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Collective Antibiotic Treatment of Trachoma

Report on Comparative Trials Leading to More Economic Methods of Treatment

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By the early 1950's, it was clear from numerous independent reports that certain of the broad-spectrum antibiotics were effective against the agent of trachoma. It seemed, however, that treatment had to be continued over long periods to effect a cure of the average case. With the assistance of WHO, comparative trials on a scale hitherto unprecedented in the disease—involving more than 9000 schoolchildren with active trachoma—have been conducted in Morocco since 1953 in order to assess the value of local treatment of trachoma with chlortetracycline and to develop simple and economic methods of treatment, for which there was a pressing need. Local application of 1% chlortetracycline ointment two or three times daily for 60 days gave almost 80% cures under reasonably favourable conditions and nearly 100% cures after re-treatment of cases not cured by the first course. Equally good results followed intermittent short-term treatment over longer periods. Relapse and reinfection rates were low.

Collective mass treatment with antibiotics is clearly a valuable method of trachoma control. The use of intermittent treatment allows for a great economy both in antibiotics and in staff and other campaign expenses and makes possible the wide expansion of mass treatment programmes.

INTRODUCTION

It is now generally accepted that certain of the antibiotics are specifically effective in the treatment of trachoma, a view which was endorsed by the WHO Expert Committee on Trachoma (1952). Maxwell-Lyons,[3] in reviewing the many controversies which existed in the early days of chemotherapy and antibiotic therapy, pointed out that response to treatment depends upon factors such as age at onset, duration of the disease, clinical types, associated infections and general environmental conditions; he furthermore drew attention to the fact that misinterpretations of results have in many cases been based on evaluations carried out too soon after the termination of treatment. Carefully conducted trials in Morocco have shown that trachoma in that country is susceptible in a high proportion of cases to treatment with chlortetracycline.

SCHOOL TREATMENT

Systematic case-finding and treatment at school has proved to be one of the most effective ways of reducing trachoma in children. It will not, however, eradicate the disease from a community if a substantial proportion of children do not attend school, as is unfortunately the case in many trachoma endemic areas. Nevertheless, schoolchildren are one of the best organized population groups and, in areas like North Africa, those suffering from trachoma can be kept under observation and medical treatment for a long period.

OBJECTIVES

The first mass campaigns in the south of Morocco had shown that prophylactic treatment with chlortetracycline ointment, applied to a whole rural

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[3] Maxwell-Lyons, F. (1955) *The evaluation of antibiotic treatment of trachoma* (unpublished working document WHO/Trachoma/65).

community, was not only effective in reducing the seasonal epidemic of conjunctivitis, but had also an appreciable effect on the evolution of trachoma (Decour, Ferrand & Reinhards, 1952). Consequently, large-scale therapeutic trials on schoolchildren were started in Marrakech, Meknès and Tiznit with the following objectives:

(1) to confirm that the different evolutive stages and clinical forms of trachoma occurring in schoolchildren in Morocco are susceptible to treatment with antibiotics;

(2) to develop a standard method of treatment which could be employed on a practicable and economically feasible basis in all schools throughout the country.

With these objectives in view, therapeutic trials were carried out as follows:

(1) in 1954-55 on a group of 3828 trachomatous children in the schools of Marrakech, using the treatment schedule recommended by the WHO Expert Committee on Trachoma (1952);

(2) in 1955-56 on three separate groups, totalling 4136 trachomatous children in the schools of Meknès, in which the results of three different schedules of treatment were studied and compared with a view to determining the minimum effective course;

(3) in 1957-58 on two separate groups, totalling 1167 trachomatous children in schools of the Tiznit province in order to assess the value of the short-term intermittent treatment of trachomatous children under rural conditions in Southern Morocco.

It was recognized that individual cases of trachoma vary in their susceptibility to antibiotics and that in any large-scale programme of collective treatment cures cannot be obtained in 100% of cases. Taking a practical view of the problem, it was agreed to work to an "acceptable limit of failure" on the grounds that it was more economical, both in supplies and personnel, to re-treat a slightly larger number of relapses than to subject all cases to an unnecessarily generous course of treatment in the first instance.

METHODS OF STUDY

Selection of cases

It was considered impossible to keep all the children collectively treated in the two towns under close observation (approximately 12 000 in Marrakech and over 7000 in Meknès). A pilot sector was therefore formed in Marrakech, covering a group of schools chosen at random, and in which some 5000 children were registered. In Meknès cases were so selected as to make possible comparison of the effect of three different treatment schedules on different evolutive stages of trachoma. All classes with children below 12 years of age were included in these trials because, in these, stages I, II and III of trachoma were fairly equally represented; in older children trachoma in stage III was predominant and too few cases of stages I and II were to be found. The greatest possible care, as indicated later, was taken to avoid experimental error. In the province of Tiznit the treatment was carried out in schools within the experimental area. Only children under the age of 12 were considered for the experiment.

Examination

All children were examined during the month preceding the start of the treatment. A simple binocular loupe was used and was adequate for most cases. All children in the pilot sectors were re-examined at the end of the treatment period and during the last weeks of June, before the schools closed for the summer holidays.

In October or November those children still at school were re-examined. It was on this final examination that conclusions as to the effect of the treatment were based.

Recording

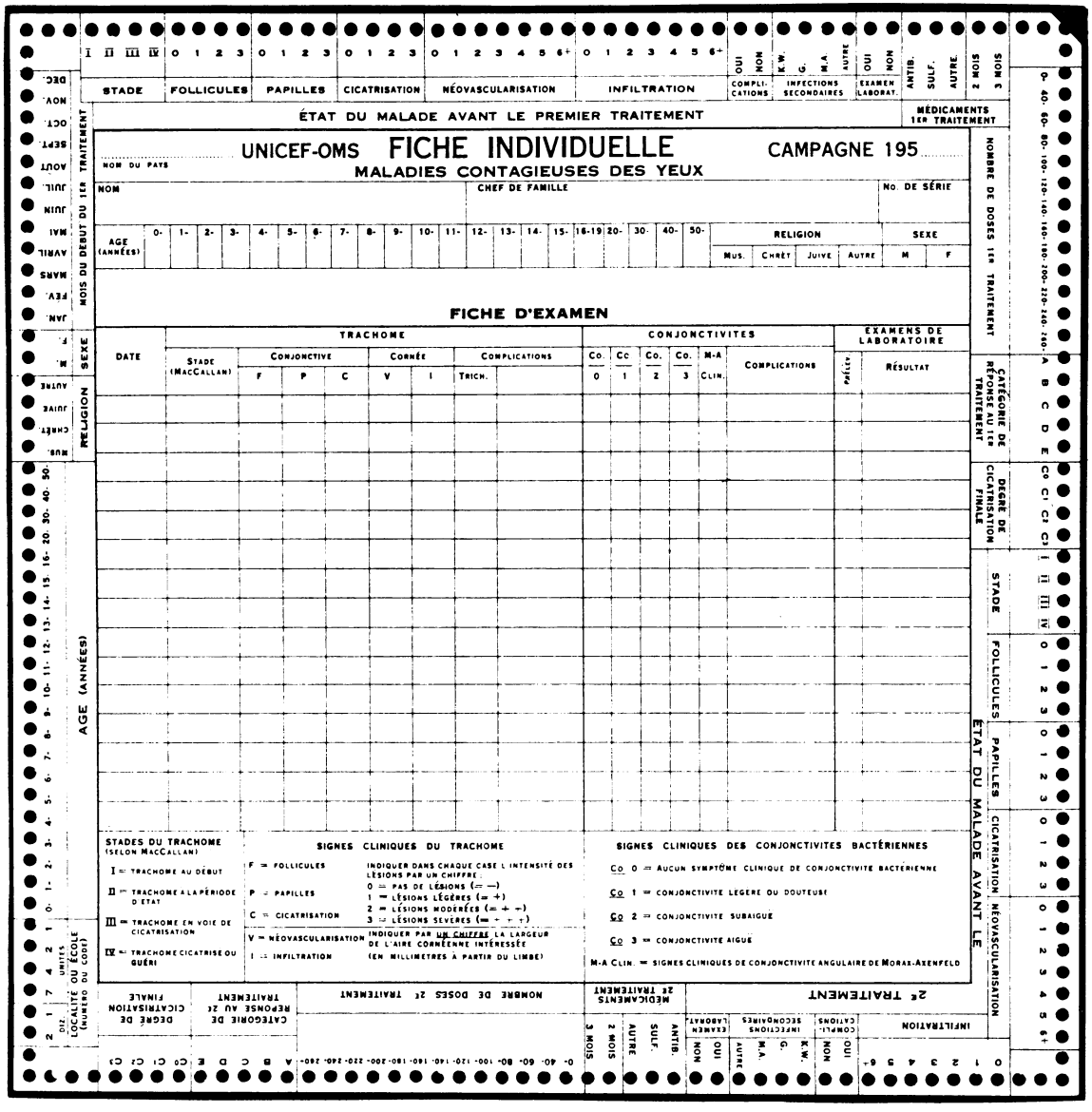
The recording, follow-up and evaluation of these trials were based on the now standardized WHO procedure.

A special record card (Fig. 1) was kept for each child suffering from trachoma, and for each child in the relatively small group of "doubtful" cases.[1] This card provides for the entry of trachoma diagnosis under the basic MacCallan classification (Tr I, II, III, IV), and for precise recording of the clinical features under the new classification of the WHO Expert Committee on Trachoma (1952; p. 14) adapted for field use. Under columns headed "follicles (F)", "papillary hypertrophy (P)", and "cicatrization (C)", the relative severity of each lesion was indicated by a number: 0, 1, 2, or 3 (nil, slight, moderate or severe). Under columns headed "neovascularization (V)" and "infiltration (I)", the elements of pannus were recorded separately in terms of millimetre extension from the upper

[1] Cases are classified as "doubtful" when the minimum requirements for a diagnosis of trachoma are not fulfilled, but when one or more of the characteristic signs is present.

