1
Clinical malaria (Suspected)	Elevated temperature/fever episodes + chills/rigors with or without splenomegaly.	2
Clinical malaria (Confirmed)	Elevated T° (fever episodes) + positive laboratory test.	3; 1
Diarrhea	More than 3 loose defecations 24 hour before the clinical examination ± unformed or fluid stool sample.	4

1: Trape et al.(1985); 2: criteria used by the examining physician; 3: Rooth and Björkman, (1992); 4: Snyder and Merson (1982).

...continued...

Table 1. (continued)

Condition	Definitions and diagnostic criteria	Reference
Low Packed Cell Volume (PCV)	0.6-4 years old PCV<32%; 5-9 years old PCV<33% 10-14 years old PCV<37%; boys > 14 years PCV<42% female > 14 years PCV<35%; pregnant female PCV<29%	5; 6
Abdominal pain	Abdominal pain at the day of visit and a history of 3 or more episodes of abdominal pain within a period of not less than two months before the clinical examination.	7
Splenomegaly	Palpable enlargement of the spleen on examination with/without inspiration.	8

5: WHO (1959); 6: Powers (1989); 7: Bury (1987); 8: Bruce-Chawatt (1990).

Table 2. The prevalence of infections by age group across all subdivisions

Age(Years)	N	Ascaris	Plasmodium	Trichuris	Hookworm	Strongyloides	Taenia	Schistosoma
0-2	145	49.6	58.6	21.3	6.2	1.3	0.7	0.0
2.1-4	128	74.2	57.8	35.9	7.0	2.3	0.8	0.0
4.1-6	116	75.8	58.6	28.4	6.9	3.4	0.0	0.0
6.1-8	125	72.0	61.6	32.8	6.4	1.6	0.4	1.6
8.1-10	111	73.8	68.5	31.5	9.0	2.7	0.0	1.8
10.1-12	110	72.7	62.7	27.2	6.3	2.7	0.9	1.8
12.1-14	90	65.5	65.6	28.8	6.6	3.3	0.1	2.2
14.1-16	94	63.8	61.7	26.6	7.4	2.1	0.2	2.1
16+	181	61.3	59.1	18.2	3.3	1.6	0.6	3.3
All ages	1100	67.0	61.2	27.2	6.3	2.2	1.1	1.4

Table 3. Prevalence and intensity of infections by subdivision (95% C.I) and mean number of parasites per infected person

Infection[1]	Subdivision I (N = 363)	Subdivision II (N = 410)	Subdivision III (N = 327)	All Subdivisions (N = 1100)
A. lumbricoides % (C.I)	63.9 (57-69)[a b]	76.3 (71-81)[a]	58.4 (52-65)[b]	67.0 (64-70)
A. lumbricoides epg (X±SE)	19125±2016[a]	31153±2202[b]	14105±1783[a]	22115±1201
Plasmodium % (C.I)	76.9 (71-82)[a]	68.8 (63-74)[a]	34.2 (28-40)[b]	61.2 (58-64)
T. trichiura % (C.I)	29.8 (24-35)[a]	25.0 (21-30)[a]	27.8 (21-33)[a]	27.2 (24-30)
T. trichiura epg (X±SE)	397±69[a]	360±59[a]	700±112[a]	473±46

[1] Different letters reflect significant differences (P<0.05)

...continued...

(Table 3. continued)

Infection[1]	Subdivision I (N = 363)	Subdivision II (N = 410)	Subdivision III (N = 327)	All Subdivisions (N = 1100)
Hookworms % (C.I)	6.6 (4-10)[a]	6.8 (4-10)[a]	5.5 (3-9)[a]	6.3 (5-8)
Hookworms (X±SE)	22±5[a]	31±6[a]	28±7[a]	27±4
S. stercoralis % (C.I)	1.7 (0.5-4)[a]	2.4 (1-5)[a]	2.8 (1-5)[a]	2.2 (1.4-3)
S. mansoni % (C.I)	0.8 (0.1-3)[a]	2.0 (0.7-4)[a]	1.5 (0.4-4)[a]	1.4 (0.8-2)
T. nana % (C.I)	1.7 (0.5-4)[a]	0.7 (0.1-2)[a]	0.9 (0.1-3)[a]	1.0(0.5-2)
Helminths/infected person (X±SE)	1.5±0.04[a]	1.4±0.03[a]	1.4±0.04[a]	1.4±0.02
Parasites/infected person (X±SE)[2]	2.0±0.05[a]	2.0±0.04[a]	1.7±0.05[b]	1.9±0.03

[1] Different letters reflect significant differences ($P<0.05$)

[2] Includes *Plasmodium*

Table 4. Crude measures of pairs association between parasite infections across all subdivisions

	A. lumbricoides	Plasmodium	T. trichiura	Hookworms	S. stercoralis
A. lumbricoides	-	13.60*	36.07*	10.10*	0.94
Plasmodium	1.6*	-	1.00	0.04	0.30
T. trichiura	2.65*	1.2	-	3.22	0.39
Hookworms	2.78*	1.0	1.59	-	37.07*
S. stercoralis	1.58	0.8	1.31	9.35*	-

Only parasites that have at least one significant association are reported. Odds ratios are in the lower area. Chi-squared ratios are in the upper area. *P<0.001.

Table 5. Age adjusted estimates of pairs association between parasite infections by subdivision

	Subdivision I	Subdivision II	Subdivision III
A. lumbricoides and *Plasmodium*	1.63*	1.33	1.29
A. lumbricoides and *T. trichiura*	2.94**	1.44	2.50**
A. lumbricoides and Hookworms	1.54*	1.43	3.07*
Hookworms and *S. stercoralis*	+**	+	+**

Only odds ratios which are significant in at least in one subdivision are reported. *P<0.05, **P<0.001. +odds ratio not calculable owing to zero values in some cells but the association is nevertheless positive.

Table 6. Rank correlation between *A.lumbricoides* epg and *T. trichiura* epg among individuals infected with both parasites.

	Subdivision I	Subdivision II	Subdivision III	All subdivisions
N	88	87	69	244
Spearman's r	0.27*	-0.002	0.42*	0.18*
Kendall's π	0.19*	-0.006	0.29*	0.12*

*P<0.01; Note the absence of correlation in subdivision II.

