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The Epidemiology of *Schistosoma haematobium* and *S. mansoni* Infections in the Egypt-49 Project Area

4. Measurement of the Incidence of Bilharziasis

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The measurement of incidence, or the rate at which people become positive, for Schistosoma haematobium *and* S. mansoni *was carried out in four parts of the Egypt-49 project area near Alexandria. For* S. haematobium, *rates as high as 22.8 % per year were found for children 0-6 years old in a rural area; in the same area, the incidence of* S. mansoni *was 8.5 % per year. The true incidence is underestimated because many cases become negative spontaneously. This loss rate of* S. haematobium *cases is 0.476 per year for children 0-4 years old, and 0.049 per year for those aged 5 and 6 years; for* S. mansoni, *the rates are 0.580 and 0.327, respectively. Despite the error, incidence is the most accurate and sensitive method of assessing the success of control operations, and is an important measurable parameter in epidemiology.*

The quantitative assessment of an endemic disease should include more factors than a statement of the *prevalence*, or proportion of people positive at a given time. A tabulation of the percentage positive in different age-groups, as in the usual age-prevalence presentation, is an improvement over a simple statement of over-all prevalence, since such a tabulation permits one to make at least a subjective evaluation of the early increase in the proportion infected with age. It is, however, much more meaningful epidemiologically to be able to make a numerical estimate of the *incidence*, or the rate at which negative persons become positive.

Incidence is thus the direct expression of the rate of transmission, and it is highly desirable to be able to obtain this important epidemiological parameter. Moreover, for many diseases, including bilharziasis, infected people may cease to show evidence of being positive. This factor results in a decline in prevalence after a peak at 15-25 years of age, which is commonly observed in areas that have been endemic for bilharziasis for long periods. The fact that some people become negative also results in an underestimation of the seriousness of the situation, as revealed by the maximum observed prevalence. It is possible to use age-prevalence data to estimate the rates of becoming positive and negative, provided that certain assumptions can be made (Hairston, 1965b). The assumptions are often valid and the calculations are not difficult, using the nomograms in Muench (1959). The principal difficulties in the use of this method of calculating epidemiological parameters are the necessity for data from large numbers of people and the fact that, if control operations are being assessed, the assumption of the long-term stability of rates is no longer justified.

Direct observation of the rate at which negative children become positive is the most useful and economical method of measuring the incidence of bilharziasis, and is obviously the method of choice for the determination of the success of control operations directed against the snail intermediate host. In those control programmes in which therapy is employed, it is necessary to follow previously uninfected children in order to detect changes in incidence, since measures based on prevalence would be confounded with a direct effect of the drug, in addition to any effect on the rate of transmission. Theoretically, the effect of therapy on transmission

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can also be assessed by successive observations on the infection rate in snails. However, in many areas, especially in Egypt, snail infection rates are so low normally that changes would be very difficult to demonstrate in a statistically satisfactory manner. Analysis of snail infection rates has the additional disadvantage of being difficult to interpret in terms of benefits to the human population.

Attention to the need for differentiation between " prevalence " and " incidence " in bilharziasis was first drawn by Pesigan et al. (1958) in connexion with studies on *Schistosoma japonicum* in the Philippines, but unfortunately these fundamentally different parameters continue to be used as synonyms in the literature on bilharziasis. An infection that runs a rapid fulminating course with a high mortality rate will naturally have a lower prevalence at a given point in time than a chronic, insidious, non-lethal infection in which the prevalence will build up and stabilize at a proportion commensurate with the rate of new infections and the death of the parasite or the host. Considering the known longevity of schistosomes and the low case-fatality rate, it is easy to show that the prevalence is certain to be higher than the incidence in the children of a community in which the disease is endemic. The situation will vary, of course, when the infection assumes epidemic proportions under special circumstances.