FIG. 1

WHO INDIVIDUAL RECORD CARD, USED FOR TRACHOMA THERAPEUTIC TRIALS



limbus. (For reasons of simplicity in the cases where the whole cornea was covered, 10 mm were registered).

Other pathological conditions of the outer eye were registered in writing or by standard symbols in the space provided.

Treatment

The treatment was started in all schools in January 1954, and 1% chlortetracycline ointment was used throughout all trials.

The schedule recommended by the Expert Committee on Trachoma (1952; p. 5) was adopted with

some modifications. The school system in Morocco does not allow of treatment being made every day, as children attend school on only five days of the week, and it was not possible to have them assembled for treatment during the two free days. It was also considered impossible to apply the ointment four times during the school hours (8 a.m. to 5 p.m.). It was therefore decided to treat the children for 60 consecutive working days three times daily. This schedule was used throughout the Marrakech trial.

During the subsequent trials in Meknès this schedule (schedule 1) was compared with two others —namely, schedule 2, involving the application of ointment twice daily on 60 consecutive working days, and schedule 3 in which ointment was applied twice daily on three consecutive days every four weeks over a period of 20 weeks, i.e., six three-day cycles of treatment. In the Tiznit trials schedules 2 and 3 were compared.

All active cases (Tr I, II and III) were treated. In these trials, as in all routine collective treatment operations, doubtful cases also received treatment. This was done to ensure that no latent cases were missed.

As it was thought that cases not cured during the first treatment might be more resistant to the treatment with chlortetracycline alone, the recommendation of the WHO Expert Committee on Trachoma (1952; p. 5) on such cases was adopted and the following year (1955) combined treatment was given to the re-treated cases. In addition to the chlortetracycline ointment, applied under the same schedule, a trisulfonamide (sulfathiazole, sulfadiazine and sulfamerazine, in combination) was given by mouth twice daily on the basis of a daily amount of 40 mg per kg of body-weight, during two periods of 20 working days separated by an interval of 10 days.

All trachomatous children newly admitted to schools were treated over the same periods with chlortetracycline alone.[1]

Methods of evaluation

Evaluation of results has been made according to the standard WHO procedure developed by Maxwell-Lyons.[2] This method is particularly suitable in evaluating mass treatment in schools. Individual response to treatment is classified as follows:

Category A (success): *clinical cure at the end of the prescribed follow-up period:*

- A 1 = cure during the course of treatment, or
- A 2 = cure during the follow-up period.

Category B (failure): *signs of active trachoma at the end of the follow-up period:*

- B 1 = marked improvement, remaining stationary short of clinical cure, or
- B 2 = improvement under treatment with subsequent relapse, or
- B 3 = no improvement.

In some cases the intermediate examination at the end of the treatment could not be made and the category of response could therefore not be determined in detail. These cases are grouped under A or B " not determined ".

The criteria by which cases were judged to be clinically cured were strictly in accordance with those later laid down for the evaluation of mass campaigns by the WHO Expert Committee on Trachoma (1956). These requirements read:

" In mass campaigns, the examination should be made by the naked eye and with a loupe. In the absence of trichiasis, the following should be considered as the minimum requirements:

(1) absence of trachoma follicles;
(2) inactive pannus (absence of corneal infiltration);
(3) absence of hyperaemia;
(4) smoothness of the conjunctiva even in the presence of scars.

[1] Thus a permanent programme of case-finding and treatment was introduced into the schools, a policy which is being gradually extended to all schools in Morocco. Year by year, all newly admitted trachomatous children will receive a course of antibiotic treatment. Resistant or relapsing cases will be re-treated in the following year, with additional sulfonamide therapy for the more serious cases.

It is well recognized that sulfonamides are active against trachoma and that the combination of antibiotics and sulfonamides is more effective than either drug given singly. It was found in Morocco, however, that the great majority of trachoma cases which were still active after a first course of antibiotics alone, were cured by a second similar course. For this reason, and in view of the high cost and potential dangers of mass treatment with sulfonamides, the routine use of the latter drugs was abandoned after the first trial in Marrakech.

Recently it was decided to give a three-day treatment with chlortetracycline ointment to all children in primary schools at the beginning of the school year in October in order to eliminate the secondary infection contracted during the summer holidays. This will facilitate the diagnosis of trachoma made immediately after this treatment.

[2] Maxwell-Lyons, F. (1955) *The evaluation of antibiotic treatment of trachoma* (unpublished working document WHO/Trachoma/65)

" In cases complicated by trichiasis, this condition must be relieved surgically before the evaluation is made. A period of at least three months and preferably six months should elapse between the end of treatment and the evaluation."

During the trials in Marrakech it was found that many cases could not be grouped after the normal follow-up period either in Category A or in Category B. Of these cases Maxwell-Lyons writes: [1]

" In the determination of cure of trachoma we are sometimes on uncertain ground. Until recent years none of us had seen trachoma cured by primary elimination of the virus, and it is not always easy to interpret the results obtained. For example, it is not uncommon to find during the post-treatment follow-up period cases which show typical scarring associated only with fine papillary hypertrophy. Many but by no means all trachomatologists consider such cases as cured. When there is an element of doubt, the period of observation should be extended or provocative tests employed, but the cases should not, as often happens, be summarily classed as failures."

These cases were grouped under:

Category X: (probable cure) Presence at the end of the follow-up period of fine papillary hypertrophy or follicles non-pathognomonic of trachoma, but with no active corneal lesions. Need for further observation or investigation.

THE SCHOOL CAMPAIGN IN MARRAKECH, 1954-1955

Marrakech was the first large town in Morocco where all trachomatous schoolchildren were given collective treatment with antibiotics. The project was a part of the mass campaign against communicable eye diseases begun in Morocco in 1953 and organized jointly by the Government, WHO and UNICEF.

MARRAKECH PILOT SECTOR

The population of Marrakech consists of some 250 000 Moslems and Jews. The trachoma rate is estimated to be over 90%.

Relatively few of the Arab and Berber children go to school: in 1953 some 9000 were registered in the primary schools. An unknown number of boys attended the small Koranic schools, which at that time were not yet under the control of the school hygiene service.

Nearly all Jewish children go to school, at least for a few years.

In December 1953 about 12 000 children were examined by Dr Chalvignac, ophthalmologist in Marrakech. By means of a random choice of schools a pilot sector of approximately 5000 registered children was formed.

Table 1 shows the distribution, stage and relative severity of trachoma in the children of the pilot sector prior to commencement of treatment. Only 5.9% of the children were free of the disease, while 7.1% were placed on the list of doubtful cases.[2]

The early forms were seen in decreasing number in the higher age-groups, being replaced by the florid stage II, and later by stage III and even by stage IV. It was also observed that the severe cases were more frequent in the lower age-groups. The severe and very severe forms seemed to be less frequent in Marrakech than those observed in the south (Ouarzazate, Zagora).

FIRST TREATMENT

In January 1954 uniform treatment was begun in all schools. Chlortetracycline was given in the form of a 1% ointment three times daily for 60 consecutive working days. Treatment was administered by young Moslem aides, supervised by the school nurses and some unqualified but already experienced team leaders from the preceding summer's campaigns in the south. In some Jewish schools instillation was done by the teachers.

[1] Maxwell-Lyons, F. (1955) *The evaluation of antibiotic treatment of trachoma* (unpublished working document WHO/Trachoma/65)

[2] In a part of these cases there was doubt whether trachoma was present. In others the signs were so few that doubt arose under which stage to classify the case. Since then, by working together, the ophthalmologists employed in the campaigns in Morocco have learnt to bring to a uniform level their opinion in the diagnosis so as to classify the cases after the classification recommended by the WHO Expert Committee on Trachoma (1952).

The doubtful cases mentioned will not be included in the general evaluation of the effect of the treatment.

TABLE 1

MARRAKECH: TRACHOMA IN SCHOOLS IN PILOT SECTOR, DECEMBER 1953, BEFORE TREATMENT

Stage of trachoma	Age (years)											TOTAL
	5	6	7	8	9	10	11	12	13	14	15	
Tr 0	12 8.2%	58 8.8%	39 6.4%	43 6.2%	28 4.1%	23 4.0%	14 3.7%	20 4.8%	9 3.6%	12 11.0%	14 13.1%	272 5.9%
Doubtful	10 6.8%	59 9.0%	48 7.9%	62 8.9%	62 9.2%	40 6.9%	10 2.7%	11 2.6%	15 6.1%	5 4.6%	8 7.5%	330 7.1%
I +	16	129	131	121	109	73	44	47	23	5	4	702 15.2%
I ++	1	2	6	3		1		1		1		15 0.3%
I +++												
Total I	17 11.6%	131 19.9%	137 22.4%	124 17.8%	109 16.1%	74 12.8%	44 11.7%	48 11.5%	23 9.3%	6 5.5%	4 3.7%	717 15.5%
II +	8	108	121	126	135	134	90	97	53	12	11	895 19.4%
II ++	41	76	43	33	31	21	10	11		1	1	268 5.8%
II +++	3	2	1	2								8 0.2%
Total II	52 35.6%	186 28.3%	165 27.0%	161 23.1%	166 24.5%	155 26.8%	100 26.6%	108 26.0%	53 21.5%	13 11.9%	12 11.2%	1 171 25.3%
III+ Fo	7	30	38	51	73	56	42	49	32	20	18	416 9.0%
III+ F+	23	118	112	173	172	159	115	120	86	31	21	1 130 24.4%
III ++	18	66	56	63	44	39	39	28	14	13	10	390 8.4%
III +++	1		1		1						1	4 0.1%
Total III	49 33.6%	214 32.5%	207 33.9%	287 41.1%	290 42.8%	254 43.9%	196 52.1%	197 47.4%	132 53.4%	64 58.7%	50 46.7%	1 940 42.0%
IV o												
IV +	4	5	9	12	14	16	5	15	3	3	12	98 2.1%
IV ++	2	5	6	9	8	16	5	15	12	5	6	89 1.9%
IV +++							2	2		1	1	6 0.1%
Total IV	6 4.1%	10 1.5%	15 2.5%	21 3.0%	22 3.2%	32 5.5%	12 3.2%	32 7.7%	15 6.1%	9 8.3%	19 17.8%	193 4.2%
TOTAL	146 100%	658 100%	611 100%	698 100%	677 100%	578 100%	376 100%	416 100%	247 100%	109 100%	107 100%	4 623 100%