Table 7. Prevalence (%) of clinical conditions among participants by age group across all subdivisions

Age (Years)	N	Abdominal pain	Diarrhoea	Low PCV	Elevated body temperature	Splenomegaly	Clinical malaria
0-2	145	25.5	29.7	38.6	8.2	0.7	7.6
2.1-4	128	39.8	22.7	36.7	11.0	1.6	9.4
4.1-6	116	31.0	17.2	31.0	16.0	2.6	14.7
6.1-8	125	41.6	21.6	25.6	10.4	2.4	10.4
8.1-10	111	42.3	27.0	32.4	10.0	1.8	9.9
10.1-12	110	38.2	20.0	15.5	11.0	0.0	10.9
12.1-14	90	41.1	21.1	21.1	10.0	1.1	10.0
14.1-16	94	29.8	11.1	24.5	6.4	0.0	6.4
16+	181	16.6	6.6	23.2	6.6	0.0	6.6
All ages	1100	32.7	19.4	28.0	10.0	1.1	9.4

Table 8. Prevalence (%) of clinical conditions by subdivision (95% C.I)

	[1]Subdivision I	Subdivision II	Subdivision III	All subdivision
Participants (N)	363	410	327	1100
Abdominal pain % (C.I)	36.9 (31-43)[a]	38.8 (33-44)[a]	20.5 (16-26)[b]	32.7 (30-36)
Diarrhea % (C.I)	24.5 (20-30)[a]	19.8 (15-24)[a b]	13.2 (9-18)[b]	19.4 (17-22)
Low PCV % (C.I)	30.9 (25-37)[a]	41.2 (36-46)[a]	8.3 (5-12)[b]	28.0 (25-31)
Elevated body Tº % (C.I)	9.6 (8-15)[a b]	13.7 (11-19)[a]	5.2 (4-9)[b]	10.0 (9-13)
Splenomegaly % (C.I)	0.6 (0.1-2)[a]	1.7 (0.6-4)[a]	0.9 (0.1-3)[a]	1.1 (0.5-2)
Clinical malaria % (C.I)	9.6 (6-14)[a b]	12.7 (9-17)[a]	4.8 (3-8)[b]	9.4 (7-12)

[1]Different superscript letters reflect significant differences ($P<0.05$).

Table 9. Crude measures of pairs association between clinical conditions

	Abdominal pain	Diarrhoea	Low PCV	Elevated body T°	Splenomegaly	Clinical malaria
Abdominal pain	-	12.0**	1.7	5.2*	0.4	4.2*
Diarrhoea	1.7**	-	6.8**	5.9*	0.9	3.4
Low PCV	1.2	1.5**	-	2.7	0.2	0.9
Elevated body T°	1.5*	1.7*	1.4	-	82.2**	†
Splenomegaly	1.5	0.4	1.3	99.8**	-	96.8**
Clinical malaria	1.5*	1.5	1.2	†	119.0**	-

Odds ratios are in the lower area. Chi-squared are in the upper area; *P<0.05; **P<0.001. †Not estimated as one variable is a component of the other.

Table 10. Logistic regression analysis of diarrhea, abdominal pain, elevated temperature and low PCV on parasite infections and other explanatory variables (N = 1100).

Independent variables	B±SE	Odds Ratio	C.I of OR	T. ratio
A-Dependent variable: Diarrhea				
1 Hookworms (yes=1; no=2)	1.21±0.26	3.35**	2.00-5.61	4.6
2 Trichuris trichiura (yes=1; no=2)	0.35±0.16	1.42*	1.02-1.97	2.07
3 Age(years)	-0.05±0.01	0.95**	0.93-0.97	-4.81
4 †SDV (SDV I=1; SDVII=2; SDV III=3¥)				
SDV I	0.79±0.21	2.20**	1.46-3.32	3.80
SDV II	0.44±0.21	1.55*	1.03-2.34	2.07
Constant (A)	-1.59			
Likelihood Ratio (Chi-Squared)	73.01			

†Subdivision. ¥Reference group. *P<0.05; **P<0.001

...continued...

Table 10. (continued)

Independent variables	B±SE	Odds Ratio	C.I of OR	T. ratio
B-Dependent variable: Abdominal pain				
1 Trichuris trichiura (yes=1; no=2)	0.31±0.14	1.36*	1.03-1.81	2.11
2 Age(years)	-0.02±0.002	0.98**	0.97-0.99	-3.34
3 †SDV (SDV I=1; SDVII=2; SDV III=3¥)				
SDV I	0.83±0.17	2.30**	1.62-3.23	4.70
SDV II	0.88±0.17	2.40**	1.73-3.37	5.14
Constant (A)	-1.19			
Likelihood Ratio (Chi-Squared)	51.65			

†Subdivision. ¥Reference group. *P<0.05; **P<0.001

...continued...

Table 10. (continued)

Independent variables	B±SE	Odds Ratio	C.I of OR	T. ratio
C-Dependent variable: Elevated temperature				
1 Plasmodium (yes=1; no=2)	1.55±0.28	4.71**	2.76-8.03	5.61
2 Age(years)	-0.03±0.01	0.97*	0.94-0.99	-2.55
Constant (A)	-3.16			
Likelihood Ratio (Chi-Squared)	49.06			
D-Dependent variable: Low P.C.V.				
1 †SDV (SDV I=1; SDVII=2; SDV III=3¥)				
SDV I	1.60±0.23	4.95**	3.15-7.78	6.93
SDV II	2.05±0.22	7.76**	5.02-12.09	9.14
Constant (A)	-2.27			
Likelihood Ratio (Chi-Squared)	113.82			

†Subdivision. ¥Reference group. *P<0.05; **P<0.001

Fig 1. Frequency distribution of single and multiple infection with A. lumbricoides, Plasmodium, T. trichiura, hookworms, S. stercoralis, S. mansoni and H. nana by subdivision.

This graph shows 37 combinations of parasites as observed among participants. Uninfected participants are presented in the first column, those infected with only A. lumbricoides are in the second column and in the third there are those infected with only Plasmodium. The ninth column shows those infected with A. lumbricoides and Plasmodium; the tenth, those infected with A. lumbricoides and T. trichiura, etc.

Note how the general patterns of polyparasitism are similar in the three subdivisions. It is an indication that control programs targeting either a single parasite species, or a range of parasite species, may not need to be customized to different subdivisions. A similar combination of drugs is likely to be useful in all.

