Mass Therapy in Attempted Control of Amebiasis in a Mental Institution

M. M. BROOKE, Sc.D., RALPH H. HEEREN, M.D., GRACE M. SAWYER, M.D., and DORTHEA STONER, B.S.

DEMONSTRATION of 25 laboratory proved cases of clinical amebiasis in an Iowa State institution for the feebleminded initiated a cooperative control program. An epidemiological investigation, including examination of stool specimens, revealed that 64 percent of the males and 34.4 percent of the females in two buildings occupied by the more retarded patients were infected with *Entamoeba histolytica*. Experience with clinical cases had shown that the problem was not limited to any one building or area of the institution and, because of the poor personal hygiene of many of the patients, it was not believed that recommended methods of improving sanitation would stop the transmission of intestinal pathogens. It was therefore decided to attempt to control the situation through mass therapy of all the institution's residents.

The Institution

The institution, a hospital and school, is situated on 1,000 acres of land 40 miles north of Des Moines, Iowa. It has dormitories for patients, school buildings, a home for employees, and an administration building with separate hospital wards for men and women and dental, X-ray, and modern medical laboratories. Auxiliary buildings house the power plant, water filtration system, dairy, and farm equipment. Patients reside in sturdily constructed 2-or 3-story brick dormitories, which are well separated on beautifully landscaped grounds. Inside, the buildings are well kept, despite overcrowding at times. Each dormitory has its own kitchen, operated by an employed cook and supervised by the dietitian. Most buildings have a dining room on each floor.

In 1951–53, the period of the study, there were approximately 1,600 feebleminded and epileptic patients in the institution, ranging in age from 1 month to 80 years. Men and women patients were approximately equal in number. The 262 employees included 22 professional individuals, among them 9 physicians, 6 registered nurses, and a dietitian, and 105 supervisors or attendants in the dormitory buildings. Patients helped in such activities as serving food, washing dishes, feeding bedridden patients, cleaning floors, and changing beds.

Patients in a given dormitory were somewhat comparable mentally and physically. The pop-

Dr. Brooke is chief of the Microbiology Section, Laboratory Branch, Communicable Disease Center, Public Health Service, Atlanta, Ga.; Dr. Heeren is director, division of preventable diseases, Iowa State Department of Health, Des Moines; Dr. Sawyer is superintendent, and Mrs. Stoner is medical technician, Woodward State Hospital and School, Woodward, Iowa. *Mrs. Sadie Johnson Geiger, Public Health Service Communicable Disease Center, gave technical assistance, and Miss Helen Bradley, formerly of the Iowa State Health Department, kept careful records during the study.*

ulation composition of the eight dormitories was:

Type of patient	Buildings: Male patients	Buildings: Female patients
Laundry, dairy, and garden workers.	Birches	Larches
School children	Hemlock	Westwood
Delinquent and low grade	Oak Hall	Maple Lodge
Low grade	Pinehurst	Elm Crest

Although the personal hygiene of patients in Birches and Larches Buildings was almost equal to that of normal individuals, the personal hygiene of those in Pinehurst and Elm Crest Buildings was very poor. Fecal incontinence was common with 67 percent of the males in Pinehurst and 49 percent of the females in Elm Crest. These patients soiled their beds and clothing with urine or feces, or both. Some were not averse to coprophagy. The personal hygiene of the patients in Oak Hall and Maple Lodge was not much better, but the hygiene of those in Hemlock and Westwood compared favorably with that of the patients in Birches and Larches. Larches was recognized as the "best building" in every respect.

A trial of mass therapy was planned in Pinehurst, the building with the known highest prevalence of *E. histolytica*. Oxytetracycline was selected for use in view of the report by Tobie and co-workers (*1*) of the virtual elimination of *E. histolytica* in a similar institution at Wassaic, N. Y., by mass therapy with this antibiotic. Two preliminary trials of mass therapy in Pinehurst Building, with 6-month followup, failed to confirm Tobie's work. Therefore, in extending mass therapy to the entire institution, it was decided to administer more than 1 drug at 6-month intervals on 2 occasions. Although the primary objective of the investigation was control of amebiasis, an effort was made to obtain information on the comparative effectiveness of the drugs employed.

Realizing that opportunities for reinfection probably varied from building to building, drugs were randomly assigned to the patients in 4 of the 8 buildings. These patients, constituting the principal study group, were examined to determine both the results of control measures and the relative effectiveness of the drugs. In the other four buildings, a single drug was used to treat all patients in a building, and patients were examined to determine the degree of control obtained by mass therapy.

Drugs

Three standard amebicidal drugs were given, singly or in combination of two of the three (*2*, *3*). These were oxytetracycline, carbarsone, iodochlorhydroxyquin, or oxytetracycline and carbarsone combined. The dosages were in accordance with the recommendations of Dr. Harry Most of New York University, Communicable Disease Center consultant.

The four therapeutic regimens were administered according to the weights of the patients (table 1). Two formulations of oxytetracyline were used. During the first treatment period in Pinehurst, the 250-mg. capsules were found to be too large for many of the younger patients to swallow, and it was sometimes necessary to mix the contents of the capsules with water. Therefore, oral drops of oxytetracycline were provided for the younger patients and others having difficulty in swallowing. The carbarsone and iodochlorhydroxyquin capsules were swallowed without difficulty. All medication was followed by a glass of water or fruit juice and by examination of the mouths of the patients to make certain that the drugs had been swallowed.