TABLE 2

MARRAKECH: CHANGES IN TRACHOMA AFTER FIRST TREATMENT, NOVEMBER 1954

AFTER TREATMENT

BEFORE TREATMENT — Stage		Tr 0	Tr doubtful	I				II				III+		III			IV					TOTAL
				+	++	+++	Total	+	++	+++	Total	Fo	F+	++	+++	Total	o	+	++	+++	Total	
Tr doubtful		127 50.4%		1 0.4%			1 0.4%	3 1.2%			3 1.2%	26 10.3%	6 2.4%			32 12.7%	10 4.0%	76 30.2%	3 1.2%		89 35.3%	252 100%
I	+			4			4 0.7%	6			6 1.1%	112	23	6		141 24.9%	175	232	9		416 73.4%	567 100%
	++											4	2			6 54.5%	2	3			5 45.5%	11 100%
	+++																					
Total I				4 0.7%			4 0.7%	6 1.0%			6 1.0%	116 20.1%	25 4.3%	6 1.0%		147 25.4%	177 30.6%	235 40.6%	9 1.6%		421 72.8%	578 100%
II	+							6			6 0.9%	210	42	8		260 37.7%	123	262	38		423 61.4%	689 100%
	++							1			1 0.6%	64	19	14		97 60.6%	8	44	10		62 38.8%	160 100%
	+++											2		1		3 100%						3 100%
Total II								7 0.8%			7 0.8%	276 32.4%	61 7.2%	23 2.7%		360 42.3%	131 15.4%	306 35.9%	48 5.6%		485 56.9%	852 100%
III+	Fo							2			2 0.7%	86	3	2		91 32.2%	23	107	50	10	190 67.1%	283 100%
	F+							1			1 0.1%	349	31	26		406 50.4%	21	212	150	15	398 49.4%	805 100%
III	++											126	10	22		158 69.0%	1	30	36	4	71 31.0%	229 100%
	+++											2				2 100%						2 100%
Total III								3			3 0.2%	563	44	50		657 49.8%	45	349	236	29	659 50.0%	1 319 100%
IV	o																					
	+											11	1	1		13 21.3%	6	32	10		48 78.7%	61 100%
	++											23				23 39.0%	1	2	23	10	36 61.0%	59 100%
	+++																			2	2 100%	2 100%
Total IV												34 27.9%	1 0.8%	1 0.8%		36 29.5%	7 5.7%	34 27.9%	33 27.0%	12 9.8%	86 70.5%	122 100%
TOTAL		127 4.1%		5 0.1%			5 0.1%	19 0.6%			19 0.6%	1 015 32.5%	137 4.3%	80 2.6%		1 232 39.4%	370 11.9%	1 000 32.0%	329 10.5%	41 1.3%	1 740 55.7%	3 123 100%

TABLE 3

MARRAKECH: CATEGORY OF RESPONSE TO FIRST TREATMENT, NOVEMBER 1954

Stage	Severity	Cured				Not cured					Doubtful (Category X)	TOTAL
		A 1	A 2	Not determined	Total	B 1	B 2	B 3	Not determined	Total		
I	+	138	258	20	416 73.4%	3	34	7		44 7.8%	107 18.9%	567 100%
	++	1	4		5 45.5%		2			2 18.2%	4 36.4%	11 100%
	+++											
Total I		139 24.0%	262 45.3%	20 3.5%	421 72.8%	3 0.5%	36 6.3%	7 1.2%		46 8.0%	111 19.2%	578 100%
II	+	93	311	19	423 61.4%	2	43	16		61 8.9%	205 29.8%	689 100%
	++	10	47	5	62 38.8%	4	16	16		36 22.5%	62 38.8%	160 100%
	+++							1		1	2	3 100%
Total II		103 12.1%	358 42.0%	24 2.8%	485 56.9%	6 0.7%	59 6.9%	33 3.9%		98 11.5%	269 31.6%	852 100%
III+	Fo	50	131	9	190 67.1%	2	6	3		11 3.9%	82 29.0%	283 100%
	F+	80	301	16	397 49.3%	18	38	13		69 8.6%	339 42.1%	805 100%
III	++	9	57	5	71 31.0%	10	13	15		38 16.6%	120 52.4%	229 100%
	+++										2	2 100%
Total III		139 10.5%	489 37.1%	30 2.3%	658 49.9%	30 2.3%	57 4.3%	31 2.4%		118 8.9%	543 41.2%	1 319 100%
TOTAL		381 13.9%	1 109 40.4%	74 2.7%	1 564 56.9%	39 1.4%	152 5.5%	71 2.6%		262 9.5%	923 33.6%	2 749 100%

TABLE 4

MARRAKECH: CATEGORY OF RESPONSE TO FIRST TREATMENT IN RELATION TO AGE, NOVEMBER 1954

Stage before treatment	Category of response	Age (years)								TOTAL
		-6	7	8	9	10	11	12	13+	
I	A	70	85	75	68	47	22	32	22	421 72.8%
	B	19	8	7	7	3	2			46 8.0%
	X	29	24	19	17	10	7	2	3	111 19.2%
	Total	118	117	101	92	60	31	34	25	578 100%
II	A	57	67	73	80	77	52	55	24	485 56.9%
	B	33	19	6	9	15	4	8	4	98 11.5%
	X	59	35	36	49	37	22	16	15	269 31.6%
	Total	149	121	115	138	129	78	79	43	852 100%
III	A	53	69	102	110	83	92	75	75	659 50.0%
	B	32	15	22	13	18	8	5	4	117 8.9%
	X	69	66	94	87	73	48	55	51	543 41.2%
	Total	154	150	218	210	174	148	135	130	1 319 100%
Total I+ II+ III	A	180 42.8%	221 57.0%	250 57.6%	258 58.6%	207 57.0%	166 64.6%	162 65.3%	121 61.1%	1 565 56.9%
	B	84 20.0%	42 10.8%	35 8.1%	29 6.6%	36 9.9%	14 5.4%	13 5.2%	8 4.0%	261 9.5%
	X	157 37.3%	125 32.2%	149 34.3%	153 34.8%	120 33.1%	77 30.0%	73 29.4%	69 34.8%	923 33.6%
	TOTAL	421	388	434	440	363	257	248	198	2 749 100%

In the pilot sector much attention was paid to registering each child's attendance for treatment, so that the total number of doses received could be noted on each card. The treatment ended in early April.

RESULTS OF FIRST TREATMENT

Unfortunately, it was not possible to see all the treated children in the pilot sector at the final examination in November 1954. Many of them had left school while others had changed classes or schools and could not be identified with certainty.

Table 2 shows the stages and severity of trachoma before treatment and after the seven months' post-treatment follow-up period.

Cures after first treatment (Table 3)

56.9% of the active cases of trachoma were clinically cured at the end of the first follow-up period.

There was a noticeable difference in the percentages cured in the different stages and degrees of severity, as shown below:

	Stage	*Percentage of cures*
Tr	I	72.8
	II+	61.4
	II++	38.8
	III+,(Fo)	67.1
	III+,(F+)	49.3
	III++	31.0

Table 3 shows how many of the cures occurred during the course of treatment (Category A1) and how many occurred during the post-treatment follow-up period (Category A2).

This late disappearance of the pathological signs and late cicatrization continuing after the end of the treatment was observed wherever mass treatment with chlortetracycline was made in Morocco. This is one reason why it is necessary to follow up cases for a longer period, after the end of treatment, if the results are to be seen in full.

Table 4 and Fig. 2 show the results of the first treatment in relation to age.

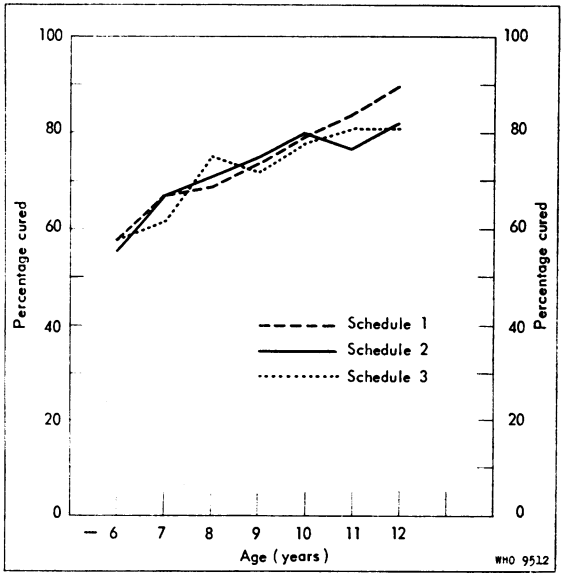
In every stage the proportions of cures showed a direct relationship to the increasing age of the subjects.

Category X

Success of the treatment was not only reflected in the obvious clinical cures. An improvement

FIG. 2

MARRAKECH : RELATION OF PERCENTAGE CURED TO STAGE OF TRACHOMA AND AGE



was observed in an important group of children in whom, besides scars, a slight papillary hypertrophy persisted as the only sign. It was for this reason that they could not be classified definitely as "clinical cures" (Tr IV), but were entered as Tr III+, Fo P+.