Fig 1. Profile of single and multiple infection by subdivision

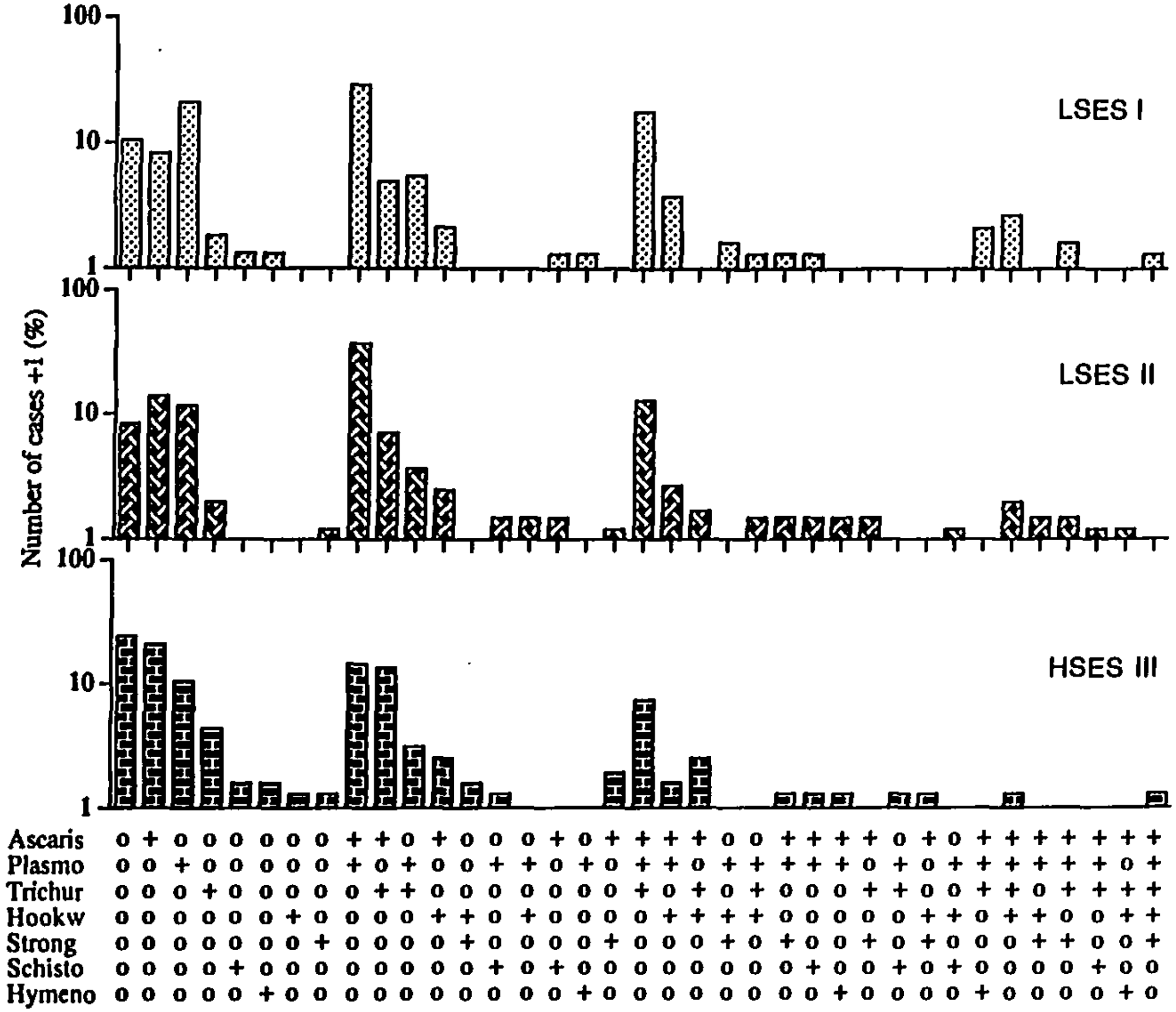
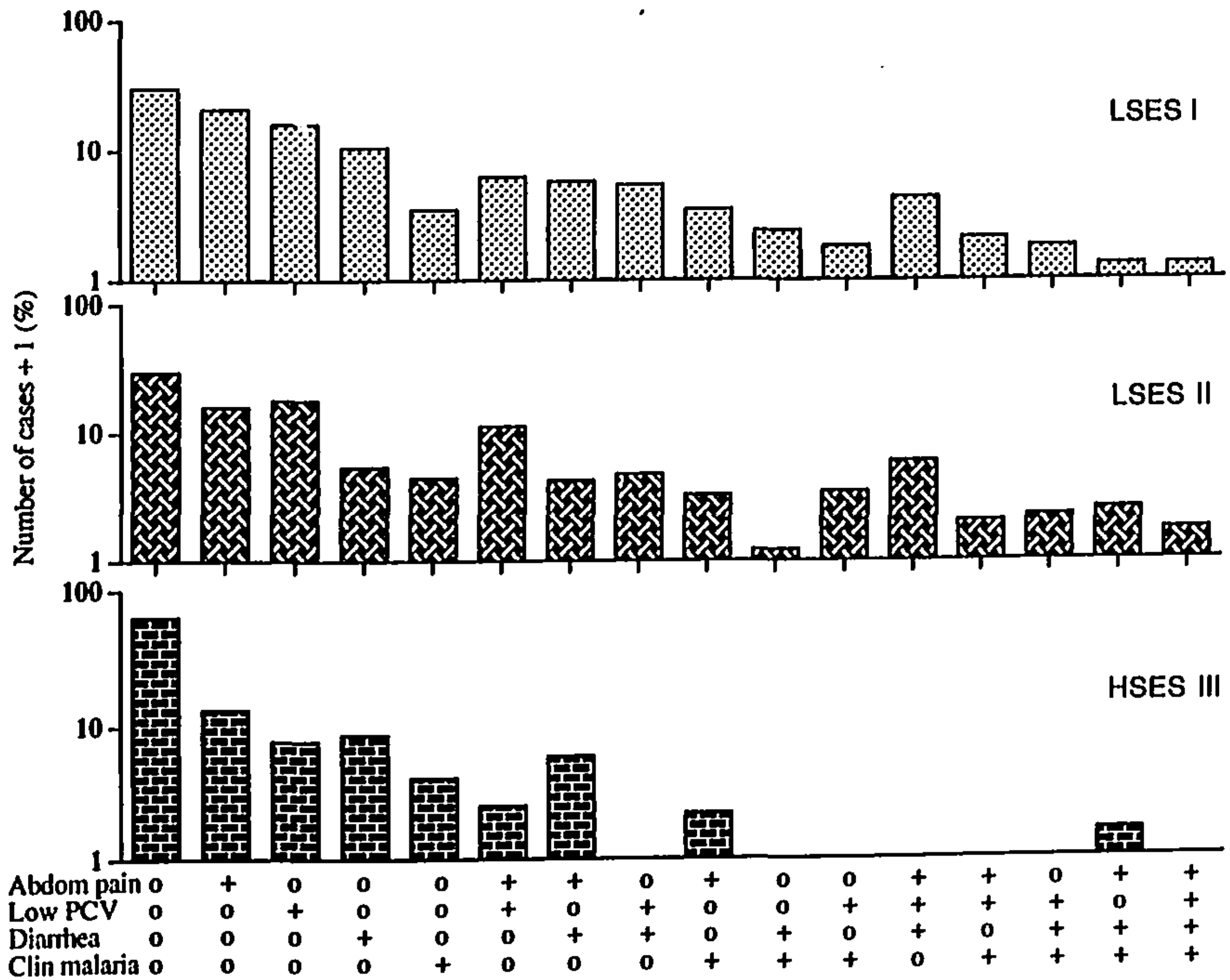


Fig 2. Frequency distribution of single and multiple clinical conditions with abdominal pain, low PCV, diarrhea and clinical malaria by subdivision.