METHODS

Observations were made in the Egypt-49 Project Area on children less than 7 years old at the time of the original prevalence survey of 1962-63.[1] A random sample of children was examined at approximately annual intervals, and a sample of infants born in the interim was added at the times of these examinations.

Parasitological examinations were carried out by sedimentation techniques for both faeces and urine. Details of the procedures have been given by Farooq & Nielsen.[2]

Annual incidence was recorded as the percentage of the group of children negative at one examination who were positive at the next examination. In cases where the period between observations was not exactly one year, the annual incidence (I) was calculated as

$$I = 1 - x^{(12/y)} \qquad (1)$$

where x is the proportion remaining negative for y months. This is multiplied by 100 to give the percentage value.

In order to obtain base-line data on incidence rates among children for the purpose of evaluating control programmes, it was considered adequate to use as " index areas " two sections (Kom Ishu and Kom el Birka) in the Rural Division, one section (Akrisha) in the Control Division, and the whole of the Reclamation and Urban Divisions. The areas are shown in Fig. 1.

Children 0-6 years old from the same households selected for the prevalence survey of 1962-63 were re-examined in the succeeding years. The sample size was doubled in Kom Ishu and Kom el Birka by including 50% of households from randomly selected villages (covering 20% of the population of the sections), thus providing a 10% sample of all 0-6-year-old children from these areas. Conversely, the sample from the Urban Division was reduced to one half (from 5% to 2.5%) by omitting alternate randomly selected households in the area. No change in sample proportions was made in Akrisha (Control Division) or in the Reclamation Division, from which a 5% random sample and a 10% systematic sample, respectively, were examined. These changes were made to ensure that adequate data were obtained for each year of age.

The number of children and the dates of survey in the different areas are shown in Table 1. Reductions in numbers observed during the second and subsequent examinations were due to children having left the village or died during the meantime. Throughout the remainder of this paper, the ages cited correspond to those noted at the first examination.

RESULTS

The annual incidence among children in the four divisions of the project area is shown in Table 2, for both *Schistosoma haematobium* and *S. mansoni*. The Control Division is economically and socially much like the Rural Division, a fact which is reflected in the similarity of the incidence figures. As would be expected, the Urban Division, composed of the town of Kafr el Dawar and adjacent factory sites, has the lowest incidence of both parasites.

The method of calculating incidence is given in detail in Table 3, using the Reclamation Division as an example. Detailed examination of the data shows that incidence rises with age, even among these preschool children. That this is not peculiar

[1] See the papers on pages 281 and 293 of this issue.

[2] See pp. 288-290 of this issue.