During preliminary trials of mass therapy in Pinehurst, one-half of the daily dosage was

Table 1. Dosages of four amebicidal drug regimens

Drug	Weight of patients (pounds)	Dosage
Oxytetracycline	>70	2 gm. per day for 10 days.
	<70	1 gm. per day for 10 days.
Oxytetracycline and carbarsone	>70	2 gm. oxytetracycline per day for 5 days. 1 gm. carbarsone per day for 10 days.
	<70	1 gm. oxytetracycline per day for 5 days. 0.5 gm. carbarsone per day for 10 days.
Carbarsone	>70	1 gm. per day for 10 days.
	<70	0.5 gm. per day for 10 days
Iodochlorhydroxyquin	>70	1 gm. per day for 10 days.
	<70	0.5 gm. per day for 10 days

given in the morning and the other half in the afternoon. During mass therapy of the entire institution, the daily dosages had to be administered at one time, usually in the morning. A record clerk was always present to record the amount of medication received. Although a physician or a registered nurse was also present, supervisors and attendants often administered the drugs since they knew the idiosyncrasies of the patients and were best able to gain their cooperation.

Before instituting mass therapy in a building, the physician in charge checked the medication for each patient and made any necessary changes. Usually, recommended dosages (table 1) were given the older patients and those in good physical condition, but for very young or debilitated patients, dosages were reduced according to body weight.

When more than one drug was given, the physician changed the randomly assigned drug for persons for whom he considered its use contraindicated. At least once a day during the treatment period, the records of each patient were examined and he was seen by the attending physician. If intolerance to the medication was observed, therapy was changed or withdrawn. However, this was done for less than 3 percent of the patients, none of whom had been selected for examination.

Employees were encouraged to participate in the amebiasis control program by taking one of the medications. If they preferred, they could submit three specimens to the hospital laboratory for examination and, if the specimen was found to be positive for *E. histolytica*, they could be treated by their private physicians.

Collecting and Examining Specimens

Identical methods of collecting and examining fecal specimens were used throughout the study. In order to insure correct identification, specimens were collected in the presence of the ward supervisor or attendant and were brought immediately to a technician stationed in the building. The technician knew the building from which the specimens originated but did not know the drug regimen received. One portion of each specimen was preserved in 5 percent formalin and another in PVA fixative (*4*), and both portions were forwarded to the parasitology laboratories of the Communicable Disease Center, Chamblee, Ga.

The portions of feces preserved in formalin were concentrated by the formalin-ether sedimentation technique (*5*). Heidenhain iron-hematoxylin-stained films were prepared from the portions of feces preserved in PVA fixative and were examined with 50× and 95× oil immersion objectives. Unstained and iodine-stained wet mounts prepared from the concentrate sediments and Heidenhain iron-hematoxylin-stained films were examined for a minimum of 15 minutes each.

Preliminary Trials

Because of the results of Tobie's study (*1*), it was planned to evaluate the effectiveness of mass therapy through observation of the patients in Pinehurst Building during a 12-month post-treatment period. However, since the infection in Pinehurst was returning to a high level at the end of 3 months, the patients were re-treated 6 months after the first medication. During the first course of therapy, the antibiotic was given in 250-mg. capsules; during the second course, in oral drops. On each occasion, all patients, supervisors, and attendants received a 10-day course of the drug, the dosage depending on the weight and general condition of the patient.

During the 6 months following therapy, new admissions to Pinehurst were kept at a minimum. Any persons who had to be placed in the building were started on a 10-day course of medication 3 days before they were admitted. Also, during this period, the physician in charge was asked to withhold amebicidal drugs from all persons except those with active clinical amebiasis.

In order to evaluate the effectiveness of mass therapy, 125 patients were randomly selected for examination prior to therapy and again 1 month, 3 months, and 6 months after therapy was started. At each examination only 1 specimen was collected from each patient.

Of these 125 patients, 101 submitted specimens at each collection period during the 12 months of the two therapeutic trials. Intesti-

nal parasites were found in 93 of 101 patients, as follows:

Entamoeba histolytica	64
Entamoeba coli	75
Endolimax nana	63
Iodamoeba buetschlii	26
Dientamoeba fragilis	3
Giardia lamblia	11
Chilomastix mesnili	19
E. histolytica, E. coli, or *E. nana* [1]	90

[1] Amebic prevalence rate (*6*).

For possible future comparison with other studies, there are included in the preceding tabulation and in table 3 figures for amebic prevalence (*6*). In determining this prevalence rate, a person infected with *E. histolytica*, *Entamoeba coli*, or *Endolimax nana* is counted as a single positive individual. Figure 1 shows the individual prevalence rates of these parasites at each examination.

Prior to the first mass therapy with oxytetracycline capsules, 64 percent of the patients in Pinehurst were positive for *E. histolytica;* 1 month after the beginning of therapy, 4 percent were positive; 3 months after, 18 percent; and 6 months after, 33 percent.