The graph shows 16 combinations of clinical conditions. In the first column, participants without any of those conditions are presented and in the second, those with only abdominal pain. In the sixth column, participants with abdominal pain and low PCV are presented, in the seventh, those with abdominal pain and diarrhea, etc.

Note how the patterns of clinical condition are similar in the lower socio-economic Subdivisions I and II and how they both differ with the higher socio-economic Subdivision III where most people have no clinical conditions. There are many empty cells in Subdivision III, yet there is none in Subdivision I and II.

Fig 2. Profile of single and multiple clinical conditions by subdivision



CHAPTER VI

GENERAL DISCUSSION AND CONTRIBUTION TO ORIGINAL KNOWLEDGE

GENERAL DISCUSSION

As a whole this study has examined the host-parasite-environment triangle in three socio-economic subdivisions of Lubumbashi, Zaire, the lower socio-economic Subdivisions I and II and the higher socio-economic subdivision III. Different parts of the data set were used to examine three points that we anticipated at the beginning of the study. The first is presented in Chapter III and discusses relationships between environmental risk factors and infections. The second is presented in Chapter IV and examines relationships between infections, socio-economic status and nutritional indicators. The third point is in Chapter V, and examines relationships between infections, socio-economic status and health outcomes.

Chapter III revealed that profiles of environmental risk factors were similarly high in Subdivisions I and II and both significantly differed with Subdivision III. It also showed generally comparable levels of helminth infections among the three subdivisions as reflected by the prevalence and/or intensity of A. lumbricoides. However, other helminths showed the same pattern in Chapter V. Investigations of health outcomes in both Chapter IV and V testify that the occurrence of health outcomes was significantly higher in subdivision I and II compared with subdivision III, although infection levels with many parasites were comparable among the three subdivisions.

Two important observations were made in this study. Although profiles of environmental risk factors by subdivision suggested a higher level of exposure to infection and disease in subdivisions I and II than in subdivision III, the level of helminth infections was generally comparable in all three subdivisions. In contrast, although the profile of infection by subdivision suggested that level of diseases should be comparable in the three subdivisions, disease was significantly less common in subdivision III than in subdivisions I and II. Both observations contradict anticipated relationships described at the beginning in Chapter III and raise interesting questions as to whether health outcomes in endemic areas are associated with infection or with environmental and living conditions. It is not clear why groups at higher risk of infection have the same level of infection as those at lower risk, nor why groups with similar levels of infection have different levels of disease.

These contrasting profiles are not the first such findings to be reported in endemic areas. Studies conducted in Southern and Western Africa (Feachem et al.,1983) revealed that, in Ndola, Zambia, hookworm and protozoal infections were comparable between groups with better living conditions (better housing, safe water, improved sanitation and better jobs) and those without; in the same study A. lumbricoides was even higher among those with the better living conditions. On the other hand, three Balinese hamlets with comparable environmental and other aspects of living conditions reportedly (Cerf et al.,1981) were equally infected with nematodes but differed in the level of PEM. The association between infection and PEM was significant only in hamlets with the least access to health care system and food availability. While these two studies provide examples of lack of association between SES and infection and between level of infection and health outcomes in different settings, what is unique in our work is that these contrasts are both described in a single setting at a single point in time. The fact that the profile of health outcomes in Chapter IV and V are consistent with the SES and the profile of risk factors for infection reported in Chapter III rather than with infection profiles is important to note. The lower frequency of poor health outcomes in subdivision III despite high levels of infection, may be due to better access to health care system and good food availability in this community. This particular finding supports the theory of multifactorial causation of diseases (MacMahon and Pugh, 1970; Friedman, 1980), but by no means suggests that infections are not related to health outcomes in Lubumbashi. Indeed, environmental and living conditions, socio-economic status, and parasitic infections, contributed each to health outcomes in the three subdivsions.

Relationships between environmental risk factors and infection, measured in the Chapter III indicate that maternal education was an important predictor of infection in all subdivisions. Additional predictors in both LSES subdivisions were related to crowding and sanitation, whereas in the HSES subdivision, the only other predictor was related to socio-cultural factors incorporated in this study as the number of relatives per family. The ratio of indirect family members (relatives) to direct family members per household was used as an index of how each household interacted with outsiders. That some predictors of infection differ between the lower and higher socio-economic subdivisions is consistent with the contrast seen between risk factors and infection patterns and indicate that different mechanisms were involved in the transmission dynamics of infection in the lower and higher socio-economic subdivisions. At the same time it lends support to speculations that relatives and live-in visitors contribute to infection transmission between the lower and higher socio-economic subdivisions. However, quantitative data on the precise transmission pattern between higher and lower socio-economic subdivisions are lacking. Our lack of understanding may cloud the issues of how the un-met needs of the urban poor impact on the health of the wealthier.

In Chapter IV and V, both infection and SES were investigated as potential predictors of health outcomes with a focus on nutritional outcomes and clinical conditions. Aside from a few variables, predictors of both nutritional and clinical conditions were generally the same.

For the first time, we have estimated the relative contribution of common parasites found in Lubumbashi, Zaire and the SES of different groups to health outcomes commonly found in that city. Hookworms, T. trichiura infection, young age, residence in LSES subdivision contributed to the occurrence of diarrhea in Lubumbashi. All but hookworms also contributed to the occurrence of abdominal pain. Plasmodium was the only parasite associated with fever and none of the parasite species was a risk factor for low PCV. Within the same population A. lumbricoides and T. trichiura were predictors of wasting, and A. lumbricoides of stunting. Kwashiorkor was linked to the presence of T. trichiura and absence of A. lumbricoides. The absence of A. lumbricoides as a risk factor for clinical conditions other than nutritional may be due to loss of information likely because of the use of binary outcome variables. In part we would have expected it to be linked with abdominal pain (Jacob et al.,1983; WHO, 1985) or even fever (Adedeji and Ogumba, 1986). These same reasons may as well explain why neither hookworms nor Plasmodium were predictors of undernutrition. Even if we did not estimate the intensity of Plasmodium infection in our studies, the fact that the majority of infected individuals were asymptomatic may explain why Plasmodium was not related with any of the PEM indicators. PEM has been reported to be more a feature of clinical malaria rather than the simple presence of Plasmodium (MacGregor et al., 1956). Even when clinical conditions were investigated, Plasmodium was a predictor only of elevated temperature which indeed is biologically plausible if elevated temperature is taken as a proxy for clinical malaria.

Our results suggest that in endemic areas where infection and morbidity are associated with various factors, the SES of a community does not necessarily equate with the level of infections in that community, but in most cases it will equate with health outcomes. A number of studies have shown that SES is a strong and consistent predictor of health outcomes (Syme and Berkman,1976; Adelstein, 1980; Adler et al.,1993). Kitagawa and Hauser (1973) even demonstrated a linear relationship between years of school, a component of SES, and mortality.

