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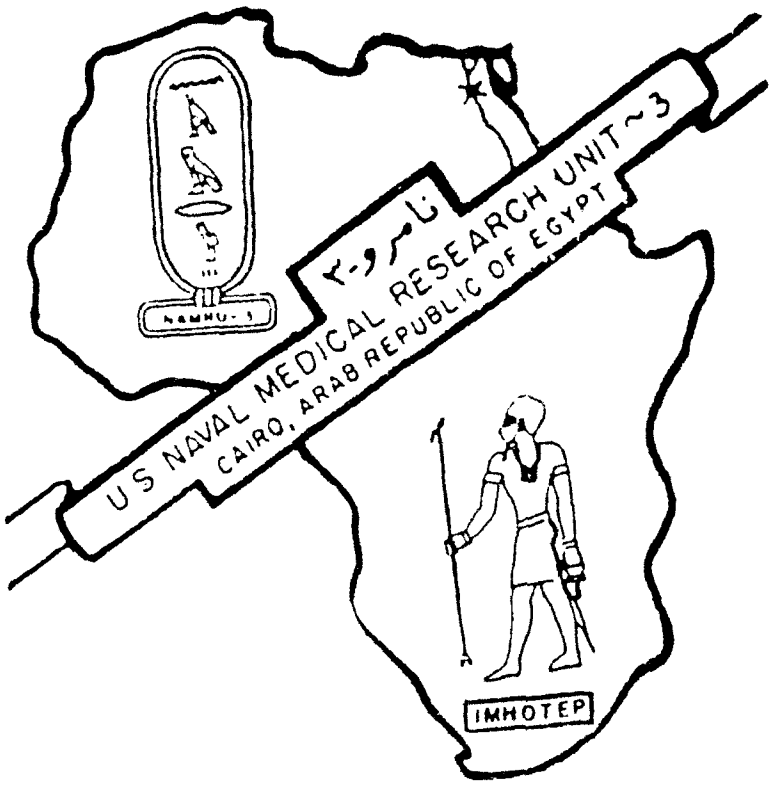
TECHNICAL REPORT

Placebo-controlled double-blind study to determine the efficacy of topical niclosamide 1% lotion in the prevention of naturally occurring Schistosoma mansoni infection in Egyptian farmers



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A randomized, double blind, placebo controlled field trial of a topical antipenetrant lotion 1% niclosamide applied daily to the upper and lower limbs of farmers occupationally exposed to S. mansoni cercarial infested water was conducted in the Nile Delta to assess safety and efficacy in preventing re-infections. Farmers aged 18-40 years were treated to cure their S. mansoni infections 3 months prior to the onset of the trial. Subjects were randomly assigned to receive niclosamide or placebo lotion which was self-applied daily for 5 months. A total of 186 subjects met the inclusion criteria and completed the trial. The exposure to schistosomal infested water occurred during routine irrigation activities from June to November 1991. Stool specimens were evaluated monthly during and for two months following the lotion application period. The subjects applying the niclosamide lotion were comparable to those applying placebo lotion in age (average of 30 years for both) total water contact (185.2 vs. 173.8 hours), reported lotion application compliance (88% vs. 92%) and reported water contact involving skin exposure other than upper and lower limbs (23% vs. 27%). The schistosomal reinfection rate was lower in the niclosamide group (53.3%) compared to the placebo lotion group (71.3%), ($p < .02$). Increased protection might be obtained with total body application for shorter, less intense water contact exposures.

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TECHNICAL REPORT

Placebo-controlled double-blind study to determine the efficacy of topical niclosamide 1% lotion in the prevention of naturally occurring Schistosoma mansoni infection in Egyptian farmers

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Summary:

A randomized, double blind, placebo controlled field trial of a topical antipenetrant lotion 1% niclosamide applied daily to the upper and lower limbs of farmers occupationally exposed to S. mansoni cercarial infested water was conducted in the Nile Delta to assess safety and efficacy in preventing re-infection. Farmers aged 18-40 years were treated to cure their S. mansoni infections 3 months prior to the onset of the trial. Subjects were randomly assigned to receive niclosamide or placebo lotion which was self-applied daily for 5 months. A total of 186 subjects met the inclusion criteria and completed the trial. The exposure to schistosomal infested water occurred during routine irrigation activities from June to November 1991. Stool specimens were evaluated monthly during and for two months following the lotion application period. The subjects applying the niclosamide lotion were comparable to those applying placebo lotion in age (average of 30 years for both) total water contact (185.2 vs. 173.8 hours), reported lotion application compliance (88% vs. 92%) and reported water contact involving skin exposure other than upper and lower limbs ((23% vs. 27%). The schistosomal reinfection rate was lower in the niclosamide group (53.3%) compared to the placebo lotion group (71.3%), ($p < .02$). Increased protection might be obtained with total body application for shorter, less intense water contact exposures.

Introduction:

Schistosomiasis is one of the most important public health problems of tropical and sub-tropical developing regions. The disease is endemic in 74 countries including extensive areas in Africa, Asia, the Middle East, South America and the Caribbean.[1] Over 200 million people are currently infected and with the recent expansion in water development resources in the developing world the number of people at risk is expanding.[2] Agricultural workers and their families in endemic areas that have continuous exposure to schistosomal cercarial infested water through farm labor, washing, bathing, and water recreation have great difficulty and perhaps no practical means of remaining free of recurrent infection. Tourists and urban dwellers that come in contact with these endemic areas are also susceptible to schistosomal infection.

Acute schistosomiasis occurs after non-infected individuals have non-protected contact with schistosomal cercarial infested waters. The exposure and infection may occur after just a few minutes of contact with cercarial infested waters. A severe disabling condition known as Katayama Fever can occur 4 to 6 weeks after initial penetration of cercarial larvae through the skin of a previously uninfected human. The infected patient manifests high remittent fever, generalized aches, weakness and

abdominal pain accompanied by hepatosplenomegaly and eosinophilia. This condition may last for several months. There is currently no well-established therapy, although steroids and praziquantel have been administered with varying success.[1] During the landing of American military personnel at Leyte in the Philippines during World War II approximately 80% of the soldiers of some units in the landing force contracted acute Katayama Fever. Currently, with the exception of avoiding potentially infested schistosomal cercarial waters or wearing suitable protective boots, gloves and non-penetrable clothing there is no effective means of preventing schistosomiasis in people that are unable to avoid contact with infested waters.

A topical lotion containing 1% niclosamide has been tested and shown to be effective in preventing schistosome cercarial penetration of the skin of hamsters and non-human primates (Cebus apella).[3,4,5] No gross dermatological effects were noted in any of the animals treated with the lotion. No skin irritation has been noted in humans during skin contact of niclosamide molluscide preparations and no sensitizing effect was seen in subjects with photoallergic reactions to tribromosalicylanilide.[6] Skin reactions were occasionally seen with applications of a 25% emulsion preparation of niclosamide which were proven to be due to other ingredients and not niclosamide.[7]

Niclosamide has been used for prophylaxis and therapy throughout the world for the past 30 years.[8] It has been used as therapy for cestode infections in man since 1960 with no reports of serious adverse reactions.[9] It is prescribed orally at a dose of 2 grams daily for 7 days in adults. It is only partially absorbed from the intestinal tract and is eliminated rapidly without adverse effects on hepatic, renal or hematological systems.[8,9,10] The absorbed fraction is eliminated by the kidneys. It is also used as a schistosomicide and molluscicide under the trade name "Mollutox".[11] In the form of a 70% dispensable powder "Bayluscide", it has been applied in spray form and used in Egypt and other parts of Africa to kill snails, snail eggs, and schistosome cercaria. The biochemical activity of niclosamide on cestodes is associated with its ability to inhibit oxidative phosphorylation in the mitochondria of these parasites. It also affects the respiration and carbohydrate metabolism of schistosome miracidia.[3] Its safety and extremely low toxicity in humans is attributable to poor dermal and gastrointestinal absorption.

In the past ten years treatment of chronic schistosomiasis has been greatly facilitated by the availability of praziquantel, a proven effective and minimally toxic therapeutic agent for S. mansoni, S. haematobium, as well as S. japonicum. A single dose of praziquantel, at 30 to 60 mg per kg body weight given orally will clear feces

and urine of viable schistosomal eggs and give cure rates ranging from 63 to 100%.[12] Praziquantel toxicity is limited to minor transient side effects including occasional nausea, vomiting, and abdominal cramping. Praziquantel is not effective for prophylaxis or chemotherapy against the immature stages of the parasite. The emergence of resistance is another potential problem with the extensive use of this drug.[13,14] Therefore, the accepted medical approach to the prevention of acute schistosomiasis is essentially the elimination of all direct skin contact with potentially infested water by strict avoidance or through the use of protective boots, gloves, and clothing impenetrable to schistosomal cercaria. The potential protective option of a topical antipenetrant preparation that can be self-applied has great practical significance. It would offer a readily accessible form of portable and inexpensive protection in potential threat areas for cercarial exposure.

Statement of Purpose:

The purpose of this study was to determine if a 1% niclosamide skin lotion was safe and protective against Schistosoma mansoni cercarial re-infection in Egyptian agricultural workers who had recently been treated by the Egyptian Ministry of Health for schistosomiasis. If the topical antipenetrant lotion was safe, effective and practical, it could be used where the threat of short term, high level cercarial contact

is anticipated. For example, it might be used during short term farm irrigation projects and by tourists and military personnel anticipating potential exposure to heavily infested cercarial waters during excursion and field operations.

Materials and Methods:

Study Design:

This study was a prospective, randomized, double blind, placebo controlled field trial.

Study Area and Study Population:

The study was conducted in the Nile Delta region of Egypt, in three rural sites in the Abu Homos District, Beheira Governorate, Egypt. Three villages: Anwar El-Mofty, Desones and Kom El-Kanater were selected due to the high prevalence of endemic Schistosoma mansoni infection detected in recent Egyptian Ministry of Health surveys. The male inhabitants of these villages were primarily farmers and did not differ greatly in respect to their living style and activities. Healthy male farmers aged 18 to 40 years who had recently been successfully treated for schistosomiasis and who fulfilled the trial inclusion criteria (Table 1), were invited to participate in the treatment trial. This treatment trial was endorsed by the Egyptian

Ministry of Health and the local health district authorities and community acceptance was high due to the local awareness that schistosomiasis is a serious health problem.

Study Medication:

The drug used in this study was a 1% solution of niclosamide formulated in an ethyl alcohol based lotion. The lotion, had the consistency of insect repellant or sunscreen lotion and was faintly yellow in color. The placebo lotion is the same formulation without the 1% niclosamide. Both lotions were identical in appearance and consistency. Study medication was manufactured by Miles Pharmaceuticals, Inc. which provided the lotion for this study under Cooperative Research and Development Agreement number DAMD17-86-0289 (U.S. Army Medical Research and Development Command). The lotion is yellow in color and was packaged in 30 ml polyethylene bottles with a screw-on caps.

Assignment of Study Medications:

The study used a double blinding procedure to assign drug to participants. The study medication and placebo were delivered to the Walter Reed Army Institute of Research, Division of Experimental Therapeutics (WRAIR-ET) by Miles Pharmaceuticals, Inc. Upon arrival at WRAIR-ET, the bottles were packaged in

containers which identified them as either active drug, or placebo. At WRAIR-ET, the bottles were individually labeled with one of ten (10) letters (A,B,C,D,F,H,J,L,U,X), and a label identifying the contents as an Investigational New Drug, was affixed. These were the only identification markings contained on the bottles as they were delivered to the study site. The medication was then delivered by air cargo service to Cairo, Egypt where it was stored in the pharmacy at United States Naval Medical Research Unit No.3 (NAMRU-3) at 25 to 28°C and issued to the field at periodic two to three week intervals.

Participants were assigned identification numbers, which were alpha-numeric with the alpha component identifying the village (three villages were included in the study) and the numeric component beginning at 001 and increasing sequentially to 200. The blinded, random assignment to study medication was provided by WRAIR, Division of Biometrics with the aid of a computerized statistical model. The blinding was blocked in groups of 20, i.e. within each group of twenty numbers each of the 10 letters would repeat exactly twice. The randomized list not only randomized the assignment of study medication (identified by letter) to the patients (identified by number), it also randomized the assignment of active drug and placebo to the letter used to identify the bottles. The study medication was transported to the field sites,

inventoried and stored in locked storage rooms at the village clinics, and was issued to the participants weekly. Each participant received a box of seven bottles of study medication per week. All drug bottles, used, unused, or partially used were returned to the study monitor weekly.

The code identifying active and placebo niclosamide lotion was held only by the Commanding Officer, NAMRU-3 (medical monitor) and the product manager (sponsor's representative) at the U.S. Army Medical Material Development Activity, Ft. Detrick, Maryland. No medical emergencies occured during the study which required the composition of a subject's lotion to be disclosed.

Dosage Range:

The dosage of niclosamide varied slightly depending on the size (body surface area) of the individual subject. A single application consisted of enough lotion to cover the upper and lower limbs. This ranged from half to one bottle per application. A subject with active niclosamide lotion received a topical dose of 15 to 30 mg of niclosamide per day.

Dosage Schedule:

Lotion was self-applied daily in the morning, before the farmers went to work in the fields seven days a week. Field monitors went to the study participants' homes three times per week on designated days and observed the lotion application and collected water contact data.

Application of Study Medication:

The study participants self-applied the lotion by removing the cap from the bottle and squeezing several milliliters from it into the hands and rubbing it in a systematic pattern over their upper limbs from the shoulder down to the hands and fingers. They also applied it to their lower limbs from the upper thigh down to the feet including the interdigital spaces of the toes and the soles.

Concomitant Medications:

Medications which were considered necessary for the patient's welfare were given at the discretion of the principal investigator or the associate investigator. Any administration of such drugs was reported in the appropriate section of the medical form.