The week following the 6-month collection of specimens, the second mass therapy with oxytetracycline (oral drops) was administered. One month later, the prevalence of *E. histolytica* was reduced to 5 percent but, again, by the end of the 6-month post-treatment period, the rate had risen to approximately one-half of the pretreatment prevalence rate, or 19 percent. The graphs for the prevalence rates of *E. coli* and *E. nana* are similar to that for *E. histolytica.* However, by the end of only 3 months after each medication, the prevalence rates for these two amebae had almost regained the pretreatment levels.

Mass therapy with oxytetracycline had a marked effect upon *Iodamoeba buetschlii*, but apparently none on *Chilomastix mesnili* and *Giardia lamblia.* Prior to the first course of therapy, 26 of the 101 patients who submitted specimens were infected with *I. buetschlii;* 1 month and 3 months after treatment with oxytetracycline, 2 infections were found but none was observed at the next 4 examinations (9 months). The infections with *Dientamoeba fragilis* were too few for consideration.

Table 2. Results of mass therapy with oxytetracycline in Pinehurst Building

Organism	Response in known positives		
	Number positive pretreatment [1]	Percent negative post-treatment	
		1 month later	6 months later
Entamoeba histolytica	97	94.8	70.1
Entamoeba coli	151	63.6	15.9
Endolimax nana	130	49.2	26.9

[1] Sum of positives prior to first and second preliminary trials of mass therapy.

Table 2 presents the observed effectiveness of mass therapy in individuals known to be positive for *E. histolytica* prior to two courses of therapy. Of the 97 patients known to be infected, 94.8 percent were "negative" 1 month later, and 70.1 percent were "negative" 6 months later. The effectiveness of therapy on *E. coli* and *E. nana* was significantly poorer, particularly at the end of 6 months.

Mass Therapy

In extending mass therapy to the entire institution, the 4 drug regimens were administered on 2 occasions 6 months apart. The second time, each patient received a different drug regimen from that he had received previously. The preliminary trials in Pinehurst had indicated that the effectiveness of mass therapy in controlling amebiasis might be determined by examining specimens collected 6 months after therapy. Therefore, specimens were examined the week prior to the first therapy, 6 months after the first therapy and just prior to the second therapy, and 6 months after the second therapy. At each examination, a single specimen was collected from as many as possible of the individuals who had been selected for examination.

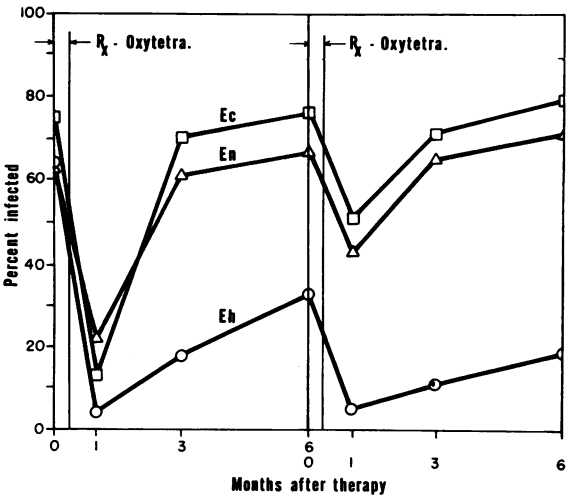
Table 3 records the intestinal parasites found in the randomly selected patients in the eight dormitory buildings prior to mass therapy throughout the institution. The prevalence rate for *E. histolytica* ranged from 7 percent in Larches to 46 percent in Oak Hall. At the time

of this examination, Pinehurst residents had already received two courses of therapy. The initial rate for this parasite in Pinehurst had been approximately 64 percent (fig. 1).

During the 12 months following the first course of therapy in the entire institution, all new admissions received the combination therapy of oxytetracycline and carbarsone for 3 days preceding admission to a dormitory.

Although control of amebiasis was the primary objective of the study, an attempt was made to obtain information on the relative effectiveness of the four drug regimens. Preliminary surveys had demonstrated that the prevalence of intestinal amebae varied from building to building in almost direct relationship to the general level of personal hygiene of the patients. Therefore, the dormitories were divided into 2 groups of 4 multiple-therapy buildings and 4 single-therapy buildings.

Figure 1. Results of two preliminary trials of mass therapy with oxytetracycline in one building of a mental institution. Incidence of Entamoeba histolytica, Entamoeba coli, and Endolimax nana prior to medication and during the 6-month post-treatment period.



Multiple-Therapy Buildings

Because the general type of patients varied from building to building, the influence of reinfection on drug evaluation was equalized by randomly assigning all 4 therapeutic regimens to the patients in 4 of the 8 buildings. Birches, Hemlock, Larches, and Westwood dormitories, which housed the higher grade patients, were selected since it was thought that reinfection would be reduced to a minimum in these buildings. Each time mass therapy was given, all

Table 3. Prevalence of intestinal parasites in a mental institution prior to mass therapy, by building