FIG. 1

EGYPT-49 PROJECT AREA, SHOWING REGIONS WHERE INCIDENCE OF BILHARZIASIS AMONG PRESCHOOL CHILDREN WAS DETERMINED

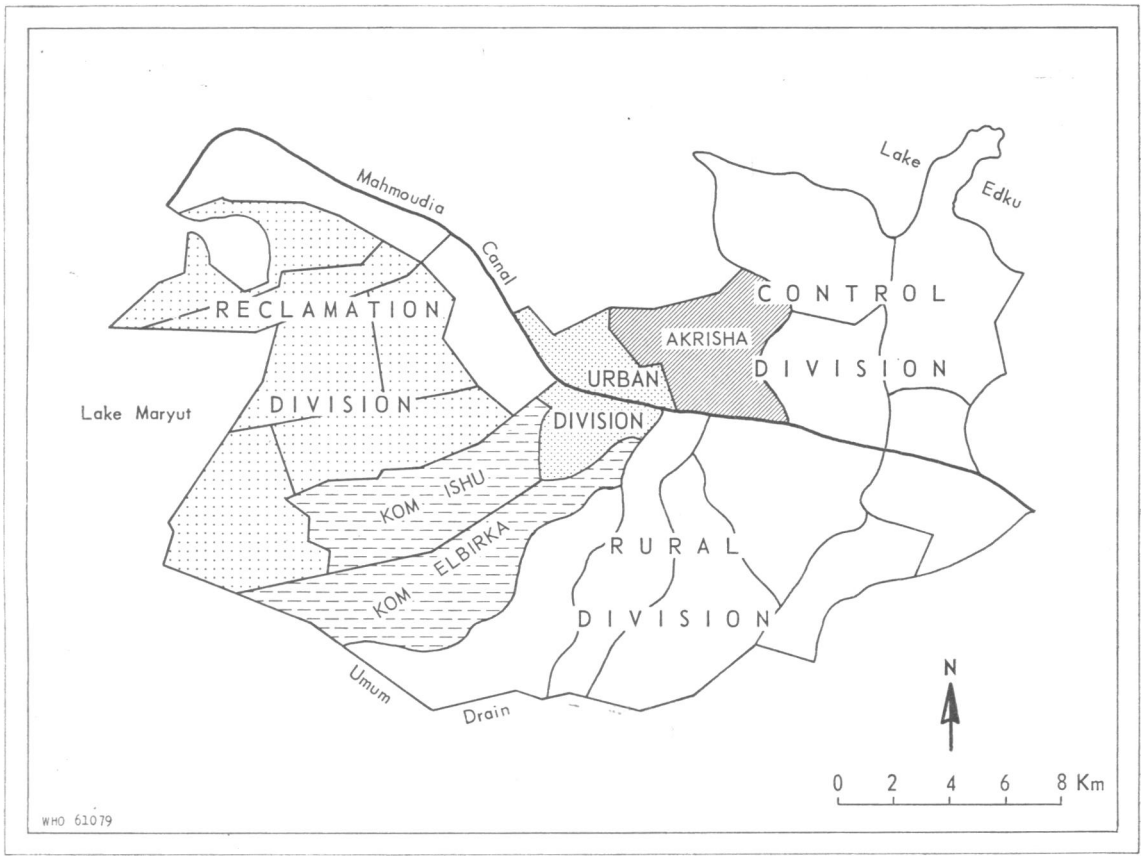

TABLE 1

PARTICULARS OF SURVEYS OF INCIDENCE OF BILHARZIASIS IN PRESCHOOL CHILDREN (0-6 YEARS OLD)

Division	Section	Dates of first examination	Dates of resurvey	Average interval (months)	Sample proportion (%)	Number examined
Rural	Kom Ishu & Kom el Birka	29.4.62-16.6.62	30.5.63-26.6.63	12.0	10.0	427 [a] (192 + 335)
Urban	All sections	30.10.62-6.3.63	1.2.64-4.3.64	13.5	2.5	589
Reclamation	All sections (Abis)	3.12.62-31.1.63	1.12.63-29.12.63	11.5	10.0	532
Control	Akrisha	21.6.62-21.8.62	27.1.64-22.2.64	18.0	5.0	282

[a] Additional 5 % sample added during 1963 resurvey.

TABLE 2

INCIDENCE OF BILHARZIASIS AMONG PRESCHOOL CHILDREN FROM THE DIFFERENT DIVISIONS OF THE PROJECT AREA

Division	Incidence (%) of infection	
	S. haematobium	*S. mansoni*
Rural	22.8	8.5
Urban	3.15	1.0
Reclamation	12.8	4.7
Control	18.0	6.4

to the Reclamation Division is shown in Fig. 2, which gives the relationship for all four divisions of the project area for *S. haematobium* infection. In all cases, the rate of increase of incidence with age is fairly regular, although subject to sampling error. This linear increase indicates that pooling the data, as was done in Table 2, gives a good estimate of the average situation in this age-group.

The estimates of incidence are subject to several potential sources of error. Some of them are the usual ones found in any epidemiological study, such as sampling error and misidentification. These can be kept within bounds by adequate sampling and by diligence. Other potential errors are specific to this study, and must be discussed separately.