Duration of the Study:

The application of study medication began on June 1, 1991 in Anwar El-Mofty and on June 8 and June 22, 1992 in Desones and Kom El-Kanater respectively. Lotion Application continued for 23 weeks terminating on November 8, 15, and 29, 1992 in Anwar El-Mofty, Desones and Kom El-Kanater respectively. The first 3 months (13 weeks) were the initial washout period. Data considered for statistical analysis on the efficacy of the lotion consisted of that collected from the end of the washout period point until two months (8 weeks) following the end of application of the study medication. Collection and analysis of stool specimens, continued for two months (8 weeks) after application of the study medication had been discontinued. The last stool collections were on February 6, 17, and 27, 1992 for Anwar El-Mofty, Desones and Kom El-Kanater respectively.

Study Procedures:

Approximately six months prior to the start of the study during November-December 1990, approximately 3000 male farmers were given a labelled 50 ml plastic centrifuge tube for urine and a wide mouthed screw-cap plastic container for stool and were asked to provide a urine and a stool specimen. The specimens were processed for examination within 6 hours of collection. Urine samples were examined by the

sedimentation concentration technique[15]. Fecal samples were examined using the Kato-Katz thick smear method[16]. Treatment was carried out during January 1991, based on the results of the urine and stool samples. Each subject with a urine and/or stool positive for Schistosoma eggs received a single oral dose of 40 mg/kg of praziquantel under the supervision of a local Ministry of Health physician. Twelve weeks after treatment, which was two months prior to the start of application of the study medication, three stool samples were collected on three consecutive days from all the treated subjects to identify eligible candidates for the study. In order to detect light infections, fecal samples were examined by the more sensitive modified Ritchie Concentration Technique[17]. Individuals found negative for S. mansoni during this re-examination were considered as potential subjects for the trial. A careful medical history and physical examination were performed on each of the potential subjects with particular attention to the presence of rashes or other skin abnormalities. From this pool of potential subjects, 600 volunteers (200 in each village) were entered into the study after providing written informed consent. The application of the study lotion began in June 1991 and continued for 23 weeks.

Clinical Evaluations:

A. General

A study physician performed a medical history and physical examination on each participant. The medical history and physical data were recorded on Standard Form 600 (Appendix 1a) and filed along with the informed consent form.

B. Dermatologic Reactions

The subject was informed at the beginning of the study and at every re-evaluation that the field monitor would ask him if he developed a skin rash during the study. The field monitor would notify the field coordinator who would evaluate the rash, noting its location, character, extent, other salient features, as well as the presence of accompanying symptoms such as nausea, dizziness or wheezing. The findings would be recorded by the field coordinator on the Dermal/Systemic Reaction Record, (Appendix 2). The field coordinator would notify the study physician of his findings by telephone or directly the same day. The physician would evaluate all adverse reactions (local and systemic) utilizing the FDA from 1639, Adverse Reaction Report, (Appendix 3). If the rash was less than 20 cm. in diameter and limited to one or two locations without serious accompanying symptoms the subject would be re-examined daily by the filed monitor and would continue to apply the test lotion and

work in the field. Daily observation would occur until the rash had significantly diminished. If the rash area was over 20 cm. in diameter, located in more than two sites, or was accompanied by serious symptoms such as severe pain, itching, swelling or weeping the study physician would be immediately contacted and would evaluate the subject that day. The subject would be instructed not to apply the test lotion or engage in water-related work until satisfactory improvement was noted by the physician. The subject would be examined daily by the physician and if satisfactory improvement was not noted within 5 days the subject would be evaluated by the study's consulting dermatologist in Cairo for appropriate investigations and therapy or the subject might select a physician of his choice for medical care. The medical care would continue until satisfactory improvement occurred and during that period the subject would not apply the test lotion or engage in water related agriculture activity until determined cured by the dermatology consultant. The subject would be compensated at the existing daily rate for loss of work due to required water avoidance procedures and related medical costs including transportation to the medical facility by the study group. If the subject was unable to safely re-apply the test lotion on the recommendation of the dermatology consultant or at the subject's choice, the subject would permanently discontinue application of the study lotion and resume normal work activities when determined medically advisable by the consulting

dermatologist.

Field Evaluation:

Each participant was issued a box containing seven 30 ml bottles of the study lotion per week. Study subjects self-applied the lotion daily to their upper and lower limbs. The lotion was applied in the morning before the study subjects left for work in the fields. Field monitors visited the study participants' houses early in the morning three times per week on designated days and observed the lotion application, inquired if the subject applied the lotion the previous day and collected data on the previous day's water contact. The study monitor made two additional visits to each participant. One visit was made during the day at the field to verify that there was no unprotected exposure (body areas other than he upper and lower limbs) to canal or irrigation water. The other visit was in the evening at the participant's house to collect total water contact information for that day and to record any adverse reactions to the lotion. The monitor recorded the data on each subjects's record log. Each monitor was responsible for observing and documenting the activities of ten study participants (five participants each day). The study subjects also were visited once a week by a field coordinator who supervised the field monitor, observed lotion application and collected data for quality control. In addition, senior study

supervisors made two to four visits to the participants per month. The principal investigators visited all participants at least once a month throughout the study duration to assess lotion application, water contact and local or systemic reactions. The data collected by the field monitor, the field coordinator, the senior supervisor and the authors were routinely compared and discrepancies were investigated to assure protocol compliance.

The principal investigators monitored 600 study participants, supervised 60 field monitors, 12 local supervision teams and 3 central supervision teams (Table 2). The field monitor, coordinator or supervisor were responsible for reporting to the principal investigators when compliance was not 100%. A missed application was defined as that in which the study drug was not applied as scheduled and water contact occurred prior to the next application. Full compliance was expected from all study participants. When full compliance was not observed, the participant was counseled and the activities were duely recorded.

Laboratory Evaluations:

A. Collection of Specimens

Fecal specimens were collected monthly after the start of lotion application and continued for 3 months after cessation of lotion application, (Appendix 4). At collection 3 and 7 urine was collected as well. A single collection consisted or three consecutive daily specimens. Samples of stool were examined by the formalin ether sedimentation procedure (The modified Ritchie technique, Appendix 5). Urine samples were examined by a sedimentation concentration technique. All participants were given a labeled 50ml plastic centrifuge tube for urine and a wide mouthed plastic screw-cap container for feces and were asked to provide the first stool specimens of the day the next morning. The containers were labeled with participant's name, study number, number of collection and the date of collection

B. Laboratory Facility

The laboratories for this study were the Abu-Homos field laboratory and the Walter Reed Army Institute of Research , Parasitology Laboratory. Specimens were transported from the field to the laboratory within two to four hours from the time of collection. Specimens then were preserved and processed followed by microscopic examination. The field laboratory was under the direct supervision of the associate

investigators.

C. Laboratory Validation

A 10% random sample of fecal collection one and two and 100% of stool specimens at collections 3 and 7 after the start of lotion application were shipped to the Parasitology Laboratory at WRAIR-ET for repeat testing as a means of assuring quality control of laboratory analysis. Any specimen identified as positive for Schistosome eggs (irrespective of which laboratory made the identification) was considered to be positive for statistical purposes.

Statistical Evaluation:

All data entry and evaluation were completed before breaking the medication code. The Epi Info microcomputer programs produced at the Centers for Disease Control and the World Health Organization were used to create questionnaires and to enter data. To assure the accuracy of data entry, a double-entry system utilized two different operators to enter all data into two separate files. The files were then compared by a special program provided by the Epi Info and any differences were identified so that the non-duplicate entries could be reviewed and reconciled in the two files. Data entry was performed in the field continuously throughout the study.

Statistical evaluations included contingency table and chi-square tests for detection of differences in re-infection rates between the treatment groups. Student's t-test was used to test for differences of means among study groups. All the statistics performed were 2-tail analyses. The odds ratios (OR) were used to estimate the protective effect and 95% confidence intervals were computed. Logistic regression analysis of data was performed using SPSS/PC V4.1 to adjust for possible confounding variables.

For the purposes of statistical analysis, a schistosomiasis-infected subject that was detected during the wash out period in the first three months of lotion application was not included in the statistical analysis to exclude the possibility of pre-infection or incomplete eradication of infection by praziquantel treatment. A subject positive for S. mansoni in any stool collection 4 months after the start of lotion application until 2 months following cessation of lotion application (in months 4-7) was considered a medication failure. The subject must be negative in each stool collection during the months 4-7 to be considered negative (medication success).

Criteria for the success of the trial included:

1) A statistically significant difference between the frequency of schistosomiasis

infection among subject using the placebo-control lotion vs those using 1% niclosamide lotion.

2) No statistically significant difference in local and systemic side effects between subjects using the placebo control lotion vs those using 1% niclosamide lotion.

Monitoring of Study:

The sponsor's representative (USAMMDA product manager) inspected all study patients' medical records and corresponding portions of case report forms twice during the study; once in June 1991, and a second time in October 1991. These inspections were for the purpose of verifying the completeness and exactness of the data being entered on the report from, and to verify proper completion of informed consent forms and medical records.

Protection of Human Subjects:

Study volunteers were selected with the consent and advice of the Ministry of Health, Arab Republic of Egypt. The purpose of the study, including the risks and benefits involved with participation, the right to withdraw at any time, and the circumstances under which the subject may be removed from the study by the principal investigator were explained to the subjects in their native Arabic language

by a study physician.

Special care was taken to insure that each volunteer understood that he had the right to withdraw from the study at any time, that he need not provide a reason for withdrawal, that withdrawal would be without prejudice, and that he would be eligible for medical care for schistosomiasis throughout the duration of the study whether or not he had completed the study.

Ethical Aspects:

A. Institutional Review Board

The protocol was reviewed and approved by the human use committees of the U.S. Naval Medical Research Unit #3 (Cairo) and the U.S. Army Surgeon General (Human Subjects Research Review Board).

B. Informed Consent

The voluntary signature of each subject was obtained on the informed consent form which was in Arabic (Appendix 6b). The Arabic consent form was an exact translation of the attached English consent form (Appendix 6a). All signatures were in black ink using a ball point pen. Felt tipped or fountain pens were not allowed,

as the ink tends to fade and/or run. Black ink only was used to facilitate photocopying.

Prior to signing of the informed consent form, the general purpose of the study was explained to the subject. Each participant had the informed consent form read to him, and had the opportunity to ask questions before signing. The consent form contained the name and address of the participant, the date the informed consent was executed, the participant's signature, and the name and signature of the witness. The field monitors, field coordinators, and the study physicians served as witnesses.

All the forms were stored in the corresponding village clinics in a locked room. At the end of the study all forms were archived with the data at NAMRU-3 in Cairo in the Clinical Investigation Division records file.

Disposition of Study Materials:

A. Drug Inventory

The central drug inventory was maintained in the central pharmacy at NAMRU-3 (Cairo). From that point, a portion of the inventory was moved to the field on a biweekly basis. The drug was dispensed by the NAMRU-3 pharmacist who maintained inventory records. The medical supplies were transported to the

village clinics, where the drug was stored in a locked room in the clinic. From the clinical sites, the field monitors dispensed drug to the participants giving each a one week supply (7 bottles) at a time. The dispensing of drug to the participant was done utilizing a master log showing the participant's study number and assigned medication code.

B. Unused Drug

All unused drug and all empty bottles were returned by the participants to the field monitors. The returned drug was recorded and all unused medications were transported to NAMRU-3 (Cairo). The returned drug was confirmed against the master log by the principal investigator and then destroyed by incineration.

C. Case Report Forms

The case report forms (Appendix 7) for each subject were initially maintained in the Abu-Homos laboratory in a secured cabinet. All entries were made in indelible black ink. All corrections that were made to the forms were made with a simple line through the error, dated and initialed with the correction written to the side. The case report forms were filed by week, with the forms maintained in a chronological order with a tracking system. The investigators reviewed the forms weekly for

compliance with the above requirements.

Results:

Of the 600 farmers participating in the study (tables 3 and 4), 404 were excluded because they did not meet the inclusion criteria (Figure 1). Of the 404 (67.3%) who were eliminated, 59 (9.8%) were poistive for Schisotsoma mansoni eggs at the the first collection, 81 (13.5%) were positive at the second collection, 235 (39.2%) were positive at the third collection and 29 (48%) discontinued participation and did not submit stool specimens for collection three. One humdred and nintey six (32.7%) subjects were negative for Schistosoma mansoni eggs in the stool at the third collection and were included in the statistical analysis. Ten of the 196 subjects discontinued participation in the study; 4 travelled outside the study area, 4 subjects stopped applying the lotion for no specific reason and 2 subjects submitted no stool specimens for the final stool collection. Reasons for exclusion and discontinuation were listed in tables 5 and 6. A total of 186 subjects were included in the analysis (Table 7). Table 8 shows the distribution of subjects in the study villages. Ninety two (49.5%) subjects were using the 1% niclosamide lotion and 94 (50.5%) subjects were applying the placebo lotion (Table 9). Six subjects in the placebo group did not have complete data on lotion application compliance, observation and water contact.

The mean age of the study subjects was 30 years; this mean was identical in the two groups. Subjects in Anwar El-Mofty (study village) were significantly younger than subjects in Desones ($P < .05$) using analysis of variance and Scheffe's multiple range test (Table 10). Eighty one subjects (88%) in the niclosamide group and 81 (92%) in the placebo group reported lotion application daily for 5 months with no more than one missed application (Table 11). There was no difference in compliance among the two groups. Lotion application was observed by study monitors in 90% or more of the occasions in 57 (62%) of the subjects in the niclosamide group versus 58(66%) of the subjects in the placebo group (Table 12). The difference in observations between the two groups was not statistically significant. There were no significant differences in mean and median total canal or irrigation water contact during the entire study period between subjects receiving niclosamide and placebo lotion, (Table 13). An analysis of variance and Scheffe's multiple range test, revealed statistical significance between mean total infested water contact in the three study villages (Table 14). Figure II, represents water contact during the study period among the two study groups. The greatest water contact occurred during the first two months of the study and decreased later. There was no significant difference in water contact during any period among the two groups. Subjects receiving niclosamide and placebo lotion were comparable in reported water

contact of skin other than upper and lower limbs (non-lotion application areas). Twenty one subjects (22.8%) in the niclosamide group versus 25 (27.2%) in the placebo group reported water contact other than the upper and lower limbs (Table 15). No statistical difference was noted in reported unprotected water contact between the two study groups.