SES is a complex of factors representing a broad spectrum of variables often conceptualized as a combination of financial, occupational, and educational variables (Green, 1970; Winkleby et al.,1992). Although these three dimensions of SES are interrelated, it has been proposed that each reflects somewhat different individual and societal forces associated with health outcomes. Occupation measures prestige, responsibility, physical activity, and risk of exposures in the work place; education indicates skills requisite for acquiring positive social, psychological, and economic resources; income reflects spending power, medical care, housing and diet (Susser et al.,1985). In this study subdivision was used as an index of SES. Indeed, at the time we conducted this work in Lubumbashi, almost every house in the subdivision III belonged to the mining company, the railway, brewery or the government. Only executive and senior officers from these organizations were accommodated in these houses which had to be vacated any time the officers lost their jobs. In contrast, subdivision I and II were generally for low paid industrial/unskilled workers, unemployed and those working in the informal sector. Thus within the Lubumbashi framework, subdivision of residence is a very good index of SES. It reflects not only the occupation of the head of household but also his income and educational level. Data on environmental and living conditions detailed in Chapter III provide a good illustration of socio-economic stratification in Lubumbashi. As far as housing is concerned, dwellings in subdivision III were similar to those in the best European or North American suburbs, whereas subdivisions I and II were slums.

Although studies supporting relationships that we found between SES and health outcomes were available in the literature (Syme and Berkman, 1976; Adelstein, 1980; Adler et al.,1993), none of them investigated the relative contribution of other factors, such as the parasites, toward these health outcomes. Similarly studies reporting associations between parasite and health outcomes in endemic areas do not usually investigate the relative contribution of factors such as the socio-economic status, or how interspecific interactions among such factors may influence outcomes. Given that infected individuals in the tropics usually harbor more than one type of parasite and suffer simultaneously from a variety of clinical conditions, the severity of such conditions may increase or decrease in specific combinations of parasites. Health outcomes deriving from such effects may also interact among themselves, thus resulting in a beneficial or detrimental effect on the host i.e., interaction between clinical malaria and iron deficiency. More interesting is that some of those health outcomes may be prejudicial to the parasite survival within the host, i.e., extreme malnutrition and gut nematodes. These critical issues are the third world realities and therefore should be addressed all at the same time in endemic areas in order to achieve a sustainable health improvement. Unfortunately such data are non existent in the literature.

This thesis provides data addressing these issues, all at the same time and in one single location. There is no indication that health outcomes investigated in Lubumbashi were more severe in multiply infected individuals compared with individuals with single infections. No health outcome protected the host against another form of health outcome, though we expected such relationship between clinical malaria and low PCV. In contrast the study suggests for the first time that kwashiorkor is negatively associated with A. lumbricoides infection. Even though the relationship conflicts with published data (Jelliffe and Jelliffe, 1978; Pawlowski, 1978), it is somewhat supported by reports that extreme malnutrition may be prejudicial to nematode recruitment and establishment in the host (Solomons and Scott, 1994). However this particular finding warrants further research. Survival of children with kwashiorkor who were also infected with A. lumbricoides may have been poorer, and therefore fewer were included in this cross-sectional study.

The definition of biological and ecological associations as provided in this study will likely contribute to the controversy around this subject. Parasites were found to be ecologically rather than biologically associated, despite similarities in their life cycle.

LIMITATIONS

A major objective of observational studies is to determine whether or not an association exists between an exposure factor and an outcome in a given community. But interpretation of such studies is difficult, particularly in cross-sectional studies, because the direction of cause and effect is difficult to assess, as the exposure factors and outcomes are assessed at a single point in time. Did the outcome affect the measured exposure level, or did the exposure factor affect the outcome? (Hennekens and Buring, 1987; Zweig and Blacke, Jr, 1988).

As public health workers, the most fundamental question is whether the frequency of a particular health outcome is influenced by changes in a known exposure factor. To understand how that change exerted that influence may call for a great deal of research (Bradford Hill, 1965). Public health workers, however, cannot sit and wait for results of such research, before deducing "causation" and taking action (Bradford Hill, 1965). Indeed in some communities, infections have been wiped out or brought under control without prior knowledge of the causative agent (Schwabe, 1984). Though the identification of the causal factor is highly desirable, epidemiologists strongly recognize that full knowledge of etiologic mechanisms is not necessary for effective control programs (Bradford Hill, 1965; Mausner and Kramer, 1985). Hennekens and Buring (1987) and Flanders et al. (1992) even claim that a cross-sectional survey can be used to address causal relationships, when the current values of the exposure factors represent the values present at the time that the outcome condition started. Factors present at birth, such as eye color or blood group (Hennekens and Buring, 1987), would be examples. However, in most cross-sectional studies, the risk factors may be subject to alteration subsequent or even consequent to the development of the outcome, and in such cases cross-sectional data can be used to formulate hypotheses, but not to test them (Mausner and Kramer, 1985; Hennekens and Buring, 1987; Zweig and Blacke, Jr, 1988).

Data presented in this thesis were collected through a carefully designed protocol and a meticulously conducted study. The study was restricted only to Zairean nationals, children (4 months-16 years old) and mothers, who had lived for not less than two years at the same address. This was done as a means of excluding those with infections contracted before moving to their current addresses. Chances of including participants harboring infections that they may have contracted before moving into their current environment were therefore very low. The selection of one index child aged 4 months-to 16 years per family to investigate relationships between infection levels and environmental risk factors added strength to the study, by controlling confounders within families. Field, laboratory and analytical components were done by different teams of people, but the same people performed the same tasks from the beginning to the end of the study. Stratified and multivariate analyses were used to adjust for complex interrelationships among variables and control for confounders. For these reasons, findings in this study deliver more than hypothesis formulation. For instance, the relationships that we found between SES and health outcomes, between maternal education and A. lumbricoides, between A. lumbricoides and wasting, etc. cannot just be said to generate testable hypotheses. Such hypotheses were formulated long ago, tested and supported (Stephenson et al.,1980; Carrera et al.,1984; Chiwuzie, 1986; Holland et al., 1988; Adler et al., 1993). Indeed, findings in this study confirm and/or refute, for the first time in Zaire, what has been confirmed in other countries through prospective or intervention studies. For instance, in 1986, WHO recognized that the presence of wasting at one point in time was a reasonable indicator of the incidence of the process that is causing it. Other studies have also supported the WHO report (Franklin et al.,1984). So do we really need intervention studies to confirm the relationship that we are reporting here between A. lumbricoides and wasting?