TABLE 3

CALCULATION OF INCIDENCE IN CHILDREN IN RECLAMATION DIVISION FOUND NEGATIVE IN DEC. 1962—JAN. 1963 AND STILL NEGATIVE IN DEC. 1963 (AVERAGE INTERVAL 11.5 MONTHS)

Age (years)	Number of children found negative for			
	S. haematobium		*S. mansoni*	
	First survey	Second survey	First survey	Second survey
0	41	40	42	42
1	62	62	66	66
2	56	51	57	56
3	65	58	65	65
4	66	55	66	65
5	54	44	68	59
6	53	38	80	71
Total	397	348	444	424
Incidence	$1 - \left(\frac{348}{397}\right)^{(12/11.5)}$		$1 - \left(\frac{424}{444}\right)^{(12/11.5)}$	
	$= 1 - 0.872$		$= 1 - 0.953$	
	$= 0.128$ or *12.8%*		$= 0.047$ or *4.7%*	

The fact that incidence changes with age requires that the age-distribution of the children be kept essentially constant from one examination period to

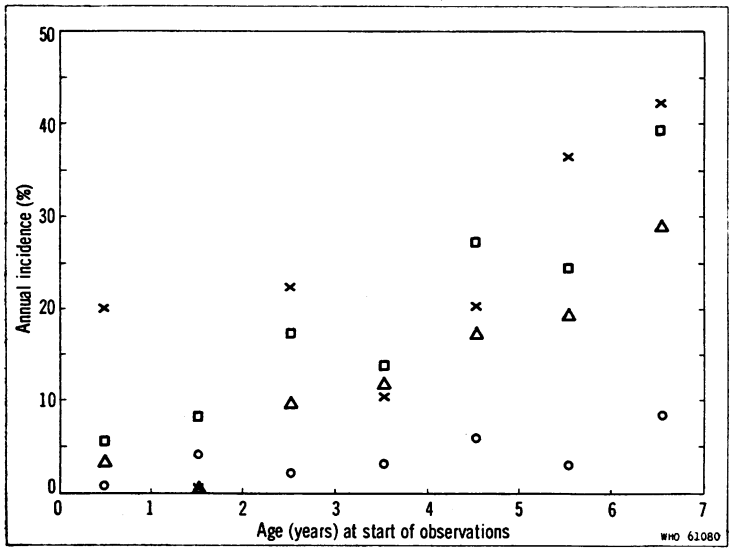

FIG. 2

INCREASE OF INCIDENCE OF *S. HAEMATOBIUM* INFECTION WITH AGE IN EACH OF THE FOUR DIVISIONS OF THE PROJECT AREA

× Rural Division
o Urban Division
△ Reclamation Division
□ Control Division

TABLE 4

DISTRIBUTION OF NEGATIVE CHILDREN (*S. HAEMATOBIUM* ONLY) OF DIFFERENT AGES AMONG THE POPULATION IN FOUR DIVISIONS OF THE PROJECT AREA

Age (years)	Number of negative children in sample in			
	Rural Division	Urban Division	Control Division	Reclamation Division
0	10	67	24	41
1	8	52	26	62
2	18	56	24	56
3	20	76	31	65
4	15	68	24	66
5	11	80	29	54
6	19	55	17	53

the next. Thus, over-representation of either older or younger ages could easily distort the over-all estimate of incidence. In the present study, the uniformity of sampling procedure in the four divisions prevented the above factor from assuming any significant importance, as shown by the initial number of children found negative for *S. haematobium* (Table 4). Statistical analysis shows that the different ages are not represented in a significantly different manner in the four divisions; χ^2 is 21.04 for 18 degrees of freedom.

It might appear at first thought that estimates of incidence would be subject to error because of the fact that not all positive persons are detected by a single examination of urine or faeces. A study to determine the reliability of a single examination was carried out on a sample of 90 persons in the Rural Division.[1] For *S. haematobium*, 86.8% of all positives were detected on the first examination; for *S. mansoni*, the figure was 79.7%. It is of special interest that no people still negative at the third examination were found positive for either parasite on the fourth or subsequent examinations.

