Trip Report Honduras 2003 5 Jan 2004
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To: Dr J Alger, Ministry of Health, Honduras
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Background
The government of Honduras (population about 8 million) was recently awarded a five year Global Fund grant for the control of HIV, tuberculosis and malaria. The objective of the malaria portion was to reduce malaria by 50% in five years. But it has yet to be determined what are the best indicators to follow, if this is the best malaria control strategy for Honduras at this time or how one shows that the reduction would actually be a result of the Global Fund intervention (rather than a natural trend dependent on, say, general development or post hurricane Mitch reconstruction). As an example of a counter argument to the 50% reduction strategy one could imagine instigating a mass, indiscriminate chloroquine chemotherapy/chemoprophylaxis campaign which would reduce the malaria transmission in the short term – but may result in the development of drug resistant *P. falciparum* in the long term.

Observations
The malaria situation in Honduras seems to be improving with an overall reduction in transmission, no indication of drug resistant falciparum and minimal mortality. Still, malaria continues as a difficult public health problem for the country because of the poverty of rural populations and limited resources to maintain control efforts.

Ministry of Health data from the malaria endemic regions of Tocoa and Trujillo indicate a great decrease in malaria over the past few years with the vast majority of cases due to vivax rather than falciparum. There were various malariametric indicators used. The surveillance system consists of passive case detection which depends on a large number of government sponsored village volunteers who treat presumtpively with chloroquine and obtain slides for confirmation (results of readings are returned within 1-4 weeks). In addition, during the past year, a large active surveillance was conducted to find cases (and carriers), who might not be detected in the passive system. Besides these government programs, there seems to be a large sector of the community diagnosed in private laboratories and treated by private pharmacies. There has not been a systematic survey to estimate the magnitude, type of clientele, type of services/drugs and referral system of this private sector. So far chloroquine seems to be efficacious against both vivax and falciaprum malaria.

Malaria indicators : Each community reported a standard set of malaria indicators, for PV and PF combined, as well as each malaria species separately. These indicators (for EACH of the passive and active surveillance systems) were: 1. the number of slides collected (for fever and/or other malaria Sx), 2. the % of slides which were positive for PF, PV or both 3. the number of positive cases (PF/PV/both) / community population. Almost all communites saw a dramatic reduction in the PV and PF malaria over the past few years according to many of the indicators and this was interpreted as reduced malaria transmission. The groups' general conclusion of reduced malaria was based more on similar reductions in nearly all of the communities rather than on any single measurement.

Assessment

Because there was some confusion regarding the interpretation of the different indicators, those attending the malaria meetings recognized the need to establish standard guidelines as to what each indicator means as well as its limits of interpretation. In additon, there was a more fundamental concern regarding how well the data represented the malaria situation. Specifically, it was pointed out that the great variation in the motivation of/access to some "volunteers" may invalidate comparisons among the different regions. It was also mentioned that standardization of microscopy slide preparation and reading should be re-emphasized. Participants suggested that a survey be done to estimate the magnitude of malaria management (diagnosis and treatment) by the private sector. For example an apparent "reduction"of malaria in the government sector could represent a shift to the private sector rather than a real reduction in malaria transmission. Finally, data was often stratified down to village level which resulted in small sample sizes, making statistical interpretation very difficult.

In general, I think that the data does show a geat reduction in malaria in the past few years with >95% of current cases due to vivax.

Recommendations

Malaria Indicators

1. Standardize slide staining and reading. Use WHO reference manuals so that comparisons can be made internationally as well as locally to detect trends over time. Set up a standardized quality control system – increase the number of slides checked to at least 600 per year (300 positives and 300 negative by first reading). In the quality control system make sure that second readings are done “blinded” to the results of the initial reading. Sometimes ELISA tests can be added to the quality control examinations, providing that an accurate vivax test is found and that any confirmatory test is read blindly.

2. Establish guidelines for what malariametric indicators to use. In general the best indicators reflect the risk to a population. This would be the number of cases divided by the number exposed (usually the community population or an appropiate sub-sample).

For **active case detection** the best indicator of risk are the % of smears which are positive for malaria. For active surveillance note that those included in the denominator will be considered a representive sample of the general community, both with and without symptoms. It is important to keep this active sample as representative and unbiased as possible. Obviously, since the number of actual cases detected depends on the sample size, the other two malaria indices, i.e. the case number and this number divided by the community population is somewhat “artificial”. The sample should be large enough to achieve a reasonable statistical certainty (95% confidence intervals determined by EPIinfo version 6). For **passive** surveillance, smears are done only one those with symptoms reporting to the community volunteers. Assuming that the community volunteers as consistently taking smears among the villages and that there is little month-to-month variation of the inclination or desire to take smears, the best indicators are the number of cases detected divided by the estimated village size. If the population is stable (there was some report of migratory workers) the absolute number of cases can be used for trend comparisons. Contrary to active detection, for passive surveilance the worse indicator is the % of smears which are positive. The problem here is that the denominator can be very dependent on variations of other febrile

illnesses in the community. The example was brought up how dengue would affect this indicator.