In contrast we do need intervention studies to confirm relationships like those we found between A. lumbricoides and kwashiorkor, and between the ratio of relatives to direct family members and A. lumbricoides, because these hypotheses have not been proposed before. Otherwise all relationships that are reported here meet requirements for valid associations laid down by Sir Bradford Hill in

1965; they are biologically plausible and coherent, strong and consistent throughout different strata from Chapter III to V. Thus given the urgent need for health care attention as reflected by these results and limitations in health care resource availability in Zaire, follow up studies to look for causal mechanisms are unnecessary, they will be time consuming, and not cost effective. Indeed, the cross sectional study is a suitable strategy for third world countries, because it is cheap, not time consuming, and can study multiple exposures and multiple outcomes.

CONCLUSION AND RECOMMENDATIONS

Findings in this work are that: (i) maternal education was the most important predictor of infection in Lubumbashi; (ii) while crowding and sanitation were associated with infection in poor neighborhoods, in the richer neighborhood, infection was associated with the community socio-cultural aspect or frequency of live-in visitors and relatives; (iii) aside from kwashiorkor, all protein energy malnutrition indicators were positively associated with infection; (iv) though the level of helminth infection was generally comparable between poor and rich neighborhoods, health outcomes including those associated with these helminths were better in the rich neighborhood; (v) SES, T. trichiura, A. lumbricoides, hookworms and Plasmodium were the most important predictors of health outcomes in Lubumbashi and children were the most affected; (vi) only positive relationships were found among parasites and all appeared to be ecological rather than biological associations; (vii) no type of morbidity protected the host against another form of morbidity.

Depending on the local need and available resources, two types of control strategies may be sought: (i) an infection oriented control strategy or (ii) a disease oriented control strategy. If the first option is adopted, emphasis should be put on improving maternal education, sanitation and some socio-cultural factors, such as those reflecting inter-community relationships. However this is a long term program and may need several years before results are seen. Thus, it should be run in parallel with short term programs based on chemotherapy targeted to young children in order to reduce major infections: T. trichiura, A. lumbricoides and Plasmodium. The selection of the drugs to be used will depend on the cost of delivery which among other factors, will also depend on drug efficacy against multiple species infections. For Plasmodium infection, this short term control program should be focussed on the elimination of adult mosquitoes/larvae rather than the use of antimalarial drugs, given controversies surrounding chemoprophylactic treatment of malaria in holo/hyperendemic areas (Bruce-Chwatt, 1980).

If the second option is adopted, emphasis should be put on improving the socio-economic status of the people, especially of those living in the poorer neighborhoods. Though such an approach will equally help control other major factors associated with health outcomes, again, it is a long term strategy and may take years before we see the results. Therefore, short term programs based on chemotherapy to control T. trichiura, A. lumbricoides and hookworm, is strongly recommended. With respect to A. lumbricoides, it is always advisable that control be infection oriented, given that one single Ascaris may be fatal to the host. Only those with clinical malaria should be treated. The high level of PEM recorded in this study also indicates a need for feeding programs for younger children, especially in the LSES communities.

While this study is an excellent illustration of the complexity of relationships between host, parasite and environmental factors, it is a challenge to policy makers and to all those with better environmental and living conditions within areas where the majority live in misery and hardships. The study supports Owen's (1927) ideas that "The individual happiness of a man can be increased and extended only in proportion as he actively endeavors to increase and extend the happiness of all around him".

CONTRIBUTION TO ORIGINAL KNOWLEDGE

1 This is the first time since the country became independent from the Belgium colonial rule in 1960, that data on environmental and living conditions, malaria, helminth infections and protein energy malnutrition are made available in Lubumbashi. It is also the first time that community based data on predominant clinical outcomes, and their correlates are made available in this city.

2 No previous studies have considered that families' level of socialization with others may be predictive of nematode infection. The "extended family index" that we have developed has been identified as a positive predictor of Ascaris infection in one of the communities that we investigated, thus opening the way for more research on the transmission dynamics of nematodes.

3 It is known that parasites depend on their host for nutritional sustenance, and that failure to satisfy the parasite's nutritional requirements may lead to negative effects on the parasite survival and/or reproductive function. Children with extreme malnutrition such as kwashiorkor, have always been reported to be heavily infected with nematodes. For the first time observation of a negative association between A. lumbricoides and kwashiorkor has been made, and both, qualitative as well as quantitative estimations are compatible with such an association.

4 Kwashiorkor and wasting are two distinct forms of extreme malnutrition. Our observation that the two were associated with A. lumbricoides but in opposite directions is a strong indication of further difference between the two indicators.

5 Parasites were found to be ecologically rather than biologically associated, despite similarities in life cycle. This finding contributes to the controversy around biological versus ecological associations among parasites.

6 The protective role of iron deficiency against clinical malaria in the tropics is well documented. Although in this study, cases of anemia and asymptomatic malaria were common, no relationship was observed between low PCV and asymptomatic cases of malaria.

7 The severity of health outcomes may increase or decrease due to a synergistic or antagonistic effects of one parasite on another. Such

types of interaction are expected to be common in endemic areas where infected people usually harbor more than one single parasite. Of the parasites that were investigated in this study, none of them increased or decreased the effect of another parasite on health outcomes.

8 Contrasts between SES and infection, and between infection and health outcomes have been each described in different areas and at different points in time. For the first time, we are reporting both contrasts in a single setting at a single point in time, as further support to the theory of multifactorial causation of diseases at the community level.

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APPENDICES

A pre-prepared study protocol is needed to begin any research work. If the study is to be conducted on human subjects, also needed are the following: a certification of ethical acceptability, a clearance from the country where the study is to be conducted and a signed consent from the participants.

What follow in this section are copies of those documents.

A1

Field work protocol, form 1, city data

This form was used in the collection of general information on Lubumbashi. We visited heads of government departments or agencies in their offices and collected data on demography, sanitation, housing, water and food supply, health care system, education, transportation, weather etc. At the end of the study, the forms were brought to Canada for analysis.