Observations	Four drug regimens				Single drug regimen				
	Larches (female)	Westwood (female)	Hemlock (male)	Birches (male)	Maple Lodge (female)	Elm Crest (female)	Oak Hall (male)	Pinehurst [1] (male)	Total
Number patients	187	267	168	247	159	179	202	207	1,616
Number examined	117	116	119	118	50	47	50	50	667
Percent positive	62.4	87.9	70.6	77.1	70.0	74.5	72.0	82.0	74.5
	Percent								
Organisms identified									
Entamoeba histolytica	6.8	49.1	23.5	27.1	24.0	29.8	46.0	[2] 34.0	28.6
Entamoeba coli	47.0	54.3	45.4	54.2	50.0	40.4	52.0	78.0	51.7
Endolimax nana	12.0	44.8	36.1	32.2	32.0	46.8	18.0	46.0	32.5
Iodamoeba buetschlii	2.6	4.3	10.1	5.9	2.0	0.0	18.0	0.0	5.5
Dientamoeba fragilis	12.0	9.5	12.6	8.5	2.0	0.0	4.0	10.0	8.7
Giardia lamblia	0.0	19.2	14.3	11.0	6.0	8.5	2.0	18.0	10.3
Chilomastix mesnili	14.5	11.2	13.4	7.6	10.0	12.8	12.0	24.0	12.6
E. histolytica, E. coli, E. nana [3]	53.8	80.2	62.2	67.8	62.0	63.8	70.0	80.0	66.9

[1] Patients in Pinehurst had been treated twice previously.
[2] Rate preceding preliminary trials, 64 percent.
[3] Amebic prevalence rate (*6*).

four drug regimens were employed in each building. For the second course of therapy, each patient received a different drug, according to the following schedule:

First course	*Second course*
Oxytetracycline	Carbarsone
Oxytetracycline and carbarsone.	Iodochlorhydroxyquin
Carbarsone	Oxytetracycline and carbarsone
Iodochlorhydroxyquin.	Oxytetracycline

To evaluate the control program within each building, approximately 30 individuals on each of the drug regimens were randomly selected for examination, or a total of approximately 120 persons on each regimen. In all, over one-half of the 869 individuals in the four buildings were selected.

Single-Therapy Buildings

In Elm Crest, Maple Lodge, Oak Hall, and Pinehurst Buildings, which housed the lower grade patients, a single drug regimen was administered at each of the two mass therapy periods. The drugs were changed in each building on the second occasion. To appraise the effectiveness of control of amebiasis, 50 individuals in each building, or approximately 200 of the 747 persons in the 4 buildings, were randomly selected to submit specimens during the 3 designated periods.

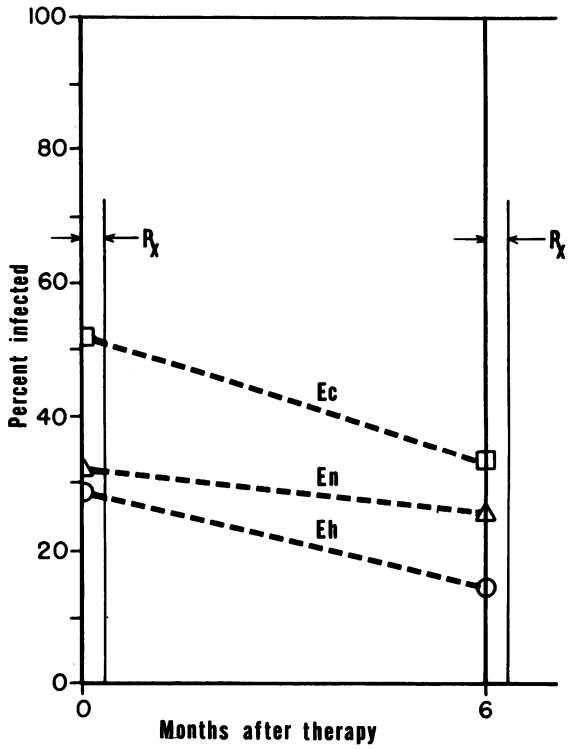
Results of Mass Therapy

The results of treatment with 4 drug regimens and with 1 drug regimen are given below.

Four Drug Regimens

Oxytetracycline, carbarsone, iodochlorhydroxyquin, and oxytetracycline and carbarsone combined were given to the patients in Larches, Westwood, Hemlock, and Birches Buildings on two occasions. Figure 2 shows the prevalence rates of *E. histolytica*, *E. coli*, and *E. nana* prior to the first course of therapy and 6 months later, based on the examination of 502 and 468 individuals, respectively. Dash lines are used in figures 2 and 3 since the lines do not indicate actual prevalence trends during the 6 months between examinations. From the experience in Pinehurst Building, it is reasonable

Figure 2. Results of mass therapy with four drug regimens in four buildings of a mental institution. Incidence of Entamoeba histolytica, Entamoeba coli, and Endolimax nana prior to medication and 6 months afterward.



to assume that an immediate decided drop in the prevalence of amebiasis after therapy was followed by a rise.

Prior to the first administration of the drugs, the average prevalence rate of *E. histolytica* in the four buildings was 28.8 percent (fig. 2). Six months later it was 14.4 percent. The prevalence of *E. coli* was also reduced significantly, but not the prevalence of *E. nana*. *I. buetschlii* was practically eliminated, being reduced from 5.7 percent to 0.5 percent; *G. lamblia* and *C. mesnili* were reduced slightly; and the rate for *D. fragilis* remained unchanged. Six months after therapy no infections of *E. histolytica* were found in the patients examined from Larches and the lower floors of Hemlock and Birches Buildings.