Thus among the children originally selected as negative, a certain number were actually passing schistosome eggs. The proportion is likely to be small, however, since a relatively small proportion of children in this age-group is infected. The error amounts to no more than 4% of the total found negative at the start of the observations. A similar error is likely to occur in evaluating the number of infections acquired by the end of the period of observation. A few simple calculations show that the net effect of failing to detect all egg-passing cases on one examination is likely to be an error of less than 10% of the calculated incidence. The error can be either positive or negative, depending upon the number of cases found positive in the initial prevalence survey.

The final source of possible error is an important one, and has interesting theoretical implications in the epidemiology of bilharziasis. It will therefore be treatep in a separate section.

[1] See page 290 of this issue.

THE RATE OF LOSS OF INFECTIONS

It can be deduced from age-prevalence curves that schistosome infections are lost spontaneously (Hairston, 1965b). In the present study, it was possible to make direct observations on the rate of loss of infections, since all children were re-examined, whether they were found positive initially or not. As with incidence, the annual rate of becoming negative can be calculated for periods of observation other than 12 months. The formula is:

$$l_x = e^{-ax} \qquad (2)$$

where l_x is the proportion remaining positive, e the base of natural logarithms, a the instantaneous rate of loss of positive cases per year and x time, in years. The finite proportion becoming negative annually can then be calculated as:

$$1 - e^{-a} \qquad (3)$$

Fig. 3 shows the results for *S. haematobium* infections in the Rural and Control Divisions for two periods each. Two striking features are revealed: the surprisingly high rate of loss of infections among young children, and the marked drop in loss rate after the age of 5 years. The large variation in results, especially for children under 5 years of age, is ascribable to the small number of children originally positive in each age-group. For this reason, and because there is no systematic variation with age among younger children, a weighted mean was calculated. The average finite rate of becoming negative for children 0-4 years old is 0.544 per year. Children 5 and 6 years old become negative at an average rate of 0.165 per year.

The error introduced into incidence figures by false negative findings, as described above, has a more important effect upon estimates of the rate at which positive cases become negative. Thus, the 32 cases remaining positive for 12 or 13 months among children 0-4 years old would represent

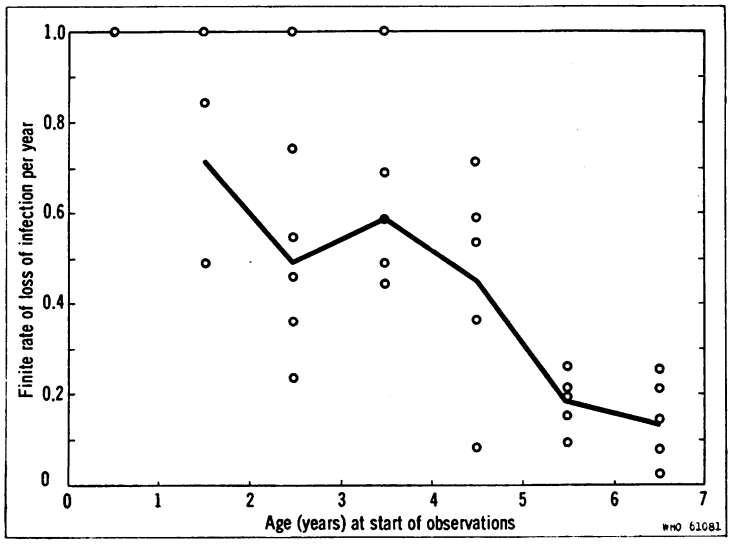

FIG. 3
RATE OF LOSS OF *S. HAEMATOBIUM* INFECTION AMONG PRESCHOOL CHILDREN [a]

o One observation of one year-class in one division

—— Weighted mean

[a] Data not corrected for cases missed on single examination.