A1

FIELD WORK PROTOCOL FORM 1 CITY DATA

Name of City ____________________ Area (km^2) _____ Altitude (m) ____

Name of Administrative Leader ______________________________________

Population ________ Number of houses ________ Urban subdivisions ______

Males ____________ Females __________ Children under 15 __________

WEATHER

Temperature: maximum from ____ to ____; minimum from ____ to ____

Rainy season from _______ to _______; dry season from _______ to _______

Average yearly precipitation (mm) ____________

SANITATION

Public Latrines (number, condition) ______________________________

____

Accessibility to public washrooms ________________________________

____

Sewage Disposal System ____

____

Garbage Collection System ____

____

HOUSING

Housing (mud / brick / other) ____________________________________

Electricity ____

WATER AND FOOD SUPPLY

Water supply system in city ______________________________________

____

(continued)

Quantity of safe water available per day ____________________

Comments ____________________

Number of public markets ________ supermarkets __________

Condition of public markets ____________________

____

Condition of supermarkets ____________________

____

HEALTH CARE SYSTEM

Number of hospitals: public ____ private ____ emergency clinics ____

beds ____ pharmacies ____ physicians: private ____ government ____

nurses ____ pharmacists ____ health related professionals ____

Current health programs ____________________

____

Environmental officers and activities ____________________

____

EDUCATION

Number of elementary schools ________ high schools __________

Capacity of elementary schools ________ high schools __________

Current enrollment of elementary schools ________ high schools ______

Health education programs on TV: Yes ___ No ___ On Radio: Yes ___ No ___

Broadcasts / wk in Swahili ____ in French ____

Number of school nurses _____

Source of Information ____________________

____

Investigator name ____________________ Title __________

Signature ____________________ Date __________ 1991

A2

Field work protocol, form 2, subdivision data

This form was used in the collection of general information on each selected sub-division. Heads of sub-divisions were interviewed and data on demography, sanitation, housing, water and food supply, health care system, education transportation etc. were recorded. At the end of the study, the forms were brought to Canada for analysis.

A2

FIELD WORK PROTOCOL FORM 2 SUBDIVISION DATA

Name of Subdivision ______________________________

Location ______________________ Area (km^2) ______________

Name of Administrative Leader ______________________________

Population ____________ Number of houses ______________

Males ____________ Females __________ Children under 15 __________

SANITATION

Public Latrines (number, condition) ______________________________

____

Sewage Disposal System ______________________________

____

Garbage Collection System ______________________________

____

HOUSING

Housing (mud / brick / other) ______________________________

Electricity ______________________________

WATER AND FOOD SUPPLY

Quantity of safe water available per day ______________________________

Distribution ______________________________

Number of public markets __________ supermarkets ____________

Condition of public markets ______________________________

____

Condition of supermarkets ______________________________

____

Cooked food sold on streets: Yes _________ No ____________

(continued)

A2 (continued)

TRANSPORTATION

Roads ____

Public transportation ____________________ Price of ticket _____

HEALTH CARE SYSTEM

Number of hospitals: public ____ private ____ emergency clinics ____

beds ____ pharmacies ____ physicians: private ____ government ____

nurses ____ pharmacists ____ health related professionals ____

Current health programs ____________________________________

____

Environmental officers and activities _________________________

____

EDUCATION

Number of elementary schools ________ high schools ____________

Capacity of elementary schools _______ high schools ___________

Current enrollment of elementary schools _________ high schools ______

Number of school nurses ____

COMMENTS

Source of Information ______________________________________

____

Investigator name ____________________ Title _________

Signature __ ____________________ Date _________ 1991

A3

Field work protocol, form 3, family data

This form was used to collect information from each selected family. Mothers or care-givers were interviewed, data on their level of education and occupation, housing and crowding, sanitation, access to safe water and food, access to health-care system and socio-cultural variables were recorded. At the end of the study, the forms were brought to Canada for analysis.

A3

FIELD WORK PROTOCOL   FORM 3   FAMILY DATA

Last Name ____________________   Family Serial # ________

First Name ____________________   Participant # ________

Head of Family __________________ Relationship to Head ________

Address ____

When did you move to this address? ________________________

Where did you live before? ________________________________

Why did you move? ______________________________________

When did you arrive in Lubumbashi? ________________________

Why did you come to Lubumbashi? ___________________________

THE HOUSE AND YARD

The walls of the house are: brick ____ mud ____ other ____________

The floor is: cement ____ dirt ____ other ____________________

The kitchen is: inside the house ____ outside the house ____

Windows are covered with mosquito netting: Yes ___ No ___ Some ____

Pests present in house: Yes ____ No ____ Identify ______________

Number of people living in house _____   Number of rooms in house ____

Crowding index: 1 (very) ____ 2 (somewhat) ____ 3 (not crowded) ____

The yard is: lawn ____ pavement ____ other ____________________

Toilet: an indoor WC ____ latrine ____ outdoor defecation area ____

Latrine: number using it _____   functional? Yes ____ No ____

What do children use? WC ____ latrine ____ area ____ indiscrimate ____

Family sewage disposal system is: private ____ collective ____

working ____   not working ____   flooded ____

Pools of sewage in: yard ____ near yard ____ neighbour's yard ____

Collective sewage system in neighbourhood is working? Yes ___ No ___

(continued)

A3 (continued)

<u>Garbage</u> dumpster in yard? Yes ___ No ____

<u>Rainwater</u> draining trenches are working? Yes ____ No ____ None ____

<u>Road</u> adjacent to house is: paved ____ dirt ____ Other ______________

Number of <u>animals</u>: dogs ___ cats ___ pigs ___ goats ___ sheep ___ fowl ___

<u>Animals live</u>: in house ___ in pens ___ fed, confined ___ unfed, free ___

WATER AND FOOD SUPPLY, EATING HABITS

<u>Source of family water</u>: tap ____ bore hole ____ other ________________

Number <u>jugs water used</u> / day: ____

<u>Drinking water</u> is: boiled ___ tap ___ bottled ___ other ___________

<u>Children eat</u> with: silverware ___ hands ___ others ______________________

<u>Adults eat</u> with: silverware ___ hands ___ others _________________________

<u>Family eats</u>: on table ___ on house floor ___ or yard ground ___

Family eats <u>cooked food sold on street</u>: Yes ____ No ____

Family <u>buys food</u> at: public markets ___ supermarkets ___ street vendors

others ____

Children <u>bath</u>: indoors ____ yard ____ rivers ____ rain water pools ____

Adults bath: indoors ____ yard ____ rivers ____ rain water pools ____

HEALTH CARE ACCESSIBILITY

Family has a <u>family doctor</u>: Yes ___ No ___ <u>witch doctor</u>: Yes ___ No ___

The family has medical <u>insurance</u> coverage for:

Doctor's visits: Yes ___ No ___ Drugs: Yes ___ No ___

Hospitalization: Yes ___ No ___

The family can buy <u>drugs</u>: whenever needed ___ sometimes ___ never ___

The family can see <u>doctor</u>: whenever needed ___ sometimes ___ never ___

Investigator name _______________________ Title ___________

Signature _______________________________ Date ___________ 1991

A4

Field work protocol, form 4, individual data

Participants' personal data and results of clinical and laboratory examinations were directly recorded in this form. At the end of the study, the forms were brought to Canada and data were entered into a Macintosh LC Computer for analysis.