After the 6-month post-treatment examination, all patients were re-treated with another drug regimen. Six months later, because of pressure of other work, stool specimens were collected only from the problem areas revealed

by earlier examination. These included all floors of Westwood and the upper floors of Hemlock and Birches. No specimens were collected from Larches. Hence, it is not possible to extend the graph in figure 2 to indicate the prevalence rates at the second 6-month post-treatment period.

The relative effectiveness of mass therapy in these buildings is demonstrated in table 4. Since there were no significant differences between the response to the first and second administrations of mass therapy, the results are combined. Therapy was significantly more effective in Larches and in Hemlock than in the other 2 buildings for practically all species except *I. buetschlii*, which was apparently eliminated in all 4 buildings. All known infections of *E. histolytica* in Larches were "negative" 6 months after the first therapy.

In table 5 are recorded the results of the individual drug regimens in reducing known infections regardless of location. In only one instance, oxytetracycline against *D. fragilis*, was one drug observed to be significantly more effective than the others. Mass therapy, regardless of the drugs administered, was more effective against certain species than against others. For example, therapy was significantly better against *E. histolytica* (62.5 percent "negative"), than against *E. coli* (50.8 percent) and *E. nana* (48.8 percent), while all known infections of *I. buetschlii* were apparently eliminated by therapy. The results of therapy in the individual buildings are based on too small a sample for analysis.

Single Drug Regimens

A single drug regimen was administered to the patients in Maple Lodge, Elm Crest, Oak Hall, and Pinehurst Buildings on each of the two occasions of mass therapy. Figure 3 presents the prevalence rates of *E. histolytica*, *E. coli*, and *E. nana* in approximately 50 randomly selected patients in each building before and 6 months after each course of therapy. At the end of 12 months a significant reduction in the prevalence of *E. histolytica* was observed in Oak Hall and Elm Crest Buildings, with possible elimination of the parasite in Maple Lodge. An increase in prevalence apparently occurred in Pinehurst during the same period.

In Maple Lodge, prior to therapy with the combination of oxytetracycline and carbarsone, the prevalence rate of *E. histolytica* was 24 per-

Table 4. Results of two courses of mass therapy with four drug regimens randomly administered to all patients in Birches, Hemlock, Larches, and Westwood Buildings

Organism	Response in known positives [1]							
	Birches		Hemlock		Larches [2]		Westwood	
	Number positive, pre-treatment	Percent negative, post-treatment [3]	Number positive, pre-treatment	Percent negative, post-treatment [3]	Number positive, pre-treatment	Percent negative, post-treatment [3]	Number positive, pre-treatment	Percent negative, post-treatment [3]
Total protozoa	237	54. 0	217	69. 1	108	79. 6	405	48. 9
Amebae	207	52. 2	177	69. 5	92	81. 5	344	46. 8
Entamoeba histolytica	45	73. 3	29	93. 1	7	100. 0	95	45. 3
Entamoeba coli	87	34. 5	72	63. 5	53	84. 9	117	40. 2
Endolimax nana	53	49. 1	49	55. 1	16	62. 5	95	43. 2
Iodamoeba buetschlii	7	100. 0	12	100. 0	2	100. 0	6	100. 0
Dientamoeba fragilis	15	80. 0	15	80. 0	14	78. 6	31	77. 4
Flagellates	30	66. 7	40	67. 5	16	68. 8	61	60. 7
Giardia lamblia	16	53. 3	21	66. 7	0	------	39	56. 4
Chilomastix mesnili	14	78. 6	19	68. 4	16	68. 8	22	68. 2

[1] Sum of positives prior to first and second mass therapy.
[2] Therapy administered on only one occasion.
[3] 6 months following treatment.