Obviously we cannot compare any single indicator between active and passive systems since the most useful indicators are NOT identical but depend on the context of sampling. **Within each system (active or passive)** we should use an agreed upon set of indicators for comparisons between communities or for trends over time within a single community. There needs to be a workshop of the district health departments to reach consensus of the concepts outlined above (assuming there is first general agreement at the National level).

Five Year Goal: The following recommendations are made to maintain/strengthen the current status of the malaria program (because it may be associated with the reduction in transmission) and to focus on falciparum malaria (eradication/delay development of drug resistance). The falciparum malaria objective is a preventive principle. Based on what has occured in other countries, Honduras would be poorly prepared to deal with a major falciparum outbreak or the development of drug resistant P. falciparum.

Present Infrastructure: About two thirds of new funds should be put towards maintaining the present malaria control infrastructure. This can be in the form of training, equipment, pay incentives, etc. The districts with malaria should be identified (regardless of recent increasing or decreasing trends) and funds made available proportionately across all levels (peripheral to central) of activities. Not only would this be "fair" and avoid a lot of interagency competition, but since it is not clear which activities are the most important regarding the recent malaria reduction, cross the board funding would at least insure that the present system is maintained.

New Initiatives: 1. Falciparum malaria: A third of new funds should be spent on "new initiatives" specifically targeting falciparum malaria. The development of drug resistance probably depends on at least three important factors: overuse of drugs, poor drug compliance and high *P. falciparum* transmission. It is very likely that a signifcant portion of those overtreated (say, influenza misdignosed and treated as malaria) will "learn" from experience that full compliance with prescribed antimalarial drugs is not neccessary. The first two factors could be addressed by performing laboratory diagnosis in the field. There is a rapid ELISA dipstick test (US 50 cents per test) which can be adapted to field settings. The last factor for drug resistance might be best addressed by attempts at focal eradication of falciparum malaria.

All three factors of falcipruam malaria control might best be addressed by use of rapid "dipstick" tests for falciparum malaria at the village level. This could begin as pilot studies in the the areas with the highest falciparum malaria rates. While it is true that the treatment of falciparum and vivax malaria are similar (chloroquine) the management of the two species may be quite different. The diagnosis of falciparum may trigger an immediate active surveillance (within hours), may initiate follow-up and test of cure to insure compliance with self administered medications, may initiate more aggressive anti-gametocyte therapy and may serve as a model for control of falicparum epidemics in the future. If falciparum is eradicated from a community then the program would move to other targeted areas.

2. Malaria Reservoir: – With such low reported rates of malaria and relatively little human migration, one wonders how the transmission cycle of malaria maintains itself. If one were to attempt a serious reduction of vivax the size of the human reservoir (asymptomatic carriers) should be estimated. The recent active surveillance (though there was some questions regarding the sensitivity of the slide readings and the quality control evaluation) detected very few asymptomatics. This result is in direct contrast to a recent study by Dr Alger showing a much larger pool of carriers. Perhaps a more definitive study incorporating PCR detection of carriers needs to be undrtaken (ref Alves FP, Am J Trop Med Hyg. 2002 Jun;66(6):641-8.)

3. Assessment/Controls: Without an adequate community control for comparison it would be very difficult to evaluate the specific effects of a specially finded program. The ideal control would show what would have happended to the **same** community over the **same** time period if the intervention had not been in place. Theoretically the "controls" may fall into three classes. The first is a historic control of the same area. Historic controls suffer from effects over time which are independent of the specific intervention. Another type of control would be a concurrent control of a different area (say, a non-intervention malarious region of Honduras). The problem here is that the region may not be identical to the intervention area, and if it is, then it might be considered unethical not to have intervened. Finally, the third type of controls are "virtual". Through interviews and "program evlauations" one determines what would have happened without the intervention. This method can be quite misleading since one can never predict "unexpected" outcomes, which so often occurs in field interventions. The real question is whether it is worthwhile to attempt a comparison with a control, with all its limitations or have no controls at all. Sometimes a poorly chosen control is very misleading and can be worse than no control at all. On the other hand one should not underestimate the value of controls. For example the new program may have a very significant effect even though the malaria rates may double during the study period (since a true control might have shown a quadrupling of transmission). My recommendation is to evaluate a number of controls which are simpler to measure rather than depending on a single, complicated one which attempts to be comprehensive.

Such controls could include:

Concurrent controls	- malaria rates of non-intervention malaria districts - malaria rates from neighboring countries
Historic controls	- a few data sets for the previous several years from the most reliable agencies/districts

Combination of Historic and Concurrent controls (ref Cunha M, Am J Trop Med Hyg. 2001 Dec;65(6):872-6).

---End report