The re-infection rate during the study was significantly lower in the niclosamide group (53.3%) than in the placebo group (71.3%), (Table 16). A Crude Odds Ratio (OR) of 0.46, ($P<.02$) was observed for the niclosamide group. However the protective effect of niclosamide lotion in preventing reinfection of S. mansoni became more significant (OR= 0.41, $P<.01$), after adjusting for total water contact which may influence the reinfection rate (Table 17).

Other factors that may influence the reinfection rate such as age, village, compliance, percent of observed lotion application and water contact other than the upper and lower limbs when entered the logistic regression model did not affect the protective Odds Ratio associated with niclosamide (Table 18).

Tables 19 and 20 represent the S. mansoni re-infection rates and Odds Ratios

associated with niclosamide lotion in the two compliance categories and in the two categories of reported water contact other than the upper and lower limbs.

An intention to treat analysis was done using 196 subjects. This includes the 10 subjects who droped from the study after being initially included. The remaining 404 subjects were excluded from the study because they did not meet the inclusion criteria (Figure 1). The reinfection rate, Odds Ratio and P-value were calculated (Table 21). The results of the intention to treat analysis did not differ from the results using only 186 subjects who completed the study (Table 16).

No generalized or dermatological side effects were reported or detected in any of the study subjects during the five month period of daily lotion application.

Discussion:

One percent niclosamide lotion was previously found to be effective in preventing schistosome cercarial penetration of the skin of laboratory animals[5-7]. The present study was conducted in one of the highest endemic areas of S. mansoni in the world. The daily lotion application regimen was well accepted by the farmers and a high level of compliance was observed. Farmers participating in the study were exposed to direct sun rays during their routine work in the field a minimum of 4 hours a day with temperatures ranging from 28 to 40°C. No skin or systemic

reactions occurred which required discontinuation of the daily lotion applications.

Although daily niclosamide lotion application was safe, well accepted and provided some protection against S. mansoni reinfection compared to the placebo (protective Odds Ratio 0.41), the level of protection was not enough to recommend its use for the control of schistosomiasis among agriculture workers in this highly endemic region. Limiting niclosamide lotion application to the upper and lower limbs only may have been a major reason for the low level of protection. Farmers in the study area were frequently exposed to canal water beyond upper and lower limbs especially during canal clearance, irrigation pump repairs, and ablution (washing of the body before Moslem prayers).

Acceptable protection might be obtained with total body application (excluding mucous membrane surfaces) to overcome the problem of water exposure beyond the upper and lower limbs. Moreover, better protection might be obtained with niclosamide lotion when used by travelers, field engineers and military forces that require less daily contact with infested water for shorter periods of time.

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TABLE 1

Inclusion Criteria

1. Anticipate exposure to schistosomal infested water during the irrigation season.
2. Agree to apply the lotion daily to upper and lower limbs for 6 months.
3. Willingness to undergo regular monitoring for adherence to the protocol.
4. Agree to avoid total body contact with potentially infested water for the duration of the study.
5. Agree to report daily water contact.
6. Agree to provide 3 consecutive daily stool samples every month for 8 months.
7. Agree to consult the study physician prior to taking any medication.
8. No history of allergies to niclosamide or related compounds.
9. No history of drug allergies, skin rash, seizures or chronic medical problems.
10. Absence of skin abnormalities or significant medical disorders.

TABLE 2

Individuals participating in field operations

600 Study participants
60 Field monitors
24 Field coordinators (12 local supervision teams)
6 Field supervisors (3 central supervision teams)

Table 3

The status of the 600 subjects participating in the study

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
M001	N	POS. IN COLLECTION 3	W	.
M002	N	POS. IN COLLECTION 3	W	.
M003	N	POS. IN COLLECTION 3	B	.
M004	N	POS. IN COLLECTION 3	B	.
M005	N	POS. IN COLLECTION 3	W	.
M006	N	POS. IN COLLECTION 3	B	.
M007	Y	.	.	.
M008	Y	.	.	.
M009	N	DISCONTINUED (1).	.	5
M010	N	POS. IN COLLECTION 3	A	.
M011	Y	.	.	.
M012	Y	.	.	.
M013	N	DISCONTINUED (2).	.	2
M014	Y	.	.	.
M015	N	POS. IN COLLECTION 3	B	.
M016	N	POS. IN COLLECTION 3	W	.
M017	Y	.	.	.
M018	Y	.	.	.
M019	Y	.	.	.
M020	N	POS. IN COLLECTION 1	A	.
M021	Y	.	.	.
M022	Y	.	.	.
M022	N	POS. IN COLLECTION 1	W	.
M024	Y	.	.	.
M025	N	POS. IN COLLECTION 3	W	.
M026	Y	.	.	.
M027	Y	.	.	.
M028	Y	.	.	.
M029	N	POS. IN COLLECTION 3	A	.
M030	N	POS. IN COLLECTION 1	W	.
M031	Y	.	.	.
M032	N	POS. IN COLLECTION 1	A	.
M033	Y	.	.	.
M034	N	POS. IN COLLECTION 3	W	.

Subject ID

The alpha component identifying the study village

M = Anwar El-Mofty.

B = Desones.

Q = Kom El-Kanater.

Lab Site:

The positive results were by:

A = Abu-Homos field laboratory.

W = Water Reed Army Institute of Research (WRAIR).

B = Both laboratories.

Reason For Exclusion:

Discontinued(1) = Travelled outside study area.

Discontinued(2) = Joined the army.

Discontinued(3) = Gave no specific reason.

Included In The Stastical Analysis

Y = Yes

N = No

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
M035	N	POS. IN COLLECTION 3	B	.
M036	N	POS. IN COLLECTION 3	W	.
M037	Y	.	.	.
M038	N	POS. IN COLLECTION 3	W	.
M039	Y	.	.	.
M040	Y	.	.	.
M041	N	POS. IN COLLECTION 3	W	.
M042	N	POS. IN COLLECTION 2	A	.
M043	N	POS. IN COLLECTION 1	A	.
M044	N	POS. IN COLLECTION 3	B	.
M045	N	POS. IN COLLECTION 3	W	.
M046	N	POS. IN COLLECTION 3	W	.
M047	N	POS. IN COLLECTION 3	W	.
M048	N	POS. IN COLLECTION 3	B	.
M049	N	POS. IN COLLECTION 3	W	.
M050	N	POS. IN COLLECTION 3	W	.
M051	N	POS. IN COLLECTION 3	W	.
M052	Y	.	.	.
M053	N	POS. IN COLLECTION 3	B	.
M054	Y	.	.	.
M055	N	POS. IN COLLECTION 3	W	.
M056	N	POS. IN COLLECTION 3	W	.
M057	N	POS. IN COLLECTION 2	A	.
M058	Y	.	.	.
M059	N	POS. IN COLLECTION 3	W	.
M060	N	POS. IN COLLECTION 3	W	.
M061	N	POS. IN COLLECTION 3	A	.
M062	N	POS. IN COLLECTION 3	W	.
M063	N	POS. IN COLLECTION 3	W	.
M064	Y	.	.	.
M065	N	POS. IN COLLECTION 3	W	.
M066	N	POS. IN COLLECTION 3	W	.
M067	N	DISCONTINUED (1).	.	1
M068	N	POS. IN COLLECTION 3	W	.
M069	N	POS. IN COLLECTION 2	A	.
M070	N	POS. IN COLLECTION 1	A	.
M071	Y	.	.	.
M072	N	POS. IN COLLECTION 3	W	.
M073	N	DISCONTINUED (3).	.	4
M074	N	DISCONTINUED (3).	.	5
M075	Y	.	.	.
M076	Y	.	.	.
M077	N	POS. IN COLLECTION 2	A	.
M078	Y	.	.	.
M079	N	POS. IN COLLECTION 3	W	.
M080	N	POS. IN COLLECTION 3	B	.
M081	N	POS. IN COLLECTION 1	A	.
M082	Y	.	.	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
M083	Y	.	.	.
M084	N	DISCONTINUED (1).	.	1
M085	Y	.	.	.
M086	N	POS. IN COLLECTION 3	A	.
M087	Y	.	.	.
M088	N	POS. IN COLLECTION 3	B	.
M089	Y	.	.	.
M090	Y	.	.	.
M091	Y	.	.	.
M092	Y	.	.	.
M093	Y	.	.	.
M094	Y	.	.	.
M095	N	POS. IN COLLECTION 1	A	.
M096	N	POS. IN COLLECTION 3	B	.
M097	N	POS. IN COLLECTION 3	W	.
M098	Y	.	.	.
M099	N	POS. IN COLLECTION 2	A	.
M100	N	POS. IN COLLECTION 3	B	.
M101	N	POS. IN COLLECTION 1	A	.
M102	N	POS. IN COLLECTION 3	W	.
M103	N	POS. IN COLLECTION 2	W	.
M104	N	POS. IN COLLECTION 1	W	.
M105	N	POS. IN COLLECTION 1	A	.
M106	N	NO WRAIR RESULTS FOR COL.3	.	.
M107	Y	.	.	.
M108	N	POS. IN COLLECTION 3	W	.
M109	N	POS. IN COLLECTION 3	W	.
M110	N	DISCONTINUED (1).	.	1
M111	N	POS. IN COLLECTION 3	W	.
M112	N	POS. IN COLLECTION 3	W	.
M113	N	POS. IN COLLECTION 3	W	.
M114	Y	.	.	.
M115	Y	.	.	.
M116	Y	.	.	.
M117	Y	.	.	.
M118	N	POS. IN COLLECTION 3	W	.
M119	N	DISCONTINUED (2).	.	1
M120	Y	.	.	.
M121	N	POS. IN COLLECTION 2	W	.
M122	Y	.	.	.
M123	N	POS. IN COLLECTION 2	A	.
M124	Y	.	.	.
M125	N	POS. IN COLLECTION 3	W	.
M126	N	POS. IN COLLECTION 3	W	.
M127	N	POS. IN COLLECTION 3	W	.
M128	N	POS. IN COLLECTION 2	A	.
M129	Y	.	.	.
M130	N	POS. IN COLLECTION 3	W	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
M131	Y	.	.	.
M132	Y	.	.	.
M133	N	POS. IN COLLECTION 2	A	.
M134	N	POS. IN COLLECTION 3	B	.
M135	N	POS. IN COLLECTION 2	A	.
M136	Y	.	.	.
M137	N	POS. IN COLLECTION 2	A	.
M138	N	POS. IN COLLECTION 3	A	.
M139	N	DISCONTINUED (1).	.	2
M140	Y	.	.	.
M141	N	POS. IN COLLECTION 3	A	.
M142	Y	.	.	.
M143	Y	.	.	.
M144	Y	.	.	.
M145	Y	.	.	.
M146	N	DISCONTINUED (1).	.	2
M147	Y	.	.	.
M148	Y	.	.	.
M149	N	POS. IN COLLECTION 3	B	.
M150	N	POS. IN COLLECTION 3	W	.
M151	Y	.	.	.
M152	Y	.	.	.
M153	N	DISCONTINUED (2).	.	1
M154	N	POS. IN COLLECTION 3	A	.
M155	Y	.	.	.
M156	N	POS. IN COLLECTION 1	A	.
M157	N	POS. IN COLLECTION 3	B	.
M158	N	DISCONTINUED (2).	.	1
M159	N	POS. IN COLLECTION 3	W	.
M160	N	DISCONTINUED (2).	.	2
M161	Y	.	.	.
M162	Y	.	.	.
M163	Y	.	.	.
M164	N	DISCONTINUED (1).	.	0
M165	Y	.	.	.
M166	N	POS. IN COLLECTION 2	A	.
M167	N	POS. IN COLLECTION 2	A	.
M168	N	DISCONTINUED (1).	.	3
M169	N	POS. IN COLLECTION 2	A	.
M170	N	DISCONTINUED (3).	.	4
M171	Y	.	.	.
M172	Y	.	.	.
M173	Y	.	.	.
M174	N	DISCONTINUED (1).	.	5
M175	Y	.	.	.
M176	Y	.	.	.
M177	N	POS. IN COLLECTION 3	W	.
M178	N	DISCONTINUED (1).	.	0