This papillary hypertrophy in most of the X cases should not be considered a sign of still active trachoma. It is not, however, quite excluded that in a few of them active trachoma may persist. In November 1954, no clear idea could be formed as to these two variants in the results of treatment, nor was it then known how to differentiate between the two conditions. The observations made in Marrakech were to bring some clarity in the evaluation of the Category X.

One group of uniform X cases was chosen [1] in which to study the effect of further treatment. Half of these children were submitted to a second course of treatment the following year, and the other half left without any further treatment (see Table 7).

[1] In order to obtain a uniform group of X cases, only those were chosen for comparison in which progressive amelioration was observed and which had not shown any tendency to relapse during the follow-up period.

It is worthy of note that treatment of the more advanced and severe forms of trachoma more often brought Category X results:

Stage in which treated	*Percentage resulting in Category X*
Tr I	19.2
II+	29.8
II++	38.8
III+,(Fo)	29.0
III+,(F+)	42.1
III++	52.4

It would seem that in long-established severe trachoma, papillary hypertrophy becomes well developed and may be very slow in disappearing, even after elimination of the infective agent and resolution of the follicles.

Failures

Definite failures are shown in the results given in Table 2 under Tr I, II, III+ with follicles, and III++. The cases of Tr III++ following treatment of stages Tr II+ or III+ are considered as aggravations.

Cases treated with apparently no success are shown in the second part of Table 3. However, there were cases in Category B1 which showed a certain amelioration. Category B2 represents relapsed cases which were perhaps not adequately treated. Some cases of reinfection may have been grouped under this category.

Those cases in which there was practically no change after treatment have been placed under Category B3. This group contains the apparently resistant cases, and in some a slight aggravation was observed. This category of response was more common in the severer cases than in the slight ones.

The proportion of failures decreases with increase in the age of the subjects. The more gross the lesions, the less favourable is the response to treatment.

In 9.5% of the 2749 children with initially active trachoma who were seen at the end of the follow-up period, trachoma was still active.

It was tentatively estimated, before treatment, that a margin of failure of 10% in Tr I and 20% in Tr II and Tr III could be accepted and would allow of successful trachoma control if the treatment were repeated in cases of failure the following year. Table 3 shows that this limit of failure was not exceeded:

Stage		*Percentage of failures*
Tr	I	8.0
	II	11.5
	III	8.9

In different stages, in cases of comparable severity, the failure rate was comparable:

Stage		*Percentage of failures*
Tr	I	8.0
	II+	8.9
	III+,(F+)	8.6
	II++	22.5
	III++	16.6

RE-TREATMENT IN SECOND YEAR

The children needing further treatment were selected after examination in November 1954, i.e., 7 months after completion of their first treatment.

Second-year treatment was started in January 1955.

All failures (Category B cases) were re-treated, but not the clinically cured cases. Half of the typical X cases were re-treated; the other half of identical cases in the same schools and classes were not treated a second time, but were kept as controls.

Trisulfonamides were given in addition to chlortetracycline ointment as already indicated. At the same time all trachomatous children newly admitted to schools were treated with chlortetracycline ointment alone.

RESULTS OF SECOND-YEAR TREATMENT

At the end of the second-year follow-up period, i.e., in October 1955, the following results were observed (Tables 5, 6 and 7).

Results among first-year failures

Cures. Out of the 145 re-treated cases which it was possible to examine in October 1955, 113 (77.9%) were clinically cured as a result of the second treatment.

As this re-treated group included a number of cases in which a certain resistance to chlortetracycline could be suspected, this must be regarded as a satisfactory result.

Category X. In 26 children (17.9%) slight papillary hypertrophy persisted as the only symptom after the second treatment.

Failures. In 6 cases (4.1%) active trachoma was still present after the second treatment. Of these 5 still had follicles.

Examination at school did not reveal the difference between these children and the others. It is possible that a few of the cases were particularly resistant to chlortetracycline and sulfonamides or, on the other

TABLE 5

MARRAKECH: CATEGORY OF RESPONSE TO SECOND TREATMENT (FIRST-YEAR FAILURE CASES)

Stage	Severity	Cured				Not cured					Doubtful (Category X)	TOTAL
		A 1	A 2	Not determined	Total	B 1	B 2	B 3	Not determined	Total		
I	+	2		1	3 100%							3 100%
	++											
	+++											
Total I		2 66.7%		1 33.3%	3 100%							3 100%
II	+	4	4	1	9 100%							9 100%
	++											
	+++											
Total II		4 44.4%	4 44.4%	1 11.1%	9 100%							9 100%
III+	₀Fo	8	4	3	15 93.8%						1 6.3%	16 100%
	F+	29	31	3	63 84.0%		1			1 1.3%	11 14.7%	75 100%
III	++	10	12	1	23 54.8%	1	3	1		5 11.9%	14 33.3%	42 100%
	+++											
Total III		47 35.3%	47 35.3%	7 5.3%	101 75.9%	1 0.8%	4 3.0%	1 0.8%		6 4.5%	26 19.5%	133 100%
TOTAL		53 36.6%	51 35.2%	9 6.2%	113 77.9%	1 0.7%	4 2.8%	1 0.7%		6 4.1%	26 17.9%	45 100%

TABLE 6

MARRAKECH: CHANGES IN TRACHOMA AFTER SECOND TREATMENT (FIRST-YEAR FAILURE CASES)

AFTER SECOND TREATMENT

AFTER FIRST TREATMENT: Stage	Tr 0	Tr doubtful	I +	I ++	I +++	I Total	II +	II ++	II +++	II Total	III+ Fo	III+ F+	III ++	III +++	III Total	IV o	IV +	IV ++	IV +++	IV Total	TOTAL
Tr doubtful																					
I +																	3			3 100%	3 100%
I ++																					
I +++																					
Total I																	3 100%			3 100%	3 100%
II +																1	8			9 100%	9 100%
II ++																					
II +++																					
Total II																1 11.1%	8 88.9%			9 100%	9 100%
III+ Fo											1				1 6.3%		10	3	2	15 93.8%	16 100%
III+ F+											11		1		12 16.0%	1	53	9		63 84.0%	75 100%
III ++											14	2	3		19 45.2%	1	15	7		23 54.8%	42 100%
III +++																					
Total III											26 19.5%	2 1.5%	4 3.0%		32 24.1%	2 1.5%	78 58.6%	19 14.3%	2 1.5%	101 75.9%	133 100%
IV o																					
IV +																					
IV ++																					
IV +++																					
Total IV																					
TOTAL											26 17.9%	2 1.4%	4 2.8%		32 22.1%	3 2.1%	89 61.4%	19 13.1%	2 1.4%	113 77.9%	145 100%

hand, these children may have become reinfected during each of the follow-up periods. With the high trachoma rate still obtaining in the town, this might have happened in certain cases.

Results among first-year Category X cases

No practical difference was observed in the re-treated and non-re-treated groups during the follow-up period.

Cures. Clinical cures were as frequently observed in the re-treated as in the non-re-treated (Table 7).

Category X. In a comparable number of cases in both groups slight papillary hypertrophy was still present.

Failures. A fairly small number of relapses or reinfections occurred in both groups.

The percentage of active trachoma present at the end of the second follow-up period was not much higher than in the 914 cases declared clinically cured in November 1954 and again examined in October 1955 (Table 7).

TABLE 7

MARRAKECH: RESULTS IN 1617 CHILDREN WITH INITIALLY ACTIVE TRACHOMA SEEN AT END OF SECOND FOLLOW-UP PERIOD, OCTOBER 1955, GROUPED ACCORDING TO CATEGORIES OF RESPONSE TO FIRST TREATMENT

	III+		III			IV					TOTAL
	Fo[a]	F+	++	+++	Total	o	+	++	+++	Total	
Clinical Cures November 1954 Not re-treated	14	6	5		25 2.7%	148	638	98	5	889 97.3%	914 100%
Category X Group for comparison Not re-treated	13	1	1		15 14.7%	1	55	28	3	87 85.3%	102 100%
Category X Group for comparison Re-treated	22		6		28 14.9%	7	104	48	1	160 85.1%	188 100%
Category X The rest Re-treated	23	1			24 9.0%	10	181	49	4	244 91.0%	268 100%
Failures November 1954 Re-treated	26	2	4		32 22.1%	3	89	19	2	113 77.9%	145 100%
TOTAL	98 6.1%	10 0.6%	16 1.0%		124 7.7%	169 10.5%	1 067 66.0%	242 15.0%	15 0.9%	1 493 92.3%	1 617 100%
		1.6%									

[a] These are Category X cases after second treatment

The 18 months which elapsed after treatment can be regarded as a period long enough to allow most relapses due to insufficient treatment to show. We may therefore conclude:

(1) that, since active trachoma was found in a very small percentage of the first year Category X cases 18 months after the end of treatment, and was observed as frequently in the re-treated as in the non-re-treated group, these active cases are more likely to be reinfections than relapses;

(2) that of the cases which in November 1954 were placed in Category X following a first course of treatment, more than 98% were, in fact, true cures.

(3) that, after appropriate treatment with antibiotics, the persistence of fine papillary hypertrophy, associated only with scarring, and in the absence of any active corneal lesions, should not be regarded as a sign of active trachoma.

Changes in cases cured after first-year treatment

914 cases declared clinically cured in November 1954 were available for re-examination a year later, i.e., 18 months after termination of treatment. Active trachoma was found in 11 of these (1.2%). In 7, the presence of small, flat, yellowish follicles of the Tr I type suggested re-infection. Although differentiation between reinfection and relapse is usually impossible, it may be supposed that there were both relapses and reinfections among these 11 cases. Even if the majority were relapses, their low number would still show that, for all practical purposes, the diagnostic criteria for clinical cure adopted had been sufficiently strict.