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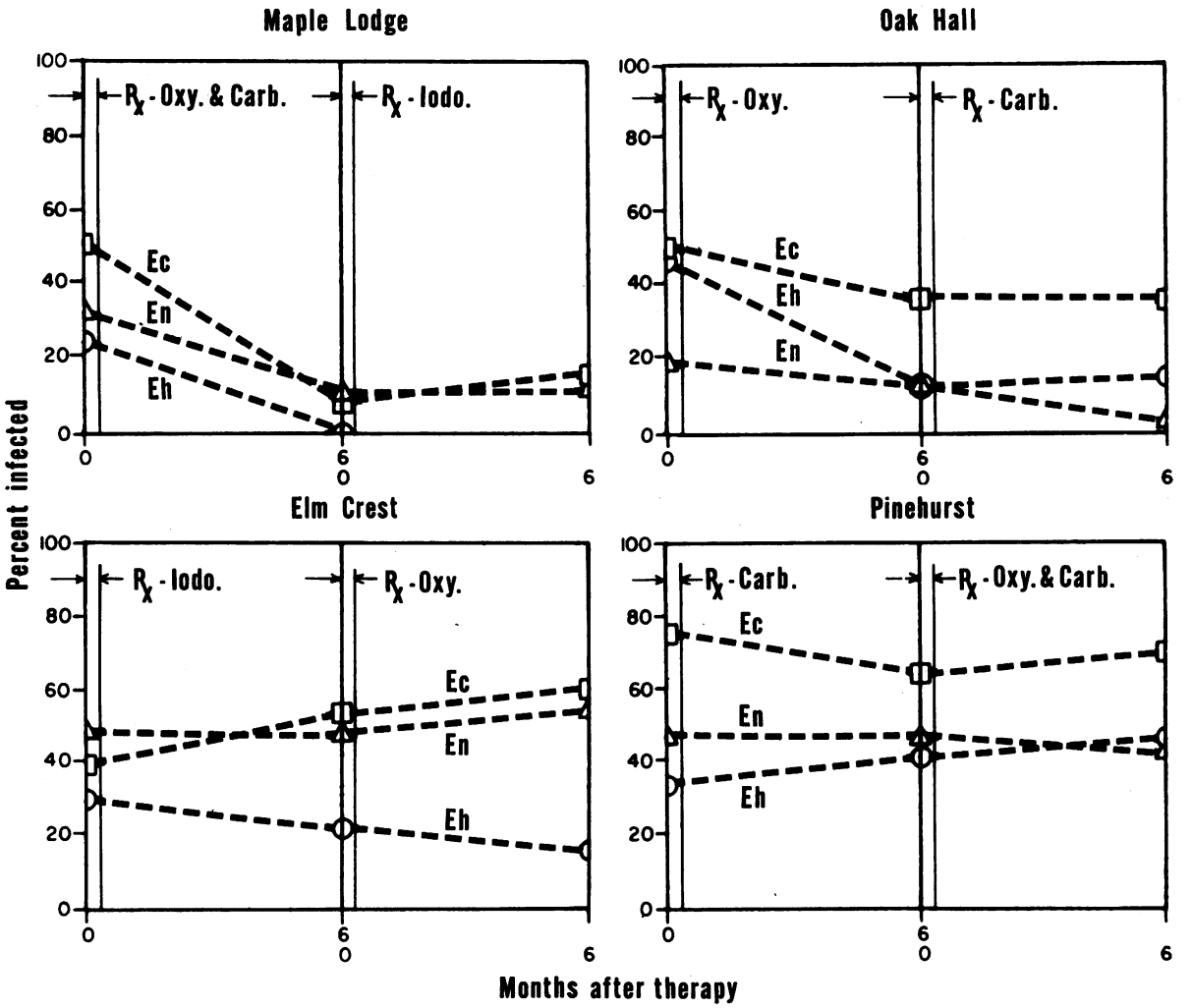
cent. Six months later, just before mass therapy with iodochlorhydroxyquin, it was zero. No *E. histolytica* infections were found 6 months after the second course of therapy but the prevalence rates of *E. coli* and *E. nana* were slightly higher than the reduced rates which were found 6 months after the first course of treatment.

In Oak Hall, prior to therapy with oxytetracycline, the prevalence rate of *E. histolytica* was 46 percent. Six months later, immediately preceding therapy with carbarsone, it was 12 percent, and 6 months after the second course it was slightly higher. The responses of *E. coli* and *E. nana* were similar, although *E. nana* seemed to be affected more by carbarsone than were the other parasites.

In Elm Crest Building, prior to therapy with iodochlorhydroxyquin, the prevalence rate of *E. histolytica* was 29.8 percent; 6 months later, just before therapy with oxytetracycline, it was 22 percent; and 6 months after the second course of treatment the rate was 16.7 percent. The prevalence of *E. nana* was practically the same at each examination while that of *E. coli* was higher 6 months after the first therapy and

Figure 3. Results of mass therapy with single drug regimens in four separate buildings of a mental institution. Incidence of Entamoeba histolytica, Entamoeba coli, and Endolimax nana prior to medication on two occasions and 6 months afterward.



Oxy.=oxytetracycline Carb.=carbarsone Iodo.=iodochlorhydroxyquin

Table 5. Results of mass therapy with four drug regimens randomly administered to all patients in Birches, Hemlock, Larches, and Westwood Buildings

Organism	Response to drug regimen in known positives [1]									
	Oxytetracycline		Oxytetracycline and carbarsone		Carbarsone		Iodochlorhydroxyquir		Total	
	Number positive, pretreatment	Percent negative, posttreatment [2]	Number positive, pretreatment	Percent negative, posttreatment [2]	Number positive, pretreatment	Percent negative, posttreatment [2]	Number positive, pretreatment	Percent negative, posttreatment [2]	Number positive, pretreatment	Percent negative, posttreatment [2]
Total protozoa	237	54. 0	239	62. 3	258	63. 2	233	52. 4	967	58. 1
Amebae	207	53. 1	199	61. 8	213	60. 0	201	52. 7	820	57. 0
Entamoeba histolytica	44	59. 1	44	65. 9	51	60. 8	37	64. 9	176	62. 5
Entamoeba coli	74	40. 5	80	56. 3	89	55. 1	86	50. 0	329	50. 8
Endolimax nana	62	45. 2	50	56. 0	46	58. 7	55	38. 2	213	48. 8
Iodamoeba buetschlii	7	100. 0	6	100. 0	8	100. 0	6	100. 0	27	100. 0
Dientamoeba fragilis	20	95. 0	19	78. 9	19	68. 4	17	70. 6	75	78. 6
Flagellates	30	60. 0	40	65. 0	45	77. 7	32	50. 0	147	64. 6
Giardia lamblia	14	50. 0	19	63. 2	25	72. 0	18	44. 4	76	59. 2
Chilomastix mesnili	16	68. 8	21	66. 7	20	85. 0	14	57. 1	71	70. 4

[1] Sum of positives prior to first and second therapy.
[2] 6 months following treatment.

practically unchanged 6 months after the second.