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
M179	N	POS. IN COLLECTION 3	W	.
M180	N	POS. IN COLLECTION 1	A	.
M181	Y	.	.	.
M182	Y	.	.	.
M183	Y	.	.	.
M184	Y	.	.	.
M185	N	POS. IN COLLECTION 1	A	.
M186	N	POS. IN COLLECTION 3	W	.
M187	Y	.	.	.
M188	Y	.	.	.
M189	Y	.	.	.
M190	N	POS. IN COLLECTION 2	A	.
M191	N	POS. IN COLLECTION 1	A	.
M192	Y	.	.	.
M193	N	POS. IN COLLECTION 2	A	.
M194	N	POS. IN COLLECTION 2	A	.
M195	N	POS. IN COLLECTION 2	A	.
M196	N	DISCONTINUED (1).	.	2
M197	N	FRACTURE RIGHT FORE-ARM.	.	1
M198	N	POS. IN COLLECTION 3	B	.
M199	Y	.	.	.
M200	N	POS. IN COLLECTION 3	W	.
B001	N	POS. IN COLLECTION 3	W	.
B002	N	POS. IN COLLECTION 1	A	.
B003	N	POS. IN COLLECTION 2	A	.
B004	N	POS. IN COLLECTION 1	A	.
B005	N	POS. IN COLLECTION 1	A	.
B006	N	POS. IN COLLECTION 1	A	.
B007	N	POS. IN COLLECTION 3	W	.
B008	N	POS. IN COLLECTION 1	A	.
B009	N	POS. IN COLLECTION 3	W	.
B010	N	POS. IN COLLECTION 1	A	.
B011	N	POS. IN COLLECTION 3	W	.
B012	Y	.	.	.
B013	N	POS. IN COLLECTION 3	W	.
B014	Y	.	.	.
B015	N	POS. IN COLLECTION 1	A	.
B016	Y	.	.	.
B017	Y	.	.	.
B018	Y	.	.	.
B019	Y	.	.	.
B020	Y	.	.	.
B021	N	POS. IN COLLECTION 3	B	.
B022	N	POS. IN COLLECTION 3	W	.
B023	Y	.	.	.
B024	N	POS. IN COLLECTION 3	A	.
B025	N	POS. IN COLLECTION 3	W	.
B026	Y	.	.	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
B027	N	POS. IN COLLECTION 2	B	.
B028	N	POS. IN COLLECTION 3	B	.
B029	N	POS. IN COLLECTION 3	B	.
B030	N	POS. IN COLLECTION 2	A	.
B031	N	POS. IN COLLECTION 3	B	.
B032	N	POS. IN COLLECTION 3	B	.
B033	N	POS. IN COLLECTION 3	A	.
B034	N	POS. IN COLLECTION 3	B	.
B035	N	POS. IN COLLECTION 3	B	.
B036	N	POS. IN COLLECTION 3	B	.
B037	N	POS. IN COLLECTION 1	A	.
B038	N	POS. IN COLLECTION 1	A	.
B039	N	POS. IN COLLECTION 2	A	.
B040	N	POS. IN COLLECTION 2	A	.
B041	N	POS. IN COLLECTION 1	A	.
B042	N	POS. IN COLLECTION 3	W	.
B043	N	POS. IN COLLECTION 3	B	.
B044	N	POS. IN COLLECTION 1	A	.
B045	N	POS. IN COLLECTION 2	A	.
B046	N	POS. IN COLLECTION 1	A	.
B047	N	POS. IN COLLECTION 2	A	.
B048	N	POS. IN COLLECTION 3	A	.
B049	N	POS. IN COLLECTION 2	A	.
B050	Y	.	.	.
B051	N	POS. IN COLLECTION 3	W	.
B052	N	POS. IN COLLECTION 3	A	.
B053	N	POS. IN COLLECTION 2	A	.
B054	N	POS. IN COLLECTION 1	A	.
B055	N	POS. IN COLLECTION 2	A	.
B056	N	POS. IN COLLECTION 2	A	.
B057	N	POS. IN COLLECTION 2	A	.
B058	N	POS. IN COLLECTION 2	A	.
B059	Y	.	.	.
B060	N	POS. IN COLLECTION 3	B	.
B061	N	POS. IN COLLECTION 2	A	.
B062	N	POS. IN COLLECTION 3	W	.
B063	N	POS. IN COLLECTION 3	B	.
B064	Y	.	.	.
B065	N	POS. IN COLLECTION 2	A	.
B066	N	DIED ON AUGUST 20, 1990	.	2
B067	Y	.	.	.
B068	N	DISCONTINUED (3).	.	2
B069	Y	.	.	.
B070	Y	.	.	.
B071	Y	.	.	.
B072	N	POS. IN COLLECTION 3	B	.
B073	N	POS. IN COLLECTION 3	W	.
B074	Y	.	.	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
B075	N	POS. IN COLLECTION 3	B	.
B076	N	POS. IN COLLECTION 3	B	.
B077	N	POS. IN COLLECTION 1	A	.
B078	N	POS. IN COLLECTION 3	W	.
B079	N	POS. IN COLLECTION 2	A	.
B080	N	POS. IN COLLECTION 1	A	.
B081	Y	.	.	.
B082	N	POS. IN COLLECTION 3	W	.
B083	N	POS. IN COLLECTION 1	A	.
B084	N	POS. IN COLLECTION 3	B	.
B085	Y	.	.	.
B086	N	POS. IN COLLECTION 3	A	.
B087	Y	.	.	.
B088	Y	.	.	.
B089	Y	.	.	.
B090	N	POS. IN COLLECTION 2	A	.
B091	N	POS. IN COLLECTION 1	A	.
B092	N	POS. IN COLLECTION 3	B	.
B093	N	DISCONTINUED (3).	.	2
B094	N	POS. IN COLLECTION 1	A	.
B095	N	POS. IN COLLECTION 3	B	.
B096	Y	.	.	.
B097	N	POS. IN COLLECTION 3	W	.
B098	N	POS. IN COLLECTION 2	A	.
B099	N	POS. IN COLLECTION 3	W	.
B100	Y	.	.	.
B101	Y	.	.	.
B102	N	POS. IN COLLECTION 3	B	.
B103	Y	.	.	.
B104	N	POS. IN COLLECTION 2	W	.
B105	N	POS. IN COLLECTION 3	B	.
B106	N	POS. IN COLLECTION 3	W	.
B107	N	POS. IN COLLECTION 3	B	.
B108	N	POS. IN COLLECTION 3	B	.
B109	Y	.	.	.
B110	N	POS. IN COLLECTION 2	A	.
B111	N	POS. IN COLLECTION 3	B	.
B112	N	SUBMITTED NO SP FOR COL.7	.	6
B113	N	POS. IN COLLECTION 3	W	.
B114	N	POS. IN COLLECTION 1	W	.
B115	N	POS. IN COLLECTION 3	W	.
B116	N	POS. IN COLLECTION 3	B	.
B117	N	POS. IN COLLECTION 2	A	.
B118	N	POS. IN COLLECTION 3	A	.
B119	N	POS. IN COLLECTION 3	B	.
B120	Y	.	.	.
B121	N	POS. IN COLLECTION 3	B	.
B122	N	POS. IN COLLECTION 2	A	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
B123	N	POS. IN COLLECTION 2	A	.
B124	N	POS. IN COLLECTION 3	W	.
B125	N	POS. IN COLLECTION 3	W	.
B126	N	POS. IN COLLECTION 3	A	.
B127	N	POS. IN COLLECTION 3	B	.
B128	N	POS. IN COLLECTION 3	B	.
B129	Y	.	.	.
B130	N	POS. IN COLLECTION 3	W	.
B131	N	POS. IN COLLECTION 3	W	.
B132	Y	.	.	.
B133	Y	.	.	.
B134	N	POS. IN COLLECTION 1	A	.
B135	N	POS. IN COLLECTION 3	A	.
B136	N	POS. IN COLLECTION 3	B	.
B137	N	POS. IN COLLECTION 2	A	.
B138	Y	.	.	.
B139	Y	.	.	.
B140	N	POS. IN COLLECTION 2	A	.
B141	N	POS. IN COLLECTION 3	B	.
B142	N	POS. IN COLLECTION 3	W	.
B143	Y	.	.	.
B144	Y	.	.	.
B145	N	POS. IN COLLECTION 2	A	.
B146	N	POS. IN COLLECTION 3	B	.
B147	Y	.	.	.
B148	N	POS. IN COLLECTION 3	W	.
B149	N	POS. IN COLLECTION 3	B	.
B150	N	POS. IN COLLECTION 2	A	.
B151	Y	.	.	.
B152	Y	.	.	.
B153	Y	.	.	.
B154	N	POS. IN COLLECTION 3	B	.
B155	N	POS. IN COLLECTION 3	B	.
B156	N	POS. IN COLLECTION 3	B	.
B157	N	POS. IN COLLECTION 3	W	.
B158	N	POS. IN COLLECTION 3	B	.
B159	N	POS. IN COLLECTION 3	B	.
B160	N	POS. IN COLLECTION 3	A	.
B161	Y	.	.	.
B162	N	POS. IN COLLECTION 3	W	.
B163	N	POS. IN COLLECTION 3	B	.
B164	N	POS. IN COLLECTION 2	A	.
B165	Y	.	.	.
B166	Y	.	.	.
B167	Y	.	.	.
B168	N	POS. IN COLLECTION 2	A	.
B169	N	POS. IN COLLECTION 3	B	.
B170	N	POS. IN COLLECTION 3	B	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
B171	N	POS. IN COLLECTION 3	W	.
B172	N	POS. IN COLLECTION 3	W	.
B173	Y	.	.	.
B174	N	POS. IN COLLECTION 3	B	.
B175	N	POS. IN COLLECTION 3	A	.
B176	N	POS. IN COLLECTION 3	B	.
B177	N	POS. IN COLLECTION 3	W	.
B178	N	POS. IN COLLECTION 2	A	.
B179	N	POS. IN COLLECTION 3	W	.
B180	N	POS. IN COLLECTION 3	W	.
B181	Y	.	.	.
B182	Y	.	.	.
B183	Y	.	.	.
B184	N	POS. IN COLLECTION 1	A	.
B185	N	POS. IN COLLECTION 3	W	.
B186	N	POS. IN COLLECTION 3	W	.
B187	N	POS. IN COLLECTION 1	A	.
B188	N	POS. IN COLLECTION 3	W	.
B189	N	POS. IN COLLECTION 2	A	.
B190	N	POS. IN COLLECTION 3	W	.
B191	N	POS. IN COLLECTION 3	W	.
B192	N	POS. IN COLLECTION 3	W	.
B193	N	POS. IN COLLECTION 1	A	.
B194	N	POS. IN COLLECTION 3	B	.
B195	Y	.	.	.
B196	Y	.	.	.
B197	Y	.	.	.
B198	N	POS. IN COLLECTION 3	B	.
B199	N	POS. IN COLLECTION 3	B	.
B200	N	POS. IN COLLECTION 3	B	.
Q001	N	DISCONTINUED (1).	.	1
Q002	N	POS. IN COLLECTION 3	W	.
Q003	Y	.	.	.
Q004	N	POS. IN COLLECTION 3	W	.
Q005	N	POS. IN COLLECTION 3	W	.
Q006	Y	.	.	.
Q007	N	POS. IN COLLECTION 3	W	.
Q008	N	POS. IN COLLECTION 3	W	.
Q009	N	HAD AN ACCIDENT.	.	2
Q010	N	POS. IN COLLECTION 2	A	.
Q011	N	POS. IN COLLECTION 3	W	.
Q012	N	POS. IN COLLECTION 3	W	.
Q013	Y	.	.	.
Q014	Y	.	.	.
Q015	N	POS. IN COLLECTION 2	A	.
Q016	Y	.	.	.
Q017	Y	.	.	.
Q018	Y	.	.	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
Q019	Y	.	.	.
Q020	N	POS. IN COLLECTION 1	W	.
Q021	N	POS. IN COLLECTION 3	W	.
Q022	N	POS. IN COLLECTION 3	W	.
Q023	N	POS. IN COLLECTION 3	W	.
Q024	Y	.	.	.
Q025	Y	.	.	.
Q026	Y	.	.	.
Q027	N	POS. IN COLLECTION 1	A	.
Q028	N	POS. IN COLLECTION 1	A	.
Q029	N	POS. IN COLLECTION 2	A	.
Q030	N	POS. IN COLLECTION 3	B	.
Q031	N	POS. IN COLLECTION 3	W	.
Q032	N	POS. IN COLLECTION 3	A	.
Q033	N	POS. IN COLLECTION 3	A	.
Q034	N	POS. IN COLLECTION 2	A	.
Q035	N	DISCONTINUED (2).	.	3
Q036	N	POS. IN COLLECTION 3	W	.
Q037	Y	.	.	.
Q038	N	POS. IN COLLECTION 3	B	.
Q039	N	POS. IN COLLECTION 1	A	.
Q040	N	POS. IN COLLECTION 3	A	.
Q041	N	POS. IN COLLECTION 3	W	.
Q042	N	POS. IN COLLECTION 2	A	.
Q043	N	POS. IN COLLECTION 3	W	.
Q044	N	POS. IN COLLECTION 3	W	.
Q045	Y	.	.	.
Q046	N	POS. IN COLLECTION 2	A	.
Q047	Y	.	.	.
Q048	N	POS. IN COLLECTION 3	W	.
Q049	N	POS. IN COLLECTION 3	W	.
Q050	Y	.	.	.
Q051	Y	.	.	.
Q052	Y	.	.	.
Q053	N	POS. IN COLLECTION 2	A	.
Q054	Y	.	.	.
Q055	N	POS. IN COLLECTION 2	A	.
Q056	N	DISCONTINUED (1).	.	0
Q057	N	POS. IN COLLECTION 1	A	.
Q058	N	POS. IN COLLECTION 1	A	.
Q059	N	POS. IN COLLECTION 1	A	.
Q060	N	POS. IN COLLECTION 2	A	.
Q061	N	POS. IN COLLECTION 3	W	.
Q063	N	POS. IN COLLECTION 3	W	.
Q064	Y	.	.	.
Q065	Y	.	.	.
Q066	N	POS. IN COLLECTION 1	A	.
Q067	N	POS. IN COLLECTION 2	A	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
Q068	N	POS. IN COLLECTION 3	W	.
Q069	Y	.	.	.
Q070	N	POS. IN COLLECTION 2	A	.
Q071	N	POS. IN COLLECTION 3	B	.
Q072	N	DISCONTINUED (1).	.	0
Q073	N	POS. IN COLLECTION 3	W	.
Q074	Y	.	.	.
Q075	N	POS. IN COLLECTION 3	B	.
Q076	N	POS. IN COLLECTION 3	W	.
Q077	N	POS. IN COLLECTION 3	W	.
Q078	N	POS. IN COLLECTION 3	B	.
Q079	N	DISCONTINUED (1).	.	0
Q080	Y	.	.	.
Q081	Y	.	.	.
Q082	N	POS. IN COLLECTION 2	A	.
Q083	N	POS. IN COLLECTION 2	A	.
Q084	N	DISCONTINUED (1).	.	0
Q085	N	POS. IN COLLECTION 3	B	.
Q086	N	POS. IN COLLECTION 1	A	.
Q087	N	POS. IN COLLECTION 3	A	.
Q088	N	POS. IN COLLECTION 2	A	.
Q089	N	POS. IN COLLECTION 3	B	.
Q090	Y	.	.	.
Q091	N	POS. IN COLLECTION 3	W	.
Q092	N	POS. IN COLLECTION 3	W	.
Q093	Y	.	.	.
Q094	N	POS. IN COLLECTION 3	W	.
Q095	N	POS. IN COLLECTION 3	W	.
Q096	N	POS. IN COLLECTION 1	A	.
Q097	Y	.	.	.
Q098	N	POS. IN COLLECTION 2	A	.
Q099	N	POS. IN COLLECTION 3	B	
Q100	Y	.	.	.
Q101	N	POS. IN COLLECTION 3	W	.
Q102	N	POS. IN COLLECTION 2	A	.
Q103	N	POS. IN COLLECTION 2	A	.
Q104	N	POS. IN COLLECTION 2	A	.
Q105	N	POS. IN COLLECTION 3	W	.
Q106	N	POS. IN COLLECTION 3	W	.
Q107	N	POS. IN COLLECTION 3	B	.
Q108	N	POS. IN COLLECTION 3	W	.
Q109	N	POS. IN COLLECTION 2	A	.
Q110	N	POS. IN COLLECTION 3	A	.
Q111	N	POS. IN COLLECTION 2	A	.
Q112	N	POS. IN COLLECTION 3	B	.
Q113	N	POS. IN COLLECTION 3	W	.
Q114	N	POS. IN COLLECTION 1	A	.
Q115	N	POS. IN COLLECTION 2	A	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
Q116	Y	.	.	.
Q117	N	POS. IN COLLECTION 3	B	.
Q118	Y	.	.	.
Q119	N	POS. IN COLLECTION 3	W	.
Q120	N	POS. IN COLLECTION 3	W	.
Q121	N	POS. IN COLLECTION 2	A	.
Q122	Y	.	.	.
Q123	N	POS. IN COLLECTION 3	W	.
Q124	N	POS. IN COLLECTION 3	B	.
Q125	Y	.	.	.
Q126	N	POS. IN COLLECTION 3	W	.
Q127	N	POS. IN COLLECTION 3	W	.
Q128	N	POS. IN COLLECTION 2	A	.
Q129	N	POS. IN COLLECTION 2	A	.
Q130	N	DISCONTINUED (3).	.	4
Q131	N	POS. IN COLLECTION 3	B	.
Q132	N	POS. IN COLLECTION 2	A	.
Q133	Y	.	.	.
Q134	N	POS. IN COLLECTION 3	W	.
Q135	N	POS. IN COLLECTION 3	A	.
Q136	N	POS. IN COLLECTION 1	A	.
Q137	N	POS. IN COLLECTION 3	B	.
Q138	N	POS. IN COLLECTION 3	A	.
Q139	N	POS. IN COLLECTION 3	B	.
Q140	N	POS. IN COLLECTION 1	A	.
Q141	N	POS. IN COLLECTION 3	B	.
Q142	N	POS. IN COLLECTION 2	A	.
Q143	Y	.	.	.
Q144	N	DISCONTINUED (1).	.	1
Q145	Y	.	.	.
Q146	Y	.	.	.
Q147	N	DISCONTINUED (1).	.	0
Q148	Y	.	.	.
Q149	Y	.	.	.
Q150	N	POS. IN COLLECTION 1	A	.
Q151	Y	.	.	.
Q152	N	POS. IN COLLECTION 1	A	.
Q153	N	POS. IN COLLECTION 3	A	.
Q154	N	POS. IN COLLECTION 1	A	.
Q155	N	POS. IN COLLECTION 1	A	.
Q156	Y	.	.	.
Q157	N	DISCONTINUED (1).	.	1
Q158	Y	.	.	.
Q159	N	POS. IN COLLECTION 2	A	.
Q160	Y	.	.	.
Q161	N	POS. IN COLLECTION 2	A	.
Q062	N	DISCONTINUED (1).	.	2
Q162	Y	.	.	.