On the other hand, even if most of these cases were reinfections, it would mean that, after cure, the reinfection risk was relatively very small in children of school age.

Trachoma in pilot sector after two years of collective control (Table 7)

Out of 1617 children with initially active trachoma who could be closely followed during the two years and who had undergone the treatment mentioned, only 26 (1.6%) probably needed further treatment. In the rest the trachoma was cured. A small number

of those still trachomatous were to be considered as resistant to the treatment given; an individual approach in their future treatment might prove useful. In others, simple reinfection would not pose any problem in regard to their future treatment by standard methods.

CICATRIZATION

In the early 1920's Robert E. Wright stated that owing to the complete lack of a specific method of treating trachoma it was the practice deliberately to destroy tissue and produce scars in the hope of inactivating the disease. Since that time much has changed. With the specific remedies capable of eliminating the virus now at our disposal we must, on the contrary, preserve the tissue and avoid as far as possible the formation of scars.

One of the essential conditions for undertaking any mass treatment of trachoma today is the availability of methods that avoid heavy scarring and diminish the risk of late complications.

The importance of this had already been grasped before the beginning of the mass campaigns in Morocco. In the WHO Individual Record Card provision is made for recording the final cicatrization. This aspect of the evaluation is made as a matter of course in each pilot project.

There is no risk of trichiasis or entropion occurring when the cure has been completed with no visible scars (Co) or with a slight superficial scarring (C+). On the other hand, heavy scarring (C+++) gives a bad prognosis. With moderate scarring (C++) the prognosis may vary.

Unfortunately many publications on trachoma therapy lack precision as to the degree of final cicatrization. In fact, however, the relative value of different treatment methods giving otherwise comparable results, may depend on the degree of cicatrization during the process of healing.

Table 8 shows the degree of cicatrization in clinically cured cases at the end of the follow-up period.

For an accurate appraisal, cases that were initially in stages I and II are considered separately from those initially in stage III and in which some scarring was already present.

Lack of any visible scarring (Co) was more frequent in cases cured by the first course of treatment than in those in which healing was delayed and obtained only as a result of a second course. This, however, is only of theoretical interest since in such cases, and in those with only slight superficial scarring (C+), the risk of late cicatricial complications is negligible. It is of more practical value to know in how many cases this risk is actually present. The number of C++ cases is comparatively low in each group, standing at 6.3% and 6.9% respectively.

The cases that were initially in stage III provided, after cure, a completely different picture. In these, considerable scarring was often present before treatment; and, after cure, the resulting cicatrization was of the order of C++ or C+++ in about 40% of cases. In cases cured by other, unknown, methods before the campaign the proportion is even more unfavourable (50%).

This comparison demonstrates the benefit of early treatment. In future all children will be treated as soon as they enter school at the age of 5-6 years. At this age, in Morocco, stages Tr I and II predominate.

THE SCHOOL CAMPAIGN AND THE COMMUNITY

The school campaign in Marrakech had a favourable influence on part of the population outside the schools. Through the children and schoolteachers, knowledge of the work done in the schools was propagated in the community and among families.

This had a very marked effect in the Jewish community, with its well-organized system of social and medical assistance for the needy. The community raised funds to inaugurate its own campaign against communicable eye diseases in all Jewish families living in Mellah, the Jewish quarter.

Treatment was given by specially instructed social workers during house-to-house visits and in an outpatient ward under the supervision of an ophthalmologist. Chlortetracycline ointment was used.

The first results of this activity became apparent in the schools in 1955, when more than a half of the young, newly admitted children had no active trachoma. (Two years earlier only some 12% of the younger children were free from trachoma.)

It is planned for the future to ensure that each child is examined and treated, so as to be cured before reaching school age. At the same time the special effort in the treatment of adults will be continued, and in this community everything possible will be done to eradicate trachoma in the families of the children treated.

TABLE 8
MARRAKECH: DEGREE OF FINAL CICATRIZATION

	Initial stage	IV				Total
		o	+	++	+++	
Clinical cures after first treatment	I	177	235	9		421 100%
	II	131	306	48		485 100%
	Total I + II	308 34.0%	541 59.7%	57 6.3%		906 100%
Failures after first treatment, but clinical cures after second treatment	I	1	24	1		26 100%
	II	1	41	4		46 100%
	Total I + II	2 2.8%	65 90.3%	5 6.9%		72 100%
Clinical cures after first treatment	III	45 6.8%	349 53.0%	236 35.8%	29 4.4%	659 100%
Cured before treatment	IV		61 50.0%	59 48.4%	2 1.6%	122 100%

COMPARATIVE TRIALS WITH DIFFERENT TREATMENT SCHEDULES IN MEKNÈS, 1955

Each year since 1954 an increasing number of schoolchildren have been collectively treated in the schools of Morocco.[1] The chlortetracycline treatment schedule used in Marrakech gave satisfactory results, but the campaign seemed rather too costly, especially in personnel. It was clearly desirable that the cost of treatment be lowered so as to enable the regular treatment of all trachomatous schoolchildren throughout the country, remembering that the number of children attending school is growing from year to year.

[1] 1954 . . . . . 31 000
1955 . . . . . 42 000
1956 . . . . . 47 000
1957 . . . . . 146 000
1958 . . . . . 263 000
1959 target number. 350 000
1960 target number. 400 000

TREATMENT SCHEDULES

In order to determine the simplest effective course of treatment for the different stages and clinical types of trachoma found in schoolchildren in Morocco, the following three treatment schedules were used in parallel trials in Meknès in 1955:

Schedule 1: Application of 1% chlortetracycline ointment three times daily for 60 consecutive working days, i.e, five days per week for 12 weeks.

Schedule 2: Application of 1% chlortetracycline ointment twice daily for 60 consecutive working days.

Schedule 3: Application of 1% chlortetracycline ointment twice daily on three consecutive days, repeated every four weeks over a period of 20 weeks, i.e., six cycles of treatment.

THE PILOT SECTOR OF MEKNÈS

All classes with children from 5 to 12 years old in the Moslem and Jewish schools of the town were included in the pilot sector. 7522 schoolchildren were examined in December 1954 and January 1955 and 4136 were found to have active trachoma. Table 9 shows the clinical findings in relation to age prior to treatment.

It should be mentioned here that the trachoma rate among schoolchildren in Meknès was not so high as in the towns of southern Morocco. The picture also differed according to the quarter of the town. In the Jewish quarters trachoma was less frequent among the schoolchildren and took less severe forms than in the Moslem part of the town.[1]

In the comparatively better-off Moslem quarters of Meknès trachoma was less frequent than in the surrounding, poor, village-type of agglomerations and in recently grown " shack " quarters.

Table 10 shows the percentage of children with active trachoma and the total number of trachomatous children in three groups of schools. (In the Moslem sector the five best schools were tentatively taken for comparison with the four worst.) It is common experience that the higher the local prevalence of trachoma, the earlier the age of onset. This finding is reflected in Table 10, where it is seen that early forms of trachoma were most frequently met in schools with the lower prevalence rates. In these schools it was not uncommon to find children in the higher classes with trachoma stage I. In districts of high trachoma prevalence the disease is usually contracted in early childhood and relatively advanced cases are to be seen among the youngest pupils in the local schools.

COMPARISON

Three groups of comparable classes were formed in each school or in groups of similar schools, care being taken to ensure that children of different ages were equally represented in each group of classes and that stages I, II and III of the trachoma cases were distributed as evenly as possible. Only classes with children below the age of 12 were chosen. The allocation of treatment schedules to groups of classes was made at random. This allowed unbiased estimates to be made of the relative effect of each schedule of treatment and considerably reduced the margin of experimental error. Each class was treated under one schedule.

Treatment of all these groups was commenced in the last days of January 1955.

FOLLOW-UP

The children under schedules 1 and 2 were again examined at the end of the treatment, early in May. All children were seen at the end of June. This moment coincided with the end of treatment under schedule 3.

In October 1955, the treated children who were still in school were re-examined, i.e., six months after the completion of treatment schedules 1 and 2, and four months after the completion of treatment schedule 3.

RESULTS

Table 11 shows the changes that occurred in trachoma cases of different stages and degrees of severity under the three treatment schedules.

The results of the three treatment schedules can best be evaluated by comparing the type of response to the treatment given. This is done first in relation to stage and severity (Table 12).

In all three treatment schedules the percentage of cures was very much the same—schedule 1: 69.6%; schedule 2: 69.6%; schedule 3: 71.1%.

Comparable results were also obtained in all three schedules whatever the stage and degree of severity of trachoma. Thus, at first sight there would appear to be little difference in the efficacy of the three treatment schedules.

Further, the total number of failures was very much the same under all three treatment schedules—7.5%, 8.5%, and 8.2% for schedules 1, 2 and 3.[2]

[1] The exact opposite was observed in the villages of southern Morocco. There, the Jewish children and the whole Jewish population were usually found to be suffering from a more severe and florid form of trachoma than the Berber population. The prevalence was 100% in both ethnic groups.

[2] The statistical analysis of these tables, made in the form of the test of homogeneity between the three treatment schedules for each of the trachoma stages and degree of severity has given a x^2 of 14.871 with 14 degrees of freedom, which is far from being significant. It may thus be assumed that all three treatment schedules gave the same percentage of *final* cures.