In Pinehurst Building, prior to therapy with carbarsone, the prevalence rate of *E. histolytica* was 34 percent; 6 months later, before therapy with the combination of oxytetracycline and carbarsone, it was 41.1 percent. Six months after the second therapy, the prevalence rate was 46.3 percent. Mass therapy with either drug regimen appeared to have little or no effect on the prevalence of *E. nana* and *E. coli.*

Since the patients in the four buildings did not receive the same medication, the relative effectiveness of mass therapy cannot be compared according to the response in known positives as was done in the case of the buildings where identical medication with four drug regimens was given (table 4). Likewise, since the type of patients varied from building to building, it is not practical to compare the effectiveness of the individual drug regimens as was done in the other buildings (table 5).

Treatment of Employees

All save 18 of the 262 employees in the institution received amebicidal drugs during the mass therapy program. The 105 employees working in the 8 dormitories generally received their medication along with the patients. Most of the 18 untreated individuals were in administrative or professional positions. Two *E. histolytica* positive employees in Elm Crest refused therapy. Prior to the mass therapy program the examination of a single stool specimen each from 128 employees revealed 3.9 percent positives for *E. histolytica.*

Toxicity of Drugs

Since only standard amebicides of known toxicity were used in this study, physicians and nurses were primarily concerned only with those side reactions which might endanger the patients or interfere with proper administration of the medication. Aversion to the oral drops of oxytetracycline was the most troublesome side reaction. Although the younger children liked the sweet, cherry flavor of the oral drops, a number of the older patients, particularly the teen-age girls, vomited immediately after the drug was administered. When the drug was given in capsules, the difficulty ended.

No serious cases of diarrhea, more than four bowel movements a day, developed either during or within a few days after medication. Also, no cases of pruritus were brought to the attention of the physicians and nurses; however, the patients in the institution are relatively insensitive to such conditions or else accept them as a matter of course.

A few minor rashes were observed in patients receiving oxytetracycline and carbarsone combined but the attending physicians questioned any connection between the rashes and the drugs. One serious rash developed in a patient receiving iodochlorhydroxyquin. Dizziness was reported by one individual on carbarsone.

Discussion

In 1951 Tobie and his co-workers (*1*) reported virtual elimination of *E. histolytica* infections from a building of Wassaic State School, an institution for mental defectives, by treating all patients with oxytetracycline. Therefore, in our study it was surprising to observe the prevalence rate of *E. histolytica* return to relatively high levels after the use of the same antibiotic in two preliminary trials of mass therapy in Pinehurst Building. In both institutions, a similar course of therapy was used and no new patients were admitted to the buildings during the post-treatment periods without first undergoing therapy.

One striking difference between the two studies which may have contributed to the diverse results was the pretreatment prevalence rates of *E. histolytica*. In Pinehurst Building, one stool examination revealed *E. histolytica* infections in 64 percent of the patients, while at Wassaic four stool examinations showed a prevalence rate of 49 percent. Since more examinations of the Pinehurst patients would undoubtedly have increased the percentage of positives, there was a decided difference in the prevalence rates of *E. histolytica* in the two populations. Inability to eradicate all infections apparently allowed a significant reservoir to remain to reinfect patients through poor personal hygiene.

When mass therapy was administered throughout the entire institution on two occasions, at 6-month intervals, the prevalence rates of *E. histolytica* were significantly lower in 7 of the 8 buildings by the end of the year's study. The effectiveness of therapy varied from building to building and appeared to be related to the prevalence of *E. histolytica* and to the general type of patients residing in the buildings. At the post-treatment examinations, *E. histolytica* was no longer found in residents of the three buildings with the lowest pretreatment prevalence rates (Larches, Hemlock, and Maple Lodge). Two of these buildings were occupied by the higher type of patients. Little or no change was noted in Pinehurst Building, which had the highest prevalence of *E. histolytica* and the most retarded patients.

Although stool examinations were not performed until 6 months after the end of mass therapy of the entire institution, from results observed in preliminary trials in Pinehurst, it is probable that a number of *E. histolytica* infections remained in each building after therapy was completed. In view of the patients' poor personal hygiene the treatment failures probably served as sources of infection. In Elm Crest, two infected employees, one of whom was a cook, may have been another source of infection.

In addition to the human reservoirs, reinfection may have occurred from organisms in the environment. In the first trials in Pinehurst the prevalence of *E. coli* returned to a high level after therapy more rapidly than did the prevalence of *E. histolytica* (fig. 1). Since both organisms were at a low level 2 weeks after therapy, the more rapid rise in prevalence of *E. coli* may indicate that cysts of *E. coli* remained viable in the environment for longer periods than did cysts of *E. histolytica*. Laboratory experimentations (*7*) have shown that cysts of *E. coli* survive desiccation to a much greater degree than do cysts of *E. histolytica*.