SUBJECT ID.	INCLUDED IN STAT. ANALYSIS	REASON FOR EXCLUSION	LAB SITE.	LAST STOOL SP. SUBMITTED
Q163	Y	.	.	.
Q164	Y	.	.	.
Q165	N	POS. IN COLLECTION 2	A	.
Q166	N	POS. IN COLLECTION 2	A	.
Q167	N	POS. IN COLLECTION 3	W	.
Q168	N	POS. IN COLLECTION 3	W	.
Q169	N	POS. IN COLLECTION 3	B	.
Q170	N	POS. IN COLLECTION 3	W	.
Q171	Y	.	.	.
Q172	Y	.	.	.
Q173	Y	.	.	.
Q174	Y	.	.	.
Q175	N	POS. IN COLLECTION 3	W	.
Q176	Y	.	.	.
Q177	Y	.	.	.
Q178	Y	.	.	.
Q179	N	POS. IN COLLECTION 3	W	.
Q180	N	POS. IN COLLECTION 3	W	.
Q181	N	POS. IN COLLECTION 3	W	.
Q182	N	POS. IN COLLECTION 3	B	.
Q183	N	POS. IN COLLECTION 1	A	.
Q184	N	POS. IN COLLECTION 3	B	.
Q185	N	POS. IN COLLECTION 2	A	.
Q186	Y	.	.	.
Q187	Y	.	.	.
Q188	N	POS. IN COLLECTION 1	A	.
Q189	N	SUBMITTED NO SP FOR COL.7	.	6
Q190	N	POS. IN COLLECTION 1	A	.
Q191	Y	.	.	.
Q192	Y	.	.	.
Q193	N	POS. IN COLLECTION 3	B	.
Q194	N	DISCONTINUED (1).	.	1
Q195	Y	.	.	.
Q196	N	POS. IN COLLECTION 3	W	.
Q197	N	POS. IN COLLECTION 3	B	.
Q198	N	POS. IN COLLECTION 1	A	.
Q199	Y	.	.	.
Q200	N	POS. IN COLLECTION 3	W	.

Table 4

Distribution of the 600 subjects by study villages

INCLUDED IN STAT. ANALYSIS	Anwar El-Mofty	Desones	Kom El-Kanater	Total
Yes	78	50	58	186
No	122	150	142	414
Total	200	200	200	600

Table 5

Reasons for exclusion and discontinuation of subjects in the study villages

REASON FOR EXCLUSION	Anwar	Kom		
	El-Mofty	Desones	El-Kanater	Total
DIED ON AUGUST 20, 1990*	0	1	0	1
TRAVELLED OUTSIDE STUDY AREA	11	0	10	21
JOINED THE ARMY	5	0	1	6
NO SPECIFIC REASON GIVEN	3	2	1	6
ACCIDENTAL INJURY	1	0	1	2
NO WRAIR RESULTS FOR COL.3**	1	0	0	1
POS. IN COLLECTION 1	15	23	21	59
POS. IN COLLECTION 2	19	31	31	81
POS. IN COLLECTION 3	67	92	76	235
NO SPECIMEN SUBMITTED FOR COLLECTION 7	0	1	1	2
Total	122	150	142	414

* DIED FROM AN ACCIDENT FALL.
** RESULTS NOT RECORDED AT WRAIR LABORATORY.

Table 6

Reasons for discontinuation and time measured by the last stool submitted by the subject

REASON FOR DISCONTINUATION	LAST STOOL SPECIMENT SUBMITTED 0	1	2	3	4	5	6	TOTAL
IED ON AUGUST 20, 1990	0	0	1	0	0	0	0	1
RAVELLED OUTSIDE STUDY AREA	7	7	4	1	0	2	0	21
OINED THE ARMY	0	3	2	1	0	0	0	6
O SPECIFIC REASON GIVEN	0	0	2	0	3	1	0	6
CCIDENTAL INJURY	0	1	1	0	0	0	0	2
O SPECIMEN SUBMITTED FOR OLLECTION 7	0	0	0	0	0	0	2	2
Total	7	11	10	2	3	3	2	38

NE HAD NO WRAIR RESULTS FOR COLLECTION 3.

TABLE 7

List of subjects included in the statistical analysis

ERIAL O.	SUBJECT ID.	AGE	TREATME CODE.	FINAL RESULT	POS COL.NO	%LOTION APPLICA	%LOTION OBSERVA	TOTAL WATER EXPOS	UN-PROT EXPOSUR	SKIN COMP
1	M007	39	1	1	4	100	100	242	1	0
2	M008	28	0	0	0	98	96	151	1	0
3	M011	27	0	1	4	100	98	131	1	0
4	M012	26	0	1	6	100	95	209	3	0
5	M014	26	0	1	6	93	86	128	3	0
6	M017	33	0	1	7	98	95	142	3	0
7	M018	31	1	1	4	96	86	116	1	0
8	M019	23	1	0	0	98	91	103	3	0
9	M021	34	0	0	0	100	90	149	3	0
10	M022	29	0	1	4	100	95	162	3	0
11	M024	30	0	0	0	100	96	138	2	0
12	M026	28	1	0	0	100	96	159	3	0
13	M027	37	1	0	0	100	96	151	2	0
14	N028	27	0	1	7	100	95	144	1	0
15	M031	22	0	1	7	100	100	178	1	0
16	M033	19	0	1	6	100	100	203	1	0
17	M037	32	0	1	4	100	100	245	4	0
18	M039	37	1	1	5	100	98	137	2	0
19	M040	24	0	0	0	100	98	119	1	0
20	M052	39	0	1	4	100	95	79	1	0
21	M054	35	1	0	0	98	95	40	1	0
22	M058	29	1	0	0	100	91	36	1	0
23	M064	23	0	1	7	98	90	173	2	0
24	M071	28	0	0	0	100	75	52	1	0
25	M075	40	1	1	4	98	60	242	3	0
26	M076	25	0	1	7	94	47	119	.	0
27	M078	25	1	0	0	100	65	172	3	0
28	M082	37	1	1	6	100	93	179	1	0

ubjects ID
e alpha component identifying the study.
M = Anwar El-Mofty.
B = Desons.
Q = Kom El-Kanater.

Treatme Code
Treatment Codey village
1 = Niclosamide
0 = Placebo.

inal Result
= Positive for S.mansoni egg.
= Negative for S.mansoni egg.

Pos Col. No
Positive At Collection Number.

% Lotion Applica
Lotion Application.

% Lotion Observa
% Lotion Observation.

otal Water Expos
otal canal or irrigation water exposure.

Skin Comp
Skin complications.

n-Prot Exposur
nprotected canal or irrigation water exposure. i.e exposure beyond the upper and lower limbs.

SERIAL NO.	SUBJECT ID.	AGE	TREATME CODE.	FINAL RESULT	POS COL.NO	%LOTION APPLICA	%LOTION OBSERVA	TOTAL WATER EXPOS	UN-PROT EXPOSUR	SKIN COMP
29	M083	29	0	1	4	100	88	101	2	0
30	M085	19	0	1	6	100	86	147	1	0
31	M087	34	0	0	0	96	80	145	2	0
32	M089	33	1	0	0	96	76	130	1	0
33	M090	28	1	1	6	98	85	103	1	0
34	M091	26	0	1	6	100	81	78	1	0
35	M092	25	1	0	0	98	85	105	3	0
36	M093	23	0	0	0	100	85	59	1	0
37	M094	35	1	0	0	100	80	125	1	0
38	M098	20	1	1	4	100	75	93	1	0
39	M107	28	1	0	0	100	93	248	1	0
40	M114	24	0	1	7	100	100	225	2	0
41	M115	31	1	0	0	98	98	231	1	0
42	M116	19	1	0	0	98	98	249	1	0
43	M117	19	0	1	7	100	100	333	3	0
44	M120	38	1	0	0	100	90	196	1	0
45	M122	29	0	0	0	100	91	329	2	0
46	M124	26	0	1	7	98	85	265	2	0
47	M129	33	1	0	0	100	90	392	3	0
48	M131	24	1	1	7	95	85	325	3	0
49	M132	31	0	1	4	100	98	329	1	0
50	M136	19	1	1	4	100	95	277	1	0
51	M140	40	1	1	5	100	85	301	1	0
52	M142	24	1	1	6	100	98	235	1	0
53	M143	19	1	0	0	100	90	233	1	0
54	M144	19	0	1	7	100	95	189	5	0
55	M145	31	0	0	0	100	95	174	3	0
56	M147	27	0	1	7	100	100	195	3	0
57	M148	20	0	1	7	100	93	93	1	0
58	M151	23	0	1	5	100	100	244	3	0
59	M152	19	1	0	0	100	100	112	1	0
60	M155	27	1	1	7	98	98	270	3	0
61	M161	32	0	1	6	100	90	69	1	0
62	M162	30	0	1	5	96	88	157	1	0
63	M163	22	1	1	6	91	80	113	1	0
64	M165	20	0	1	4	81	73	96	3	0
65	M171	34	0	1	7	92	79	185	.	0
66	M172	27	0	1	6	98	86	190	2	0
67	M173	40	1	1	5	98	91	175	1	0
68	M175	31	1	0	0	96	66	132	1	0
69	M176	27	0	1	4	100	71	291	1	0
70	M181	39	0	1	4	100	96	318	3	0
71	M182	40	1	0	0	98	98	323	2	0
72	M183	23	0	1	5	100	90	229	1	0
73	M184	27	1	1	7	100	93	235	1	0
74	M187	24	0	1	7	98	98	322	1	0
75	M188	40	0	1	7	98	98	310	1	0