TABLE 9

MEKNÈS: TRACHOMA IN THE PILOT SECTOR, BEFORE TREATMENT

Stage of trachoma		Age (years)							TOTAL
		6	7	8	9	10	11	12	
Tr 0		766 43.8%	555 37.4%	540 38.3%	371 41.2%	321 39.4%	256 33.4%	140 35.0%	2 949 39.2%
Doubtful		24 1.4%	19 1.3%	21 1.5%	13 1.4%	9 1.1%	11 1.4%	3 0.8%	100 1.3%
I	+	132	72	57	30	13	13	2	319 4.2%
	++	13	8	3		1	1	1	27 0.4%
	+++								
	Total I	145 8.3%	80 5.4%	60 4.3%	30 3.3%	14 1.7%	14 1.8%	3 0.8%	346 4.6%
II	+	177	92	83	48	46	38	16	500 6.6%
	++	284	155	108	35	28	34	12	656 8.7%
	+++	35	15	16	2	4		2	74 1.0%
	Total II	496 28.4%	262 17.7%	207 14.7%	85 9.4%	78 9.6%	72 9.4%	30 7.5%	1 230 16.4%
III+	+ Fo	135	267	285	226	217	213	127	1 470 19.5%
	+ F+	99	137	131	67	68	67	27	596 7.9%
III	++	75	112	97	57	45	74	24	484 6.4%
	+++		4	4	2				10 0.1%
	Total III	309 17.7%	520 35.1%	517 36.7%	352 39.1%	330 40.5%	354 46.2%	178 44.5%	2 560 34.0%
IV	+	8	44	49	40	47	48	34	270 3.6%
	++	1		14	8	15	8	11	57 0.8%
	+++		2	1	2	1	3	1	10 0.1%
	Total IV	9 0.5%	46 3.1%	64 4.5%	50 5.5%	63 7.7%	59 7.7%	46 11.5%	337 4.5%
TOTAL		1 749 100%	1 482 100%	1 409 100%	901 100%	815 100%	766 100%	400 100%	7 522 100%

TABLE 10
MEKNÈS: TRACHOMA IN THREE DIFFERENT GROUPS OF SCHOOLS, BEFORE TREATMENT

	Doubtful	Trachoma I	Trachoma II	Trachoma III	Total active trachoma	Trachoma IV	Total[a] treated for trachoma	Free of trachoma	Total examined
Jewish schools	55 2.6%	151 7.1%	172 8.1%	235 11.1%	558 26.3%	16 0.8%	629 29.7%	1 491 70.3%	2 120 100%
5 best Moslem schools	13 0.8%	68 4.0%	256 14.9%	534 31.1%	858 49.9%	88 5.1%	959 55.8%	759 44.2%	1 718 100%
4 worst Moslem schools	3 0.3%	26 2.3%	327 29.0%	604 53.6%	957 85.0%	88 7.8%	1 048 93.1%	78 6.9%	1 126 100%

[a] The total number of children treated for active trachoma, doubtful trachoma and trachoma in Stage IV.

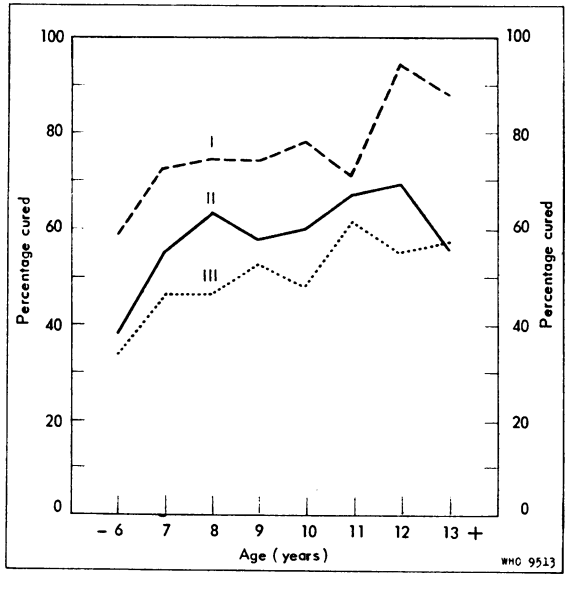
In schedule 3 relatively more cures occurred during the course of treatment. Category A1 responses occurred in 48.6% of all cures of an identified type in schedule 1, in 44.8% in schedule 2, and in 80.2% in schedule 3.

The duration of the treatment period under schedule 3 was 20 weeks as against 12 weeks in schedules 1 and 2 so that more time was available for resolution of the lesions. This also seems to indicate that the suppressive effect of intermittent application of the antibiotic on the virus was operative from an early stage of treatment.

It is of importance to know whether children of all age-groups reacted in a comparable manner to these three treatment schedules. From Table 13 it can be seen that, in general, the younger children (6-7) reacted less well than the older ones (8-12). The percentage of cures tends to show a regular increase with age, the percentage of failures showing a corresponding decrease. This appears regularly in every stage of trachoma and is comparable in all three treatment schedules, so that no weak point in relation to age of the children could be detected in any of these schedules (Fig. 3).

The different reactions of different age-groups to treatment may well be due to the fact that trachoma in younger children occurred more often in severe forms and was frequently complicated by secondary infection.

FIG. 3
MEKNÈS: RELATION OF PERCENTAGE CURED TO SCHEDULE OF TREATMENT AND AGE



The above data obtained from the present trials may be of importance, in Morocco at least, in planning future operations in schools since: (1) they demonstrate that in any evaluation of trachoma the age of the person treated may be of great importance,

TABLE 11
MEKNÈS: CHANGES IN TRACHOMA AT END OF FOLLOW-UP PERIOD
Treatment Schedule 1

AFTER TREATMENT

BEFORE TREATMENT: Stage	Tr 0	Tr doubtful	I: +	I: ++	I: +++	I: Total	II: +	II: ++	II: +++	II: Total	III+: Fo	III+: F+	III: ++	III: +++	III: Total	IV: o	IV: +	IV: ++	IV: +++	IV: Total	TOTAL
Tr doubtful	3 11.1%										1 3.7%		1 3.7%		2 7.4%	5 18.5%	17 62.9%			22 81.5%	27 100%
I +											14	3			17 23.3%	11	45			56 76.7%	73 100%
I ++																3	9			12 100%	12 100%
I +++																					
Total I											14 16.5%	3 3.5%			17 20.0%	14 16.5%	54 63.5%			68 80.0%	85 100%
II +											28	4	1		33 25.2%	11	87			98 74.8%	131 100%
II ++											49	13	10		72 46.8%	8	70	4		82 53.2%	154 100%
II +++											12	1	4		17 77.3%		1	4		5 22.7%	22 100%
Total II											89 29.0%	18 5.9%	15 4.9%		122 39.7%	19 6.2%	158 51.5%	8 2.6%		185 60.3%	307 100%
III+ Fo											45	2	12		59 19.1%	14	187	44	5	250 80.9%	309 100%
III+ F+											28	6	5		39 31.2%	6	73	6	1	86 68.8%	125 100%
III ++											33	1	6		40 46.5%	1	26	16	3	46 53.5%	86 100%
III +++																					
Total III											106 20.4%	9 1.7%	23 4.4%		138 26.5%	21 4.0%	286 55.0%	66 12.7%	9 1.7%	382 73.5%	520 100%
IV o																	1 100%			1 100%	1 100%
IV +											1				1 1.7%		56	1		57 98.3%	58 100%
IV ++																	13	3		16 100%	16 100%
IV +++																		1	2	3 100%	3 100%
Total IV											1 1.3%				1 1.3%		70 89.7%	5 6.4%	2 2.6%	77 98.7%	78 100%
TOTAL	3 0.3%										211 20.7%	30 2.9%	39 3.8%		280 27.5%	59 5.8%	585 57.5%	79 7.8%	11 1.1%	734 72.2%	1 017 100%

TABLE 11 (continued)

Treatment Schedule 2

AFTER TREATMENT

BEFORE TREATMENT Stage		Tr 0	Tr doubtful	I				II				III+		III			IV					TOTAL
				+	++	+++	Total	+	++	+++	Total	Fo	F+	++	+++	Total	o	+	++	+++	Total	
Tr doubtful			1 4.5%														3 13.6%	18 81.8%			21 95.5%	22 100%
I	+											16	2			18 20.7%	22	47			69 79.3%	87 100%
	++											2	1			3 60.0%		2			2 40.0%	5 100%
	+++																					
Total I												18 19.6%	3 3.3%			21 22.8%	22 23.9%	49 53.3%			71 77.2%	92 100%
II	+											15	6	4		25 19.4%	14	89	1		104 80.6%	129 100%
	++											45	6	22		73 46.5%	7	69	8		84 53.5%	157 100%
	+++											4		7		11 91.7%		1			1 8.3%	12 100%
Total II												64 21.5%	12 4.0%	33 11.1%		109 36.6%	21 7.0%	159 53.4%	9 3.0%		189 63.4%	298 100%
III+	Fo											61	2	6		69 17.0%	15	290	28	5	338 83.0%	407 100%
	F+											43	5	5		53 35.3%	5	78	14		97 64.7%	150 100%
III	++											51	1	26		78 55.7%		35	27		62 44.3%	140 100%
	+++											1				1 50.0%		1			1 50.0%	2 100%
Total III												156 22.3%	8 1.1%	37 5.3%		201 28.8%	20 2.8%	404 57.8%	69 9.9%	5 0.7%	498 71.2%	699 100%
IV	o																					
	+											1		1		2 3.2%	2	57	1		60 96.8%	62 100%
	++																	7	3		10 100%	10 100%
	+++																		1		1 100%	1 100%
Total IV												1 1.4%		1 1.4%		2 2.7%	2 2.7%	64 87.7%	5 6.8%		71 97.3%	73 100%
TOTAL			1 0.1%									239 20.2%	23 1.9%	71 6.0%		333 28.1%	68 5.7%	694 58.6%	83 7.0%	5 0.4%	850 71.8%	1 184 100%

TABLE 11 (concluded)