In comparing results of the four drug regimens in the four buildings on parallel therapy, the only observed difference in drug activity was against *D. fragilis*. Oxytetracycline was significantly more effective than any of the other medications in reducing the prevalence of this parasite. All of the regimens apparently eliminated the few known infections of *I. buetschlii* and were more effective against *E.*

histolytica than against *E. coli* or *E. nana*. This selective action of amebicides in man, particularly the ease of eliminating infections of *I. buetschlii*, has been observed by others (*1*, *8*).

The fact that no significant differences were observed in the activity of the four regimens against *E. histolytica* does not, of course, mean that none existed. The four drugs were randomly assigned to patients in four buildings since it was realized at the outset that differences in opportunity for reinfection would make it difficult to compare groups of patients receiving different medications. By randomization, reinfection opportunities were made more nearly equal. The results suggest that reinfections occurred frequently in most of the buildings so that even if certain drugs were significantly more effective than others, the differences may have been masked by the time post-treatment examinations were made. If the investigation had been directed specifically toward drug evaluation rather than toward control, more frequent post-treatment examinations would have been made. This would have required additional technical help, which was not available.

Some differences in drug activity are suggested by the results obtained in the buildings on single therapies. For example, oxytetracycline alone or combined with carbarsone appeared somewhat more effective than the other drugs (fig. 3). Although the superiority of this combination was observed in the treatment of acute amebiasis in Korea (*3*), caution must be exercised in drawing conclusions from results in the single therapy buildings since the patients were not similar in each building, and in some instances the drugs were given at different times of the year.

Although other workers have reported on mass therapy of patients in selected buildings of mental institutions (*1*, *9*, *10*), to our knowledge, this investigation constitutes the first attempt to control amebiasis in an entire institution by mass therapy. Although only limited success was obtained, the authors still believe that mass therapy constitutes the only practical approach to control in mental institutions with amebiasis problems.

Theoretically, the administration of a 100 percent effective drug, combined with a thorough cleanup campaign, would solve the problem. Lacking these two, perhaps idealistic, conditions, the administration of less effective drugs at intervals more frequent than 6 months may accomplish the elimination of *E. histolytica* in such relatively confined populations as exist in mental institutions. Berberian and coworkers (*9*) found that, after mass therapy with bismuth glycolylarsanilate and chloroquine phosphate, weekly administration of the same combined therapy to one part of the initial population reduced the infection rate of *E. histolytica* to 25 percent and daily administration to another group reduced the rate to 10 percent of the pretreatment levels. Although these results are encouraging, the intervals between treatments are too frequent for practical application in most institutions.

Summary

In an institution of approximately 1,600 mentally deficient patients living in 8 separate buildings, examination of single stool specimens from 667 individuals indicated that at least 29 percent harbored *Entamoeba histolytica*. Prevalence rates ranged from 7 to 64 percent from building to building.

Preliminary tests of mass therapy in the building with the highest prevalence of *E. histolytica* showed that single courses of oxytetracycline did not eradicate all infections and that the incidence of infection rose to one-half of the pretreatment level by the end of 6 months.

When mass therapy was extended to the entire institution, each patient was given 1 of 4 drug regimens—carbarsone, iodochlorhydroxyquin, oxytetracycline, and a combination of oxytetracycline and carbarsone—on 2 occasions 6 months apart. On the second occasion, the drug was changed for each person. Results of examinations performed 6 months after each medication indicated that mass therapy was successful in reducing the prevalence of *E. histolytica* in 7 of the 8 buildings but that the species apparently was "eliminated" in only 3 buildings. The effectiveness of therapy appeared to be related to the prevalence rate of *E. histolytica* in each building prior to medication and to the general level of personal hygiene of the patients.

No significant differences were observed in the relative effectiveness of the four drug regimens against *E. histolytica.* However, since the study was primarily concerned with control of infections and was not specifically designed for the evaluation of drugs, this result cannot be taken as conclusive.

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SUPPLY REFERENCE

Charles Pfizer and Co., Brooklyn, N. Y., Eli Lilly and Co., Indianapolis, Ind., and Ciba Pharmaceutical Products, Summit, N. J., provided the drugs used in the tests.

Conference on Nurse Traineeship Program

A national conference to evaluate the professional nurse traineeship program of the Public Health Service (title II, P. L. 84–911) will be held in Washington August 13–15, 1958. The program provides financial aid to graduate nurses preparing for teaching, supervisory, or administrative positions in nursing. Since its inception in 1956, the program has awarded 1,387 traineeships through 60 schools of nursing and public health. Funds allocated by Congress total $5 million.

About 80 recognized authorities from the fields of nursing education, medicine, hospital and public health nursing service, hospital administration, education, and public health administration will participate in the conference. They will determine the adequacy of the traineeship program in meeting the need for administrators and teachers of nursing and make recommendations as to possible modifications in the program.

Dr. John Millett, previously on the President's Committee on Administrative Management, the Social Science Research Council, and the National Resources Planning Board, and currently president of Miami University, Oxford, Ohio, will serve as chairman of the conference.