SERIAL NO.	SUBJECT ID.	AGE	TREATME CODE.	FINAL RESULT	POS COL.NO	%LOTION APPLICA	%LOTION OBSERVA	TOTAL WATER EXPOS	UN-PROT EXPOSUR	SKIN COMP
76	M189	25	1	1	7	98	96	350	1	0
77	M192	38	0	0	0	100	88	169	1	0
78	M199	38	1	0	0	100	91	162	2	0
79	B012	26	1	1	6	100	75	379	1	0
80	B014	18	1	1	6	100	80	272	1	0
81	B016	40	0	1	4	100	70	321	1	0
82	B017	38	1	0	0	100	61	327	1	0
83	B018	39	0	1	7	100	86	311	1	0
84	B019	25	1	1	7	100	81	280	1	0
85	B020	35	0	1	7	100	65	393	2	0
86*	B023	26	0	0	0	100	96	228	1	0
87*	B026	40	0	1	7	100	73	132	1	0
88	B050	34	1	1	7	100	91	257	1	0
89	B059	40	0	0	0	100	100	141	2	0
90	B064	32	0	0	0	96	61	131	1	0
91	B067	40	1	1	7	100	60	180	4	0
92	B069	25	1	1	6	100	65	165	2	0
93	B070	34	0	0	0	98	76	131	1	0
94	B071	22	1	1	7	100	91	143	2	0
95	B074	32	0	1	6	96	90	203	3	0
96	B081	29	1	1	7	100	86	269	1	0
97	B085	40	0	1	4	100	88	273	3	0
98	B087	31	0	1	4	100	88	285	4	0
99	B088	39	1	0	0	100	81	243	1	0
00	B088	32	1	1	7	100	81	254	4	0
01	B096	37	0	1	7	100	90	151	4	0
02	B100	37	1	0	0	100	88	194	4	0
03	B101	34	0	0	0	100	96	216	1	0
04	B103	30	0	1	7	100	96	235	1	0
05	B109	38	1	1	7	96	93	237	1	0
06	B120	20	1	1	6	100	88	199	1	0
07*	B129	28	0	1	5	100	88	189	1	0
08	B132	33	1	0	0	100	83	135	2	0
09	B133	28	1	1	7	100	55	166	1	0
10	B138	38	0	1	4	98	70	134	2	0
11	B139	28	1	1	5	93	70	201	1	0
12	B143	18	1	1	5	100	96	188	2	0
13	B144	18	1	0	0	100	91	223	1	0
14	B147	26	0	1	5	100	86	258	1	0
15	B151	40	1	0	0	100	96	362	3	0
16	B152	25	0	1	7	100	96	321	1	0
17	B153	19	1	1	6	100	95	312	1	0
18	B161	30	0	1	6	100	91	267	2	0
19	B165	35	1	1	7	100	98	267	3	0
20	B166	38	1	0	0	100	98	271	1	0
21	B167	39	0	1	7	100	100	226	1	0
22	B173	37	1	1	7	96	93	250	2	0

ERIAL O.	SUBJECT ID.	AGE	TREATME CODE.	FINAL RESULT	POS COL.NO	%LOTION APPLICA	%LOTION OBSERVA	TOTAL WATER EXPOS	UN-PROT EXPOSUR	SKIN COMP
23	B181	40	1	0	0	100	100	243	2	0
24	B182	35	1	1	7	100	96	80	1	0
25	B183	24	1	1	7	100	100	183	1	0
26	B195	39	0	1	7	100	100	164	2	0
27	B196	19	0	1	7	100	100	137	1	0
28	B197	39	0	1	7	100	100	165	3	0
29	Q003	33	0	0	0	98	96	61	1	0
30	Q006	28	0	0	0	100	100	81	1	0
31	Q013	40	1	1	6	100	90	104	1	0
32	Q014	32	1	0	0	100	95	151	1	0
33	Q016	18	0	0	0	98	98	84	1	0
34	Q017	20	0	1	7	100	98	118	1	0
35	Q018	21	1	1	6	100	100	145	3	0
36	Q019	18	0	1	7	100	98	112	1	0
37	Q024	40	0	1	7	98	96	227	2	0
38	Q025	35	1	0	0	93	91	214	3	0
39	Q026	33	1	0	0	96	96	230	2	0
40	Q037	40	0	0	0	100	83	135	3	0
41	Q045	25	1	1	4	100	98	251	1	0
42	Q047	38	1	0	0	98	96	199	1	0
43	Q050	29	0	1	4	98	98	244	2	0
44	Q051	26	1	0	0	100	100	17	1	0
45	Q052	40	0	1	6	100	100	71	2	0
46	Q054	30	0	1	4	96	91	89	1	0
47	Q064	20	1	0	0	100	95	124	1	0
48	Q065	24	0	0	0	100	93	122	1	0
49	Q069	30	1	1	4	100	91	118	3	0
50	Q074	40	1	1	4	100	98	49	1	0
51	Q080	29	1	1	4	100	96	79	3	0
52	Q081	33	0	0	0	100	100	384	1	0
53	Q090	28	1	1	7	100	100	289	2	0
54	Q093	33	0	1	7	100	80	127	1	0
55	Q097	32	0	1	7	100	86	102	1	0
56	Q100	25	1	1	6	100	95	171	1	0
57	Q116	32	1	0	0	98	93	111	1	0
58	Q118	22	1	0	0	100	93	60	1	0
59	Q122	40	0	1	5	98	86	48	3	0
60	Q125	32	0	1	4	100	96	63	3	0
61	Q133	20	1	0	0	98	85	171	1	0
62	Q143	40	1	1	6	100	95	179	3	0
63	Q145	39	0	1	6	100	98	149	1	0
64	Q146	28	1	1	4	98	93	152	2	0
65	Q148	27	0	0	0	100	96	160	1	0
66	Q149	20	1	1	4	100	96	190	3	0
67	Q151	31	1	1	6	100	78	83	4	0
68	Q156	32	0	0	0	100	85	91	1	0
69	Q158	34	0	1	4	100	80	109	2	0
70	Q160	19	0	0	0	100	96	43	1	0

ERIAL O.	SUBJECT ID.	AGE	TREATME CODE.	FINAL RESULT	POS COL.NO	%LOTION APPLICA	%LOTION OBSERVA	TOTAL WATER EXPOS	UN-PROT EXPOSUR	SKIN COMP
.71	Q162	36	1	1	7	100	91	123	1	0
.72	Q163	38	1	0	0	100	88	162	3	0
.73	Q164	28	0	1	7	100	91	189	3	0
.74	Q171	39	1	0	0	100	81	100	1	0
.75	Q172	33	0	1	7	100	81	183	3	0
.76	Q173	33	1	0	0	100	55	35	2	0
.77	Q174	40	1	0	0	98	75	104	2	0
.78	Q176	32	0	0	0	100	76	153	1	0
.79	Q177	31	1	0	0	96	65	76	1	0
.80	Q178	18	1	1	6	100	76	153	2	0
81	Q186	39	0	0	0	100	88	45	1	0
82	Q187	20	1	0	0	98	85	68	2	0
83	Q191	29	0	1	7	100	98	125	3	0
84	Q192	34	1	0	0	100	100	96	1	0
85	Q195	28	0	0	0	100	98	112	3	0
86	Q199	32	0	1	7	100	100	93	1	0

. Data are recorded until the 17th week.
. Data are recorded until the 19th week.
Data are recorded until the 13th week.

TABLE 8
Distribution Of Subjects By Study Villages

Anwar El-Mofty	Desones	Kom El-Kanater	Total
78(41.9%)	50(26.9%)	58(31.2)	186(100%)

TABLE 9

Distribution Of Subjects By Study Medication

Among The Three Villages

Study	Anwar		Kom	
Medication	El-Mofty	Desones	El-Kanater	Total
Niclosamide	35(44.9%)	27(54%)	30(52.7%)	92(49.5%)
Placebo	43(55.1%)	23(46%)	28(48.3%)	94(50.5%)
Total	78(100%)	50(100%)	58(100%)	186(100%)

TABLE 10

Subject's Mean Age In Years By Study Medications

In The Three Villages

Study Medication	Anwar El-Mofty	Desones	Kom El-Kanater	Total
Niclosamide	29.89	30.22	30.13	30.01
Placebo	27.58	33.61	30.78	30.06
Total	28.62[a]	31.78[a]	30.45	30.04

[a]. $P < .05$ (Scheffe's multiple range test)

TABLE 11
Lotion Application Compliance Among Study Groups In The Three Villages

%Lotion Application	Study Medication	Anwar El-Mofty n= 75(100%)	Anwar Desones n= 47(100%)	Kom El-Kanater n=58(100%)	Total n= 180*(100%)
98-100%	Niclosamide	30	24	27	81
	Placebo	36	18	27	81
	Total	66(88%)	42(89.4%)	54(93.1%)	162(90%)
90-97%	Niclosamide	5	3	3	11
	Placebo	3	2	1	6
	Total	8(10.7%)	5(10.6%)	4 (6.9%)	17(9.4%)
< 90%	Niclosamide	0	0	0	0
	Placebo	1	0	0	1
	Total	1(1.3%)	0(0.0%)	0(0.0%)	1(0.6%)

* 6 Subjects had incomplete data

TABLE 12
Lotion Application Observation By Study Monitors

Among Study Groups In The Three Villages

% Lotion Observation	Study Medication	Anwar El-Mofty n= 75(100%)	Desones n= 47(100%)	Kom El-Kanater n=58(100%)	Total n= 180*(100%)
90-100%	Niclosamide	23	13	21	57
	Placebo	28	11	19	58
	Total	51(68%)	24(51.1%)	40(69%)	115(63.9%)
80-89%	Niclosamide	7	8	4	19
	Placebo	9	4	8	21
	Total	16(21.3%)	12(25.5%)	12(20.7%)	40(22.2%)
< 80%	Niclosamide	5	6	5	16
	Placebo	3	5	1	9
	Total	8(10.7%)	11(23.4%)	6(10.3%)	25(13.9%)

* 6 Subjects had incomplete data

TABLE 13

Mean and median values of water contact in hours during the entire study period by study groups

Study Group	No. of Subjects	Mean	Standard Deviation	Median
Niclosamide	92	184.5	84.5	177
Placebo	88	173.8	85.3	152
	180*	179.3	84.8	165

* 6 Subjects had incomplete data

TABLE 14

Mean Infested Water Contact In Hours During The Whole Study Period By Study Medication In The Three Villages

Study Medication	Anwar El-Mofty	Desones	Kom El-Kanater	Total
Niclosamide	191.20	232.59	133.47	184.52
Placebo	182.82	223.15	125.71	173.82
Total	186.73[a]	228.57[a]	129.72[a]	179.29

a. $P < .05$ (Scheffe's multiple range test)

TABLE 15

Water Contact Episodes Invoving Areas Other Than The Upper And Lower Limbs Reported From The Study Groups In The Three Villages

Unprotected Water Contact Episodes	Study Medication	Anwar El-Mofty n= 75(100%)	Desones n= 47(100%)	Kom El-Kanater n=58(100%)	Total n= 184*(100%)
None	Niclosamide	23	16	15	54
	Placebo	20	13	17	50
	Total	43(56.6%)	29(58%)	32(55.2%)	104(56.5%)
1-2	Niclosamide	4	6	7	17
	Placebo	8	5	4	17
	Total	12(15.8%)	11(22%)	11(18.9%)	34(18.5%)
> 2	Niclosamide	8	5	8	21
	Placebo	13	5	7	25
	Total	21(27.6%)	10(20%)	15(25.9%)	46(25%)

* 2 Subjects had incomplete data

TABLE 16

S.mansoni Reinfection Rates And Odds Ratio Associated With Niclosamide Lotion In The Three Villages

		Anwar El-Mofty			Desones			Kom El-Kanater			Total		
		S.mansoni			S.mansoni			S.mansoni			S.mansoni		
		+	-	TOTAL	+	-	TOTAL	+	-	TOTOAL	+	-	TOTAL
	Niclosamide	16	19	35	19	8	27	14	16	30	49	43	92
	Placebo	33	10	43	18	5	23	16	12	28	67	27	94
Reinfection Rate	Niclosamide	46.7%			70.4%			46.7%			53.3%		
	Placebo	76.7%			78.3%			57.1%			71.3%		
	Odd Ratio	0.26			0.66			0.66			0.46		
	95%CI	(0.08,0.75)			(0.15,2.86)			(0.20,2.12)			(0.24,0.88)		
	P-VALUE	0.004			0.52			0.42			0.011		

TABLE 17

Odds Ratio of *S. mansoni* infection associated with niclosamide

Study Group	*S.mansoni* +	*S.mansoni* -	Crude Odds Ratio	(95% CI)	Adjusted Odds Ratio*	(95%CI)
Niclosamide	49	43	0.46	(0.24,0.88)[a]	0.41	(0.22,0.77)
Placebo	67	27	1.00		1.00	

*. adjust for reported total water contact

[a]. P<.012

[b]. P<.006

Table 18

Result of muliple logistic Regression analysis on major study varibles

VARIABLE	BETA	STANDARD ERROR	ODDS RATIO	P-VALUE
-NICLOSAMIDE/PLACEBO	-0.9035	0.3287	0.4052	0.0060
-STUDY VILLAGE	-0.0038	0.1981	0.9962	0.9849
-SUBJECT AGE	-0.0383	0.0240	0.9624	0.1099
-TOTAL INFESTED WATER CONTACT	0.0059	0.0022	1.0060	0.0058
-LOTION APPLICATION COMPLIANCE	-0.0469	0.0873	0.9541	0.5908
-LOTION APPLICATION OBSERVATION	-0.0036	0.0155	0.996'	0.8185
-WATER CONTACT OTHER THAN UPPER AND LOWER LIMBS	0.2639	0.1770	1.3019	0.1361
-CONSTANT	5.6262	8.3693		0.5014

Table 19

S.mansoni Reinfection Rates And Odds Ratios Associated With Niclosamide in Different Compliance Categories

		98-100% Compliance			< 98% Compliance			Total		
		S.mansoni			S.mansoni			S.mansoni		
		+	-	TOTAL	+	-	TOTOAL	+	-	TOTAL
	Niclosamide	43	38	81	6	5	11	49	43	92
	Placebo	57	24	81	5	2	7	62	26	88*
Reinfection Rate	Niclosamide	53.1%			54.5%			53.3%		
	Placebo	70.4%			71.4%			70.5%		
	Odds Ratio	0.48			0.48			0.48		
	95%CI	(0.24,0.96)			(0.04,5.34)			(0.24,0.93)		
	P-VALUE	0.023			0.47			0.018		

* 6 Subjects had incomplete data

TABLE 20

S.mansoni Reinfection Rates And Odds Ratio Associated With Niclosamide In The Different Categories Of Reported Water Contact Other Than The Upper And Lower Limbs