Treatment Schedule 3

BEFORE TREATMENT / AFTER TREATMENT

Stage		Tr 0	Tr doubtful	I				II				III+		III			IV					TOTAL
				+	++	+++	Total	+	++	+++	Total	Fo	F+	++	+++	Total	o	+	++	+++	Total	
Tr doubtful												1 3.8%	2 7.7%			3 11.5%	3 11.5%	20 76.9%			23 88.5%	26 100%
I	+											5	4			9 11.0%	17	55	1		73 89.0%	82 100%
	++												1			1 16.7%	2	3			5 83.3%	6 100%
	+++																					
Total I												5 5.7%	5 5.7%			10 11.4%	19 21.6%	58 65.9%	1 1.1%		78 88.6%	88 100%
II	+											25	5	1		31 24.6%	11	83	1		95 75.4%	126 100%
	++											50	9	18		77 49.4%	7	70	2		79 50.6%	156 100%
	+++											5		7		12 66.7%		5	1		6 33.3%	18 100%
Total II												80 26.7%	14 4.7%	26 8.7%		120 40.0%	18 6.0%	158 52.7%	4 1.3%		180 60.0%	300 100%
III+	Fo											63	3	12		78 20.9%	10	224	58	3	295 79.1%	373 100%
	F+											31	5	5		41 27.3%	7	86	16		109 72.7%	150 100%
III	++											45	4	10		59 49.6%		28	29	3	60 50.4%	119 100%
	+++													1		1 50.0%		1			1 50.0%	2 100%
Total III												139 21.6%	12 1.8%	28 4.3%		179 27.8%	17 2.6%	339 52.6%	103 16.0%	6 0.9%	465 72.2%	644 100%
IV	o																					
	+																1	97	4		102 100%	102 100%
	++																	3	5		8 100%	8 100%
	+++																			2	2 100%	2 100%
Total IV																	1 0.9%	100 89.3%	9 8.0%	2 1.8%	112 100%	112 100%
TOTAL												225 19.2%	33 2.8%	54 4.6%		312 26.7%	58 5.0%	675 57.7%	117 10.0%	8 0.7%	858 73.3%	1 170 100%

TABLE 12
MEKNÈS: CATEGORIES OF RESPONSE TO TREATMENT

Treatment Schedule 1

Stage	Severity	Cured				Not cured					Doubtful (Category X)	TOTAL
		A 1	A 2	Not determined	Total	B 1	B 2	B 3	Not determined	Total		
I	+	32	19	5	56 76.7%		2	1		3 4.1%	14 19.2%	73 100%
	++	5	7		12 100%							12 100%
	+++											
Total I		37 43.5%	26 30.6%	5 5.9%	68 80.0%		2 2.4%	1 1.2%		3 3.5%	14 16.5%	85 100%
II	+	49	40	9	98 74.8%		5			5 3.8%	28 21.4%	131 100%
	++	17	59	6	82 53.2%		17	6		23 14.9%	49 31.8%	154 100%
	+++		5		5 22.7%		2	3		5 22.7%	12 54.5%	22 100%
Total II		66 21.5%	104 33.9%	15 4.9%	185 60.3%		24 7.8%	9 2.9%		33 10.7%	89 29.0%	307 100%
III+	Fo	127	105	18	250 80.9%		10	4		14 4.5%	45 14.6%	309 100%
	F+	45	39	2	86 68.8%		11			11 8.8%	28 22.4%	125 100%
III	++	13	31	2	46 53.5%	1	5	1		7 8.1%	33 38.4%	86 100%
	+++											
Total III		185 35.6%	175 33.7%	22 4.2%	382 73.5%	1 0.2%	26 5.0%	5 1.0%		32 6.2%	106 20.4%	520 100%
TOTAL		288 31.6%	305 33.4%	42 4.6%	635 69.6%	1 0.1%	52 5.7%	15 1.6%		68 7.5%	209 22.9%	912 100%

TABLE 12 (continued)

Treatment Schedule 2

Stage	Severity	Cured				Not cured					Doubtful (Category X)	TOTAL
		A 1	A 2	Not determined	Total	B 1	B 2	B 3	Not determined	Total		
I	+	33	28	8	69 79.3%		2			2 2.3%	16 18.4%	87 100%
	++		2		2 40.0%		1			1 20.0%	2 40.0%	5 100%
	+++											
Total I	Total I	33 35.9%	30 32.6%	8 8.7%	71 77.2%		3 3.3%			3 3.3%	18 19.6%	92 100%
II	+	48	43	13	104 80.6%		8	2		10 7.8%	15 11.6%	129 100%
	++	22	57	5	84 53.5%	1	18	9		28 17.8%	45 28.7%	157 100%
	+++		1		1 8.3%		4	3		7 58.3%	4 33.3%	12 100%
Total II	Total II	70 23.5%	101 33.9%	18 6.0%	189 63.4%	1 0.3%	30 10.1%	14 4.7%		45 15.1%	64 21.5%	298 100%
III+	Fo	159	146	33	338 83.0%		6	2		8 2.0%	61 15.0%	407 100%
	F+	40	51	6	97 64.7%	1	9			10 6.7%	43 28.7%	150 100%
III	++	6	50	6	62 44.3%	2	21	4		27 19.3%	51 36.4%	140 100%
	+++		1		1 50.0%						1 50.0%	2 100%
Total III		205 29.3%	248 35.5%	45 6.4%	498 71.2%	3 0.4%	36 5.2%	6 0.9%		45 6.4%	156 22.3%	699 100%
TOTAL		308 28.3%	379 34.8%	71 6.5%	758 69.6%	4 0.4%	69 6.3%	20 1.8%		93 8.5%	238 21.9%	1 089 100%

TABLE 12 (concluded)

Treatment Schedule 3

Stage	Severity	Cured				Not cured					Doubtful (Category X)	TOTAL
		A 1	A 2	Not determined	Total	B 1	B 2	B 3	Not determined	Total		
I	+	60	8	5	73 89.0%		2	2		4 4.9%	5 6.1%	82 100%
	++	2	2	1	5 83.3%		1			1 16.7%		6 100%
	+++											
Total I		62 70.5%	10 11.3%	6 6.8%	78 88.6%		3 3.4%	2 2.3%		5 5.7%	5 5.7%	88 100%
II	+	65	13	17	95 75.4%		6			6 4.8%	25 19.8%	126 100%
	++	55	15	9	79 50.6%	2	13	12		27 17.3%	50 32.1%	156 100%
	+++	3	2	1	6 33.3%		3	4		7 38.9%	5 27.8%	18 100%
Total II		123 41.0%	30 10.0%	27 9.0%	180 60.0%	2 0.7%	22 7.3%	16 5.3%		40 13.3%	80 26.7%	300 100%
III+	Fo	203	36	56	295 79.1%		12	3		15 4.0%	63 16.9%	373 100%
	F+	70	27	12	109 72.7%		4	6		10 6.7%	31 20.7%	150 100%
III	++	32	18	10	60 50.4%	2	8	4		14 11.8%	45 37.8%	119 100%
	+++	1			1 50.0%	1				1 50.0%		2 100%
Total III		306 47.5%	81 12.6%	78 12.1%	465 72.2%	3 0.5%	24 3.7%	13 2.0%		40 6.2%	139 21.6%	644 100%
TOTAL		491 47.6%	121 11.7%	111 10.8%	723 70.1%	5 0.5%	49 4.7%	31 3.0%		85 8.2%	224 21.7%	1 032 100%

TABLE 13

MEKNÈS: CATEGORIES OF RESPONSE TO TREATMENT IN RELATION TO AGE AND TO STAGE OF TRACHOMA

Treatment Schedule 1

Stage before treatment	Category of response	Age (years)							TOTAL
		6	7	8	9	10	11	12	
I	A	27	21	11	4	2	2	1	68 80.0%
	B	1	1		1				3 3.5%
	X	5	4	4			1		14 16.5%
	Total	33	26	15	5	2	3	1	85 100.0%
II	A	69	44	26	16	11	14	5	185 60.3%
	B	24	5	4					33 10.7%
	X	39	23	15	4	5	3		89 29.0%
	Total	132	72	45	20	16	17	5	307 100.0%
III	A	37	63	77	58	53	62	32	382 73.5%
	B	6	9	8	4	4		1 2.8%	32 6.2%
	X	22	20	20	18	8	15	3	106 20.4%
	Total	65	92	105	80	65	77	36	520 100.1%
Total I+ II+ III	A	133 57.8%	128 67.4%	114 69.1%	78 74.3%	66 79.5%	78 80.4%	38 90.5%	635 69.6%
	B	31 13.5%	15 7.9%	12 7.3%	5 4.8%	4 4.8%		1 2.4%	68 7.5%
	X	66 28.7%	47 24.7%	39 23.6%	22 21.0%	13 15.7%	19 19.6%	3 7.1%	209 22.9%
	TOTAL	230 100.0%	190 100.0%	165 100.0%	105 100.1%	83 100.0%	97 100.0%	42 100.0%	912 100.0%

TABLE 13 (continued)

Treatment Schedule 2

Stage before treatment	Category of response	Age (years)							TOTAL
		6	7	8	9	10	11	12	
I	A	33	14	7	10	3	3	1	71 77.2%
	B	2		1					3 3.3%
	X	12	3	2	1				18 19.6%
	Total	47	17	10	11	3	3	1	92 100.1%
II	A	56	41	30	18	25	15	4	189 63.4%
	B	27	7	6		5			45 15.1%
	X	28	18	10	1	4	2	1	64 21.5%
	Total	111	66	46	19	34	17	5	298 100.0%
III	A	44	117	103	59	71	77	27	498 71.2%
	B	12	10	8	5	6	4		45 6.4%
	X	20	46	30	22	10	22	6	156 22.3%
	Total	76	173	141	86	87	103	33	699 99.9%
Total I+ II+ III	A	133 56.8%	172 67.2%	140 71.1%	87 75.0%	99 79.8%	95 77.2%	32 82.1%	758 69.6%
	B	41 17.5%	17 6.6%	15 7.6%	5 4.3%	11 8.9%	4 3.3%		93 8.5%
	X	60 25.6%	67 26.2%	42 21.3%	24 20.7%	14 11.2%	24 19.5%	7 17.9%	238 21.9%
	TOTAL	234 99.9%	256 100.0%	197 100.0%	116 100.0%	124 99.9%	123 100.0%	39 100.0%	1 089 100.0%