FIELD WORK PROTOCOL   FORM 4   INDIVIDUAL DATA

Last Name ____________ ____________   Family Serial # ________

First Name ____________ ____________   Participant # ________

Relationship to head of family ______________________________

Age (yrs) ____ Birth Date: Yr ____ Mm ____ Dy ____ Sex (M/F) ____

Birth Place ____________________ Citizenship ____________________

Race: Black ____ White ____ Asian ____ Other ____

ADULTS: Married ____ Divorced ____ Separated ____ Single ____

Employment ______________ Working Place ______________

Hours / day at work __________ Day / wk at work __________

Highest level of education achieved __________

Read: Yes ___ No ___   Write: Yes ___ No ___

CHILDREN: Day-care / school ______________________ Grade ____

Hours / day at school ______ Hours / day at home ______

Most common play-place ______________________________

CLINICAL EXAMINATION

Weight (kg) ______ Height (cms) ______ Body temperature _____°C

Number bowel movements yesterday? ______

Finish eating food available? Yes ___ No ___ Still hungry? Yes ___ No ___

Anemia: Yes ___ No ___   Edema: Yes ___ No ___

Potbelly: Yes ___ No ___   Jaundice: Yes ___ No ___

Lymphadenopathy: Yes ___ No ___   Splenomegaly: Yes ___ No ___

River blindness: Yes ___ No ___   Onchocerca nodules: Yes ___ No ___

Referral to ____________________ for ____________________

Investigator's Name ________________   Title ________________

Signature ______________________   Date ____________ 1991

(continued)

LABORATORY SAMPLE COLLECTION

	STOOL SAMPLE		BLOOD SMEAR thick/thin	HEMATOCRIT	SEROLOGY filter paper
Date Received					
Receiver					
Date Prepared	KATO	SMEAR			
Date Examined					
Examiner					

LABORATORY RESULTS

Stool Sample: Solid ____ Semi-Liquid ___ Liquid ____ Blood ____

PARASITE	INIT	RESULT				TREATMENT		
		1	F/T	2	F/T	Drug	Dose	Date
Ascaris (ep5mg)								
Trichuris (ep5mg)								
Hookworm (ep5mg)								
Taenia (Y/N)								
S mansoni (ep5mg)								
E histolytica (Y/N)								
Giardia (Y/N)								
S haematobium (Y/N)								
Wuchereria (Y/N)								
P falciparum (Y/N)								
P malariae (Y/N)								
Trypanosoma (Y/N)								
Hematocrit (%)								

Comments:

Field work protocol, form 5, hospital data

Copies of this form were distributed to local hospitals and medical laboratories authorities to record infection, morbidity and mortality due to parasites in their institutions from June 01/91 to August 30 1991. At the end of the study, forms were returned to us.

A5

FIELD WORK PROTOCOL   FORM 5   HOSPITAL DATA

Nom de hospital ______________________________

Adresse ______________________________

En cas de confusion, contacter le Dr. José–Gaby Tshikuka.

Pour chaque mois, indiquez le nombre des personnes dans les catégories suivantes.

CONDITION	JUIN 1991	JUILLET 1991	AOÛT 1991
Malades en consultation externe			
Hospitalisations			
Mortalités Totale			
Mortalité du			
à la malaria			
aux autres infections parasitaires			
Malades traité pour:			
Onchocercose			
Wuchereriose			
Ascariose			
Trichuriose			
Ankilostomiase			
Taenia			
Hydaticose			
Schistosomiase (mansoni)			
Schistosomiase (haematobium)			
Amebiase			
Giardia			
Malaria (falciparum)			
Malaria (malariae)			
Trypanosomiase			

AU VERSO, S'IL VOUS PLAIT

(continued)

A5 (continued)

Provenance des données ______________________________

____

____

Autre commentaire:

Nom du repondant ____________________ Position ______________

Signature __________________________ Date ____________ 1991

Investigator _______________________ Title _________________

Signature __________________________ Date ____________ 1991

A6

Certification of ethical acceptability for research involving human subjects

The study protocol, was reviewed by the McGill Ethical Community. This certificate was granted to us as prof that the study was ethically sound and acceptable to be conducted on human subjects.

Authorization to conduct the study in Lubumbashi

The study proposal was reviewed by the Zairean ministry of health. This letter is a clearance to conduct the study throughout the sub-region of Lubumbashi.

Informed consent

This form was read by/to the head of the family. Additional explanations were provided to ensure that he/she fully understood the content of the form. A family was investigated only when the head of the family gave his/her written or verbal consent.

A8

Informed Consent

Institute of Parasitology, Macdonald College, McGill University Montreal PQ, Canada H9X 3V9 TL (514) 398-7722

Laboratoire Médical Central de Lubumbashi, Region du Shaba, République du Zaire

ENQUETE SANITAIRE PILOTE DE LA VILLE DE LUBUMBASHI

juin 1991 - août 1991

Chercheur principal Dr J.G. Tshikuka

AVIS DE PARTICIPATION

Madame/Monsieur

Nous avons le plaisir de vous anoncer que votre résidence figure parmi tant d'autres qui ont été tirées au hazard pour entrer dans l'enquête sanitaire qui se tient du mois de juin au mois d' août 1991, dans la ville de Lubumbashi. Cette enquête a pour objet: l'évaluation des changements causés par l'urbanisation, leurs implications dans la santé commu- nautaire, l'élucidation des déterminants ou les facteurs responsables des infections parasitaires ainsi que les mécanismes appropriés pour leur contrôl et la promotion sanitaire.

Si nous avons choisi la ville de Lubumbashi comme le lieu de l' enquête, c'est précisément à cause de son importance dans l'économie nationale.

Nos investigations consisteront à l'obtention auprès de participants, des réponses aux questions liées à l'habitat, à l'obtention des échantillons des selles que les participants ameneront avec eux dans notre centre pilote. Au centre sanitaire pilote les participants seront examinés par un medecin et quelque gouttes de sang seront prélèvées du bout de leur doig. Les tests de laboratoire séront executés gratuitement par un personnel médical qualifié. Les résultats de ces examens leur seront communiqué le jour suivant. Un traitement approprié des infections parasitaires diagnostiquées sera donné gratuitement aux participants selon nos moyens. Dans le cas contraire, une prescription médicale leur sera remise pour acquerir des produits pharmaceutiques à leur frais personnel.

Votre participation madame/monsieur nous aidera à comprendre et à évaluer les problèmes de santé communautaire de notre chère ville, afin de trouver des solutions appropriées.

Nous vous garantissons que toutes les données seront confidentielles.

Veuillez ainsi remplir et signer le bas de la page pour approuver votre participation. Toute fois, vous avez le droit de vous retirer de l'enquête au cas où votre décision changeait plus tard. Nous vous remercions d'avance madame/monsieur pour votre collaboration.

Dr J.G. Tshikuka

Je soussigné____________________résident sur la rue________ ____________#______dans la zone urbaine de ____________, ville de Lubumbashi, avoir accepté de faire partie de l'enquête sanitaire qui se tient à Lubumbashi du mois de juin au mois d'août 1991. J'accepte aussi avoir bien compris le contenu de cette enquête.

Date__________________Signature____________________