		NO OR VERY LOW LEVEL EXPOSURE			MODERATE TO HIGH LEVEL EXPOSURE			Total		
		S.mansoni			S.mansoni			S.mansoni		
		+	-	TOTAL	+	-	TOTOAL	+	-	TOTAL
	Niclosamide	37	34	71	12	9	21	49	43	92
	Placebo	44	23	67	21	4	25	65	27	92*
Reinfection	Niclosamide		52.1%			57.1%			53.3%	
Rate	Placebo		65.7%			84%			70.6%	
	Odds Ratio		0.57			0.25			0.47	
	95%CI		(0.27,1.20)			(0.05,1.12)			(0.24,0.91)	
	P-VALUE		0.10			0.05			0.015	

* 2 Subjects had incomplete data

Table 21

S.mansoni Reinfection Rates And Odds Ratio Associated With Niclosamide Lotion In An Intention To Treat Analysis

	S.mansoni +	S.mansoni -	TOTAL
Niclosamide	55	43	98
Placebo	71	27	98

Reinfection Rate	
Niclosamide	56.1%
Placebo	72.5%
Odds Ratio	0.48
P-VALUE	0.023

FIGURE I. DESCRIPTION OF STUDY SUBJECTS

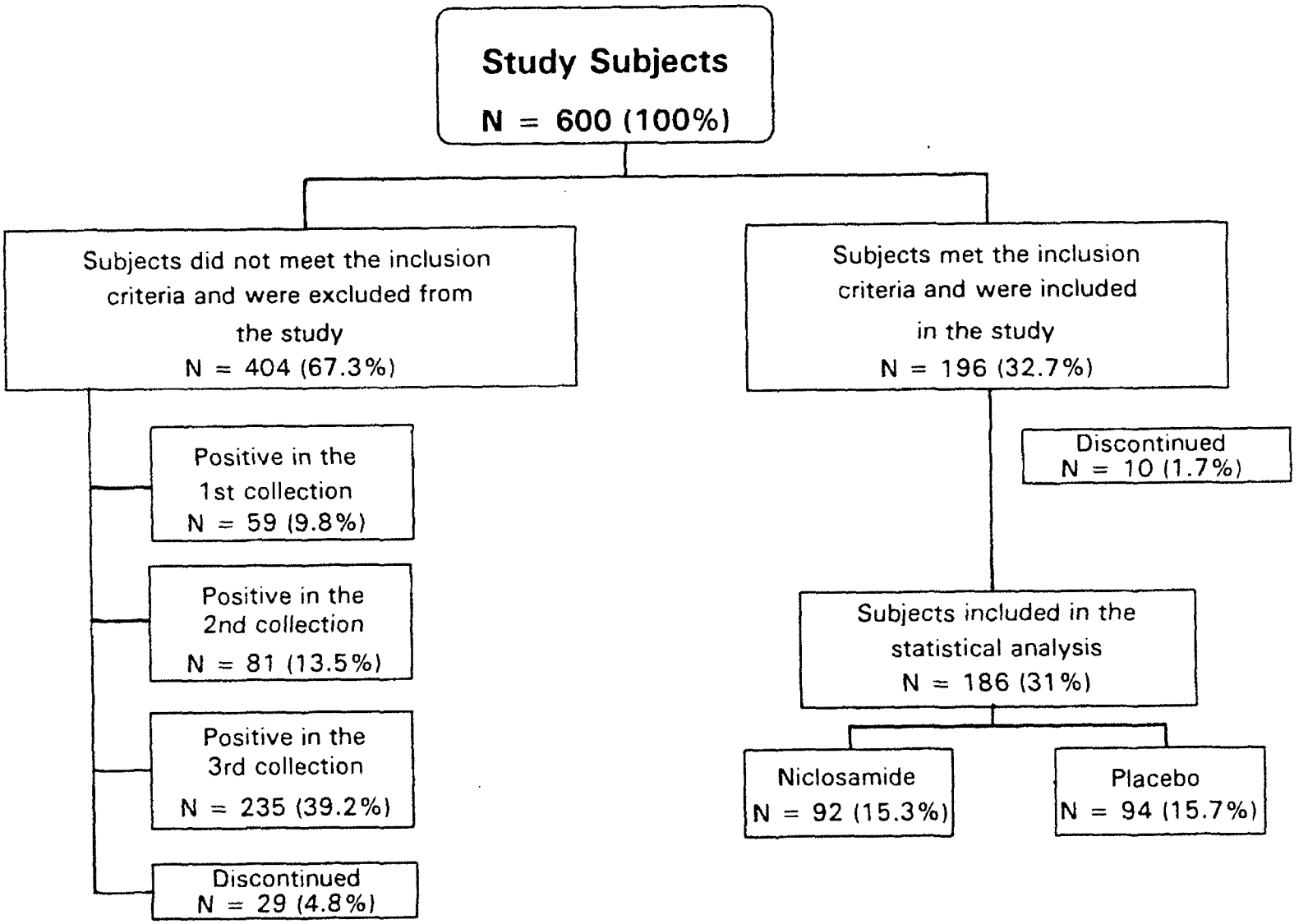
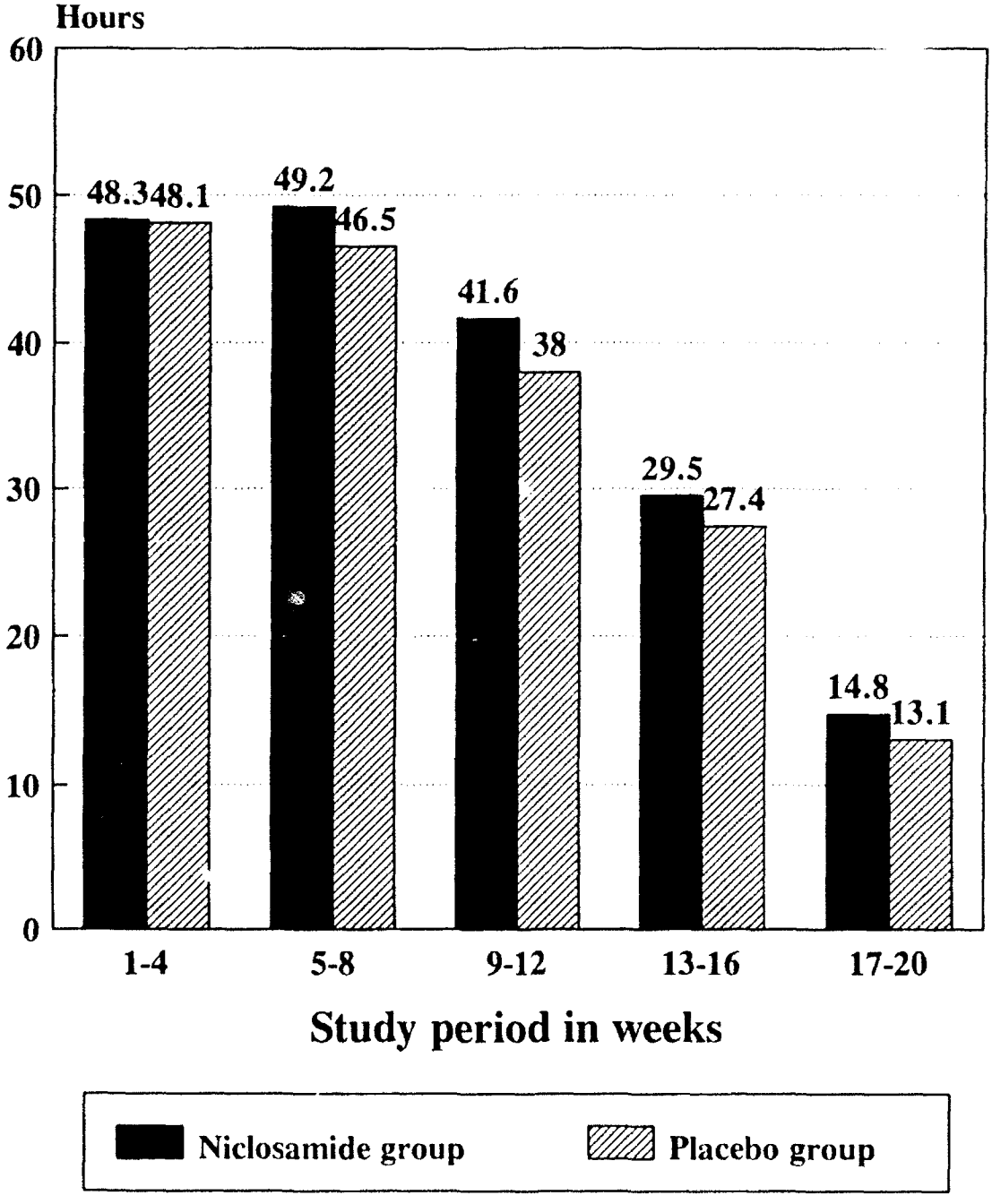


Figure II Mean water contact in hours during the study period among the Niclosamide and Placebo groups



NSN 7540-00-634-4178

HEALTH RECORD

DATE

APPENIX-1A
REPORT OF MEDICAL EXAMINATION

NOR MAL	CLINICAL EVALUATION (Check each item as appropriate or enter "NS" if not evaluated.)	ABNOR MAL
	HEAD, FACE, NECK AND SCALP	
	NOSE	
	SINUSES	
	MOUTH AND THROAT	
	EARS—GENERAL (Ext. & ext. canals) (Auditory acuity under items 70 and 71)	
	DRUMS (Perforation)	
	EYES—GENERAL (Visual acuity and refraction under items 39, 40 and 67)	
	OPHTHALMOSCOPIC	
	PUPILS (Equality and reaction)	
	OCULAR MOTILITY (Associated parallel movements, nystagmus)	
	LUNGS AND CHEST (Include breasts)	
	HEART (Thrust, size, rhythm, sounds)	
	VASCULAR SYSTEM (Varicosities, etc.)	
	ABDOMEN AND VISCERA (Include hernia)	
	ANUS AND RECTUM (Hemorrhoids, fistulae) (Prostate, if indicated)	
	ENDOCRINE SYSTEM	
	G-U SYSTEM	
	UPPER EXTREMITIES (Strength, range of motion)	
	FEET	
	LOWER EXTREMITIES (Except feet) (Strength, range of motion)	
	SPINE, OTHER MUSCULOSKELETAL	
	IDENTIFYING BODY MARKS, SCARS, TATTOOS	
	SKIN, LYMPHATICS	
	NEUROLOGIC (Equilibrium tests under item 78)	
	PSYCHIATRIC (Specify any personality deviation.)	

NOTES (Describe every abnormality in detail. Enter pertinent item number before each comment. Continue in item 73 and use additional sheets if necessary.)

History of seizures Yes No

History of skin rash Yes No

History of allergy to Niclosamide or any other drug Yes No

History of any chronic medical problems Yes No

Date of last praziquantel treatment

Signature of examining physician Date

Do not write below this line (For Use of this space for Mechanical

RECORDS MAINTAINED AT:

PATIENT'S NAME (Last, First, Middle initial) | SEX

RELATIONSHIP TO SPONSOR | STATUS | RANK/GRADE

SPONSOR'S NAME | ORGANIZATION

DEPARTMENT/SERVICE | SSN/IDENTIFICATION NO. | DATE OF BIRTH

CHRONOLOGICAL RECORD OF MEDICAL CARE

STANDARD FORM 600 (Rev. 8-84)
Prescribed by GSA and ICMR

N 7540-00-634-4178 600-10a

HEALTH RECORD	CHRONOLOGICAL RECORD OF MEDICAL CARE
DATE	SYMPTOMS, DIAGNOSIS, TREATMENT, TREATING ORGANIZATION *(Sign each entry)*

PATIENT'S IDENTIFICATION *(Use this space for Mechanical Imprint)*

RECORDS MAINTAINED AT: ▶			
PATIENT'S NAME *(Last, First, Middle initial)*			SEX
RELATIONSHIP TO SPONSOR	STATUS		RANK/GRADE
SPONSOR'S NAME		ORGANIZATION	
DEPART./SERVICE	SSN/IDENTIFICATION NO.		DATE OF BIRTH

CHRONOLOGICAL RECORD OF MEDICAL CARE **STANDARD FORM 600** (Rev. 8-84)
Prescribed by GSA and ICMR
FIRMR (41 CFR) 201-45.508

APPENDIX 2
DERMAL/SYSTEMIC REACTION RECORD

ame: _____
Subject Number: _____
Date Lotion Started: _____

	Date of Lesion	Date of Follow-up	Date of Follow-up	Date of Follow-up
Location of lesion				
Size of lesion				
Erythema formation:				
None				
Barely perceptible				
Well-defined				
Moderate to severe				
Severe (beet red)				
Edema formation:				
None				
Barely perceptible				
Slight (edges well-defined)				
Moderate (raised approx. 1.0 mm)				
Severe (raised beyond 1.0 mm)				
Other findings:				
Tender				
Weeping				
Abraded				
Generalized symptoms (describe)				
Signature of examiner, date, time				

APPENDIX 3

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION (HFN 730)
ROCKVILLE, MD 20857

ADVERSE REACTION REPORT
(Drugs and Biologics)

Form Approved OMB No. 0910-0230

FDA CONTROL NO.

ACCESSION NO.

I. REACTION INFORMATION

1. PATIENT ID/INITIALS *(In Confidence)*
2. AGE YRS
3. SEX
4-6. REACTION ONSET MO DA YR

7. DESCRIBE REACTION(S)

8-12. CHECK ALL APPROPRIATE

[ ] PATIENT DIED

[ ] REACTION TREATED WITH Rx DRUG

[ ] RESULTED IN, OR PROLONGED, INPATIENT HOSPITALIZATION

[ ] RESULTED IN PERMANENT DISABILITY

[ ] NONE OF THE ABOVE

13. RELEVANT TESTS/LABORATORY DATA

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) *(Give manufacturer and lot no. for vaccines/biologics)*
15. DAILY DOSE
16. ROUTE OF ADMINISTRATION
17. INDICATION(S) FOR USE
18. DATES OF ADMINISTRATION *(From/To)*
19. DURATION OF ADMINISTRATION
20. DID REACTION ABATE AFTER STOPPING DRUG?