32/0.868 or 37 total positives out of the 78 such cases observed. The true rate of becoming negative would be 0.526 instead of the directly calculated 0.590. When all such corrections are made and properly weighted for the number of cases, the estimated finite rates of becoming negative are 0.476 for children 0-4 years old and 0.049 for those 5 and 6 years old. These estimates apply to *S. haematobium* infections only.

Children infected with *S. mansoni*, especially those aged 5 and 6 years, lose their infections more rapidly than do those infected with *S. haematobium*. After the necessary corrections for missed positive cases have been made, the weighted mean rates of loss of infection are 0.580 for children under 5 years of age and 0.327 for those 5 years old and above.

The fact that older children lose their infections less rapidly than younger children confirms a prediction made by one of us (Hairston, 1962, 1965a, 1965b). The prediction was based on the hypothesis that the rate of loss of infection would be inversely related to the number of parasites harboured, and would be equal to the finite death rate of female parasites raised to the power of the number of females present in the majority of cases under consideration. Since the older children would be expected to have acquired more worms than younger ones, they would be expected to lose their infections at a much lower rate. The prediction would include, by implication, the higher rate of loss of infections of *S. mansoni* than of *S. haematobium* among older children, since the lower incidence of *S. mansoni* infections would indicate a lower accumulation of parasites.

It is evident that acquired immunity would have the opposite effect of the one observed, and in children it is therefore not regarded as a factor of epidemiological importance, although it may well be significant among adults.

The spontaneous loss of infections by young children is a potential source of error in the estimation of incidence. Since the rate of becoming negative is surprisingly high, especially in the early years, it is possible that some of the children found negative at the end of the period of observation had acquired and lost the infection in the meantime. If the survey was taken just before the main season of becoming positive, this factor could mean a loss of as much as 45%-50% of those actually becoming positive. If the survey was taken half-way between the annual peaks of transmission, the loss would be about 26.5%. For the older children the loss would be less: 5% as a maximum estimate and 4.3% as a median value.

Inasmuch as a large proportion of new cases are in the older age-group, the error is less than might have been supposed. Under more or less average timing of surveys, the over-all underestimate of incidence would amount to 21%, but because of highly seasonal transmission and if surveys were taken immediately before the newly exposed children become positive, the underestimate could be nearly 40% of the true incidence. Table 5 gives the corrected values of incidence shown in Table 2, based on the

TABLE 5

CORRECTED INCIDENCE OF BILHARZIASIS AMONG PRESCHOOL CHILDREN FROM THE DIFFERENT DIVISIONS OF THE PROJECT AREA [a]

Division	Corrected incidence (%) of infection	
	S. haematobium	*S. mansoni*
Rural	27.6	12.2
Urban	4.0	1.4
Reclamation	15.5	6.7
Control	21.8	9.2

[a] Corrected to allow for children who become positive and then negative between consecutive examinations; compare with uncorrected rates in Table 2.

foregoing considerations. The error is twice as great for *S. mansoni* as for *S. haematobium*, because of the higher rate of loss of infections.

DISCUSSION

Observations on the incidence of bilharziasis, and analyses of the factors influencing the measurement of incidence, have shown such studies to be important from the standpoint of the evaluation of control efforts and from that of epidemiological theory.

It is becoming appreciated in epidemiology, and in population studies generally, that the most meaningful parameters are the rate functions, as opposed to the static measures of numbers or proportions. It is the rates of becoming positive and negative that determine the number of people infected at any given time, and it is through changing these rates that control of the disease will become possible.

The calculated values of incidence and rate of loss of infection give rise to one important contradiction, which we hope will be resolved by further study. It will be recalled that the incidence of *S. mansoni* infections is lower than that of *S. haematobium* infections, whereas the rate of loss is higher. In the absence of modifying factors, this combination of facts would require a lower prevalence for *S. mansoni* for the age-group under consideration. This is not found, at least in the Control Division. The paradox could be resolved if there were a sufficiently high incidence of *S. mansoni* among people who have been infected once and have lost their infections. At present, this is only a hypothetical explanation, supported by very indirect evidence (Hairston, 1965b), but it should be possible to make the necessary observations.