[ ] YES [ ] NO [ ] NA

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?

[ ] YES [ ] NO [ ] NA

III. CONCOMITANT DRUGS AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION *(Exclude those used to treat reaction)*
23. OTHER RELEVANT HISTORY *(e.g. diagnoses, allergies, pregnancy with LMP, etc.)*

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24. NAME AND ADDRESS OF MANUFACTURER *(Include Zip Code)*

24a. IND/NDA NO. FOR SUSPECT DRUG

24b. MFR. CONTROL NO.

24c. DATE RECEIVED BY MANUFACTURER

24d. REPORT SOURCE *(Check all that apply)*

[ ] FOREIGN [ ] STUDY [ ] LITERATURE

[ ] HEALTH PROFESSIONAL [ ] CONSUMER

25. 15 DAY REPORT?

[ ] YES [ ] NO

25a. REPORT TYPE

[ ] INITIAL [ ] FOLLOWUP

V. INITIAL REPORTER *(In confidence)*

26, 26a. NAME AND ADDRESS OF REPORTER *(Include Zip Code)*

26b. TELEPHONE NO. *(Include area code)*

26c. HAVE YOU ALSO REPORTED THIS REACTION TO THE MANUFACTURER?

[ ] YES [ ] NO

26d. ARE YOU A HEALTH PROFESSIONAL?

[ ] YES [ ] NO

Submission of a report does not necessarily constitute an admission that the drug caused the adverse reaction.

NOTE: Required of manufacturers by 21 CFR 314.80

FORM FDA 1639 (7/86)   PREVIOUS EDITION MAY BE USED

APPENDIX 4

DATES FOR SPECIMEN COLLECTION

	Anwar-El-Mofty	Desones	Kom El-Kanater
First Collection	Sat 6/29 Sun 6/30 Mon 7/01	Tue 7/09 Wed 7/10 Thur 7/11	Sat 7/20 Sun 7/21 Mon 7/22
Second Collection	Tue 7/30 Wed 7/31 Thur 8/01	Sat 8/10 Sun 8/11 Mon 8/12	Tue 8/20 Wed 8/21 Thur 8/22
Third Collection	Sat 8/31 Sun 9/01 Mon 9/02	Tue 9/10 Wed 9/11 Thur 9/13	Sat 9/21 Sun 9/22 Mon 9/23
Fourth Collection	Tue 10/01 Wed 10/02 Thur 10/03	Sat 10/13 Sun 10/14 Mon 10/15	Tue 10/22 Wed 10/23 Thur 10/24
Fifth Collection	Sat 11/02 Sun 11/03 Mon 11/04	Tue 11/13 Wed 11/14 Thur 11/15	Sat 11/22 Sun 11/23 Mon 11/24
Sixth Collection	Tue 12/03 Wed 12/04 Thur 12/05	Sat 12/14 Sun 12/15 Mon 12/16	Tue 12/24 Wed 12/25 Thur 12/26
Seventh Collection	Sat 1/04 Sun 1/05 Mon 1/06	Tue 1/14 Wed 1/15 Thur 1/16	Sat 1/25 Sun 1/26 Mon 1/27
Eighth Collection	Tue 2/04 Wed 2/05 Thur 2/06	Sat 2/15 Sun 2/16 Mon 2/17	Tue 2/25 Wed 2/26 Thur 2/27

APPENDIX 5

FORMOL-ETHER CONCENTRATION METHOD FOR S. MANSONI

1,2) Add 1 ml (exactly) of feces to 7 ml of 10% formol-saline (0.9%) in a calibrated 15 ml centrifuge tube (by displacing the liquid level to the 8 ml line) and mix thoroughly.

3) Place a small circular piece of stainless steel wire mesh (40 mesh/in^2) directly into a plastic funnel. Strain feces through the wire mesh and collect in another 15 ml centrifuge tube.

4) Use a trigger spray bottle for the formol saline solution to break up large particles and force them through the mesh.

5) Centrifuge for 3 minutes at 2,000 rpm and decant.

6) Add formol-saline to the sediment up to 12 ml, mix well, centrifuge for another 3 minutes at 2,000 rpm and decant again.

7) Add 8 ml of buffered alcohol solution, break up the sediment with an applicator stick, and add 4 ml of ether.

8) Shake well and then centrifuge at 1,500 rpm for 1 minute.

9) Decant ether, debris, and solution and wipe the inside of the tube clean with a cotton swab.

10) Dilute sediment with about 3 ml of normal saline.

11) Strain through the 200/in^2 screen into a clean 15 ml centrifuge tube.

12) Force the sediment through the screen with the help of a trigger-spray bottle. To facilitate the procedure, affix the screen to the inside of a short length of plastic tubing (Fig 1).

13) Sediment the filtrate by gravity for 15 minutes.

14) Draw off the supernatant by means of a vacuum or pipette.

15) Remove the sediment to the slide with a Pasteur pipette.

16) Rinse the tube with a few drops of saline to help remove the last bit of sediment.

17) Stain slightly with Lugol's solution.

18) Place 22 X 60 mm cover slip on the sediment.

19) Count the eggs in the entire sediment.

APPENDIX 6A

INFORMED CONSENT

PATIENT NAME: _____ TODAY'S DATE: _____

PATIENT ADDRESS: _____ DATE OF BIRTH: _____

PROJECT TITLE: Placebo-controlled double blind study to determine the efficacy of topical niclosamide 1% lotion in the prevention of naturally occurring schistosomiasis in Egyptian farmers

PROCEDURES:

1. I have been asked to participate in a medical research study being conducted by NAMRU-3 and the Ministry of Health Field Research Section on the prevention of schistosomiasis by means of a lotion applied daily to the arms and legs to prevent schistosome penetration of skin. The experimental preparation is being used under the regulations of the U.S. Food and Drug Administration.

2. I understand that total avoidance of potentially schistosome infested fresh water is the best measure to avoid infection. Also the use of protective boots, gloves and clothing would offer protection against infection. Fully aware of this information, I choose to work in water associated agriculture activities without water avoidance or protective measures as a matter of personal choice. I will participate in this study and apply a lotion to my arms and legs as part of an evaluation of a new medication-lotion that may be effective in preventing infection.

3. I understand that voluntary participation is requested and if I agree to participate the following procedures will be conducted:

a. An entry physical examination.
b. Regular observations by study monitor of lotion application for 6 months.
c. Regular reporting of daily water contact to study monitor.
d. Immediate reporting of any skin reactions or generalized responses to lotion.
e. Follow-up for four months following lotion application with an initial and final urine specimen and stool specimens provided every four weeks.
f. Discontinuation of lotion and notification of monitor on the development of a skin reaction.
g. Notification of study physician prior to taking any medications during the study period.

4. I understand that I will receive by chance, according to a number I am assigned, either niclosamide lotion or plain lotion without niclosamide, to be applied daily to my arms and legs.

5. I understand that I will allow a study observer to show me how

to apply the lotion and observe me apply it. I will apply the lotion as instructed. I will also provide 3 consecutive daily stool samples every four weeks for nine months and 3 consecutive daily urine samples at the start and the end of the study. Also I will inform the study observer of the total amount of hours each day I am in contact with irrigation water.

DISCOMFORTS AND RISKS:

I understand that some side effects may occur from the lotion such as a rash, itching, redness, or swelling. I agree to notify the study monitor very soon after the occurence of such skin reactions and will not use the lotion or contact irrigation water until my skin is clear and I am given permission from the study physician. I also understand that NAMRU-3 will provide the necessary health care for medical problems resulting from treatment with lotion including general reactions and skin reactions.

BENEFITS:

I understand that this study will be of no direct benefit to me with the exception of obtaining free diagnosis and treatment for schistosomiasis infection.

CONFIDENTIALITY:

I understand that medical information obtained during my participation in this study will be kept confidential and my name will not be used in any published report. Representatives of the Egyptian Ministry of Health, U.S. Food and Drug Administration and the U.S. Army Medical Research and Development Command may inspect the records of this study.

STATEMENT OF VOLUNTARY PARTICIPATION:

I understand that participation in this project is entirely voluntary. I may refuse or discontinue participation at anytime. I understand that NAMRU-3 will provide all necessary medical care for injury or illness which is the direct result of application of the study lotion. I have recieved a copy of this consent form. I agree to participate in this project.

SIGNATURE OF PATIENT: _____ DATE: _____

TYPED/PRINTED NAME OF PATIENT: _____

PERMANENT ADDRESS OF PATIENT: _____

_____

SIGNATURE OF WITNESS: _____ DATE: _____

TYPED/PRINTED NAME OF WITNESS: _____

SIGNATURE OF CARE PROVIDER OBTAINING CONSENT: _____

APPENDIX-6b

اقرار بالموافقة على الإشتراك في الدراسة

اسم المريض: ____________ التاريخ: ____________

العنوان: ____________ تاريخ الميلاد: ____________

عنوان الدراسة: دراسة عشوائية مزدوجة لتحديد مدى فاعلية الدهان الموضعي الذي يحتوي على ١% نيكلوساميد للوقاية من مرض البلهارسيا الذي يصيب المزارعين المصريين.

الإجراءات:

١. لقد طلب مني الإشتراك في الدراسة الطبية التي تجريها وحدة الأبحاث الطبية للبحرية الأمريكية رقم ٣ "نامرو٣" والإدارة العامة لمكافحة البلهارسيا بوزارة الصحة للوقاية من البلهارسيا وذلك باستخدام دهان يوضع يوميا على الذراعين و الساقين للحيلولة دون اختراق السركاريا للجلد، وقد استخدم المركب التجريبي طبقا للوائح الخاصة بهيئة الأغذية و العقاقير الأمريكية.

٢. انا اعلم أن أفضل وسيلة للوقاية من البلهارسيا هي تجنب المياه العذبة التي بها عدوى البلهارسيا كما أن استخدام الأحذية العالية (البوت) و القفازات و الملابس الواقية توفر الحماية من هذا المرض. ورغم علمي بذلك فانني اخترت أن استعمل هذه المياه في أعمال الزراعة بدون استخدام أي وسائل وقائية. و سوف اشترك في هذه الدراسة بوضع الدهان على ذراعي و ساقي بهدف تقييم فاعلية هذا العلاج الجديد الذي قد يكون فعال لمنع الإصابة بالبلهارسيا.

٣. كما اعلم أن هذه الدراسة تتطلب اشتراكي التطوعي، و اذا ما وافقت على الإشتراك سوف التزم بالآتي:

ا - اجراء كشف طبي في بداية اشتراكي بالدراسة.

ب - ملاحظة دورية بواسطة مسئول البحث لإستخدام الدهان بشكل سليم.

ج - ابلاغ مسئول البحث على نحو منتظم بمدة التعرض للمياه يوميا.

د - الإبلاغ فورا عن أي مضاعفات جلدية أو عامة للدهان.

ه - المشاركة لمدة اربعة شهور بعد وضع الدهان مع تقديم عينات الدم و عينات البول و عينات من البراز كل اربعة اسابيع.

و - الإمتناع عن الدهان و ابلاغ مسئول البحث عند حدوث أي تطورات في المضاعفات الجلدية.

ز - ابلاغ الطبيب المسئول عن البحث قبل أخذ أي نوع من الادوية خلال فترة البحث.

٤. انا افهم انني سوف اعطى على نحو عشوائي حسب رقمي اما دهان يحتوي على النيكلوساميد أو دهان غير فعال لا يحتوي على مادة النيكلوساميد و ذلك لدهان الذراعين و الساقين يوميا.

APPENDIX 7a
SUBJECT DAILY LOG

Name _____ Subject No. __ __ __ __

Village _____ Week No. __ __

Date	___/___/___	___/___/___	___/___/___
Time of visit	_____	_____	_____

	Yes	No	Yes	No	Yes	No
Application of lotion	[]	[]	[]	[]	[]	[]
Lotion application observed	[]	[]	[]	[]	[]	[]
Presence of local skin reactions	[]	[]	[]	[]	[]	[]
Presence of systemic reactions	[]	[]	[]	[]	[]	[]

Estimated time spent in irrigation or canal water contact in previous day _____ _____ _____

	Yes	No	Yes	No	Yes	No
Used vials (7) collected	[]	[]	[]	[]	[]	[]

1st Observation
Time _____ _____ _____
Activity Observed _____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____

2nd Observation
Time _____ _____ _____
Activity Observed _____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____

Time of evening interview _____ _____ _____

Estimated time spent in irrigation or canal water contact this day _____ _____ _____

Name of field monitor _____ _____ _____

APPENDIX 7B

نموذج التسجيل اليومي

الاسم : _____ الرقم : ____/____

اسم القرية : _____ رقم الأسبوع : __ __

التاريخ : ____/____/____ ____/____/____ ____/____/____

وقت الزيارة : _____ _____ _____

	نعم	لا	نعم	لا	نعم	لا
هل تم الدهان بالكريم	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
مشاهدة الدهان بالكريم	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
وجود مصانع بلدية	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]
وجود مصانع خاصة	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]

الوقت الذي قضي في الري _____ _____ _____
او صيان الشرقة في _____ _____ _____
اليوم السابق

	نعم	لا	نعم	لا	نعم	لا
تم جمع العينات الغارقة	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]

المشاهدة الاولى
الوقت _____ _____ _____
نوع العمل _____ _____ _____
_____ _____ _____
_____ _____ _____

المشاهدة الثانية
الوقت _____ _____ _____
نوع العمل _____ _____ _____
_____ _____ _____
_____ _____ _____

وقت التدخين المستخدم _____ _____ _____

الوقت الذي قضي في الري _____ _____ _____
او صيان الشرقة اليوم _____ _____ _____

اسم المشرف _____ _____ _____