The direct measurement of the rate of becoming positive is an important feature of epidemiological studies or control efforts. In the interests of economy and accuracy, it seems worth while to consider the subdivisions of the population most suitable for study. First consideration must go to the requirements of the method, which include the use of people negative at the start of the period of observation. This means that children should be the group examined, since older persons who are negative are very likely to have once been positive, a factor that would be unwelcome to the study.

Among children, two opposing considerations must be weighed against each other. The older group, more than 5 years old, are, as has been shown, likely to yield data that are less subject to error, but they also have a much greater area of activity, so that, with increasing age, there is a decreasing assurance that the children actually acquired new infections within the area of study.[1] Exactly the converse conditions apply to children less than 5 years old. Thus, there are advantages and disadvantages connected with both groups, and it appears that the most complete information would be obtained if all ages, at least up to 7 years, are followed.

It is important, moreover, to record data separately by year of age. Complete separation of data in this fashion may be slightly wasteful of effort, since it appears that only two epidemiological groups are readily recognized: children less than 5 years old and those 5 years old and above. Use of two groups would provide statistically valid data with the examination of fewer individuals. For many purposes, estimates derived from studies on relatively few children are more revealing than are those derived from the examination of much larger numbers covering the entire population.

[1] See the paper on page 369 of this issue.

ACKNOWLEDGEMENT

The wholehearted co-operation received from Dr S. A. Samaan and Dr A. A. Allam and their teams of technicians in conducting the surveys is gratefully acknowledged.

RÉSUMÉ

Dans ce quatrième article sur l'épidémiologie des infections à *Schistosoma haematobium* et à *S. mansoni* dans la région du projet pilote de lutte contre la bilharziose dans le delta du Nil, les auteurs étudient l'incidence des infections bilharziennes. La méthode choisie a consisté à examiner par randomisation un groupe d'enfants âgés de 0 à 6 ans et à réexaminer 12 mois plus tard ceux chez lesquels le premier examen était négatif. L'examen parasitologique des selles et des urines a été effectué en utilisant les techniques de sédimentation. Selon les auteurs l'évaluation d'une situation épidémiologique se fait d'une façon plus sensible et plus fidèle en mesurant l'incidence d'une infection qu'en en établissant la prévalence à un moment donné.

L'incidence des deux infections a présenté des variations importantes suivant les différents secteurs définis dans la région du projet, mais elle a été comparable entre deux secteurs dont les conditions socio-économiques étaient très semblables. C'est dans les zones rurales que l'on a observé la plus forte incidence de l'infection à *S. haematobium* (22,8 % par an) et de l'infection à *S. mansoni* (8,5% par an). L'examen minutieux des données a montré une augmentation continue de l'incidence avec l'âge, même dans le groupe d'âge préscolaire.

Parmi les causes d'erreurs qui peuvent entraver la mesure de l'incidence, la plus importante est le taux élevé des infections à guérison spontanée. Pour *S. haematobium*, ce taux a été estimé à 0,476 par an chez les enfants de 0 à 4 ans et à 0,049 par an chez les enfants de 5 et 6 ans, et pour *S. mansoni*, respectivement à 0,580 et à 0,327. On pense que ces chiffres reflètent le taux de mortalité des vers et que, chez l'enfant, le taux des guérisons spontanées n'est pas influencé par l'immunité: entre deux examens, certains enfants peuvent devenir positifs puis négatifs. L'incidence réelle serait ainsi sous-estimée dans la proportion de 21% pour *S. haematobium* et de 40% pour *S. mansoni.*

Malgré ces erreurs, les auteurs estiment que la mesure de l'incidence est un paramètre épidémiologique important pour l'étude de l'infection et l'évaluation quantitative des résultats des opérations de lutte.

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