TABLE 13 (concluded)

Treatment Schedule 3

Stage before treatment	Category of response	Age (years)							TOTAL
		6	7	8	9	10	11	12	
I	A	18	21	24	8	2	4	1	78 88.6%
	B	1	1	2		1			5 5.7%
	X	5							5 5.7%
	Total	24	22	26	8	3	4	1	88 100.0%
II	A	50	36	43	18	12	15	6	180 60.0%
	B	20	12	5		1	2		40 13.3%
	X	27	22	18	6	3	2	2	80 26.7%
	Total	97	70	66	24	16	19	8	300 100.0%
III	A	42	85	104	64	65	65	40	465 72.2%
	B	5	15	6	5	2	4	3	40 6.2%
	X	19	37	25	24	16	12	6	139 21.6%
	Total	66	137	135	93	83	81	49	644 100.0%
Total I+ II+ III	A	110 58.8%	142 62.0%	171 75.3%	90 72.0%	79 77.5%	84 80.8%	47 81.0%	723 70.1%
	B	26 13.9%	28 12.2%	13 5.7%	5 4.0%	4 3.9%	6 5.8%	3 5.2%	85 8.2%
	X	51 27.3%	59 25.8%	43 18.9%	30 24.0%	19 18.6%	14 13.5%	8 13.8%	224 21.7%
	TOTAL	187 100.0%	229 100.0%	227 99.9%	125 100.0%	102 100.0%	104 100.1%	58 100.0%	1 032 100.0%

and should always be recorded and taken into account; (2) in an established school campaign, when it is chiefly the new entrants each year that need treatment (the older children having already been treated and cured), the percentage of cures may be lower than in the first year when pupils of all ages were treated together.

Table 14 shows the results according to category of response in the three different groups of schools in Meknès to which reference was made earlier.

CICATRIZATION

As already mentioned, the value of different trachoma treatment methods which give otherwise comparable results may depend on the degree of the cicatrization during the healing process.

In the three treatment schedules the therapeutic agent is the same, though the rhythm and intensity of the treatment may influence the cicatrization. The possibility may be admitted, in treatment schedule 1, of the virus being eliminated sooner than in schedule 3, thus enabling an earlier resolution of the lesions, which might cause a difference in the degree of final cicatrization.

Table 15 shows how this is reflected in the final quantity of scar tissue present.

The resolution in cases initially in stages I and II produces a percentage of cures with no visible scars (using a binocular loupe for detection) much the same in all three treatment schedules. Slight scarring of no practical importance (C+) is the result most frequently observed. More evident scarring (C++) occurred in all three treatment schedules in a comparatively small number of cases.

Much more marked scarring is observed after cure in cases initially in stage III, often with gross scarring present at the first examination. Here the extent of scarring after treatment depends not so much on the type of treatment as on the fact that the treatment leading to cure came late, when much cicatrization was already present. Thus by comparing the degree of cicatrization resulting in Tr I and II with the result in Tr III, the marked benefit of treating children early with antibiotics can be seen immediately.

Comparison of the degree of scarring after cure by antibiotic treatment with that seen in children in the same schools cured by unknown methods, or spontaneously, shows that the antibiotic treatment has given the more favourable results.

In the series of cases that were treated the percentage of moderately heavy scarring (C++) is, for Tr I cures, 0.5%, and for Tr II cures, 3.8%, as against 16.9% of moderately heavy scarring, plus 3.0% of the heaviest scarring in the group cured by other means before the campaign. This would indicate that the risks may for the future be diminished by the antibiotic treatment of the children at as early an age as possible and before the development of the advanced stages of trachoma.

LATE FOLLOW-UP EXAMINATION

At the end of June 1956—12-14 months after end of treatment—1154 children who were declared clinically cured on October 1955 were re-examined. In eleven out of this number trachoma follicles were found besides scars. The follicles in eight of these cases were of the Tr I type, which seems to indicate that a new infection was present. In the three other cases there appeared to be nothing to indicate whether a new infection or a relapse had occurred. In nine further cases papillary hypertrophy alone was present in a form in which the possibility of active trachoma could not be excluded.

Thus, the relapse rate after a year could be estimated at not more than 1.1% and reinfections at not more than 0.7%.

Table 16 shows the number of reinfections and/or relapses recorded one year after termination of the treatment under the three different schedules.

The comparatively small number of possible relapses in all three treatment schedules would not suggest any difference in lasting effect in any one of them. It indicates, moreover, that the criteria of cure have been sufficiently strict.

REPETITION OF THE TRIAL WITH DIFFERENT TREATMENT SCHEDULES UNDER RURAL CONDITIONS, TIZNIT, 1957-58

In order to assess the value of the short-term intermittent treatment of trachomatous children in rural schools in southern Morocco another comparative trial with two different schedules was carried out in schools in the Tiznit province in 1957-58.

TABLE 14

MEKNÈS: CATEGORIES OF RESPONSE TO TREATMENT IN THREE DIFFERENT GROUPS OF SCHOOLS

Jewish Schools (Mellah)

Category of response	Schedule 1				Schedule 2				Schedule 3			
	Tr I	Tr II	Tr III	Total	Tr I	Tr II	Tr III	Total	Tr I	Tr II	Tr III	Total
A	30 76.9%	34 79.1%	42 82.4%	106 79.7%	28 77.8%	37 77.1%	50 86.2%	115 81.0%	36 87.8%	29 70.7%	53 82.8%	118 80.8%
B	2 5.1%	1 2.3%	2 3.9%	5 3.8%		6 2.5%	1 1.7%	7 4.9%	4 9.8%	3 7.3%		7 4.8%
X	7 17.9%	8 18.6%	7 13.7%	22 16.5%	8 22.2%	5 10.4%	7 12.1%	20 14.1%	1 2.4%	9 22.0%	11 17.2%	21 14.4%
Total	39 100%	43 100%	51 100%	133 100%	36 100%	48 100%	58 100%	142 100%	41 100%	41 100%	64 100%	146 100%

5 Best Moslem Schools

Category of response	Schedule 1				Schedule 2				Schedule 3			
	Tr I	Tr II	Tr III	Total	Tr I	Tr II	Tr III	Total	Tr I	Tr II	Tr III	Total
A	16 94.1%	56 66.7%	120 72.7%	192 72.2%	16 72.7%	36 60.0%	106 71.1%	158 68.4%	16 84.2%	46 67.6%	110 80.3%	172 76.8%
B		4 4.7%	7 4.2%	11 4.1%	2 9.1%	9 15.0%	9 6.0%	20 8.7%	1 5.3%	9 13.2%	5 3.6%	15 6.7%
X	1 5.8%	24 28.6%	48 29.1%	63 23.7%	4 18.2%	15 25.0%	34 22.8%	53 22.9%	2 10.5%	13 19.1%	22 16.1%	37 16.5%
Total	17 100%	84 100%	165 100%	266 100%	22 100%	60 100%	149 100%	231 100%	19 100%	68 100%	137 100%	224 100%

4 Worst Moslem Schools

Category of response	Schedule 1				Schedule 2				Schedule 3			
	Tr I	Tr II	Tr III	Total	Tr I	Tr II	Tr III	Total	Tr I	Tr II	Tr III	Total
A	3 75.0%	26 33.8%	43 56.6%	72 45.9%	5 71.4%	34 50.0%	114 60.0%	153 57.7%	3 100%	37 50.0%	94 59.1%	134 56.8%
B	1 25.0%	15 19.4%	8 10.5%	24 15.2%		16 23.5%	17 8.9%	33 12.5%		14 18.9%	14 8.8%	28 11.9%
X		36 46.8%	25 32.9%	61 38.9%	2 28.5%	18 26.5%	59 31.1%	79 29.8%		23 31.1%	51 32.1%	74 31.4%
Total	4 100%	77 100%	76 100%	157 100%	7 100%	68 100%	190 100%	265 100%	3 100%	74 100%	159 100%	236 100%

TABLE 15

MEKNÈS: COMPARISON OF DEGREE OF FINAL CICATRIZATION AFTER CURE OF TRACHOMA UNDER THREE DIFFERENT TREATMENT SCHEDULES IN RELATION TO STAGE AND SEVERITY

Stage	Treatment schedule 1					Treatment schedule 2					Treatment schedule 3					Total				
	Co	C+	C++	C+++	Total cured	Co	C+	C++	C+++	Total cured	Co	C+	C++	C+++	Total cured	Co	C+	C++	C+++	Total cured
Total I	14 20.6%	54 79.4%			68 100%	22 31.0%	49 69.0%			71 100%	19 24.4%	58 74.4%	1 1.3%		78 100.1%	55 25.3%	161 74.2%	1 0.5%		217 100%
II+	11	87			98 99.9%	14	89	1		104 100.1%	11	83	1		95 100%	36 12.1%	259 87.2%	2 0.7%		297 100%
II++	8	70	4		82 100.1%	7	69	8		84 99.9%	7	70	2		79 100%	22 9.0%	209 85.3%	14 5.7%		245 100%
II+++		1	4		5 100%		1			1 100%		5	1		6 100%		7 58.3%	5 41.7%		12 100%
Total II	19 10.3%	158 85.4%	8 4.3%		185 100%	21 11.1%	159 84.1%	9 4.8%		189 100%	18 10.0%	158 87.8%	4 2.2%		180 100%	58 10.5%	475 85.7%	21 3.8%		554 100%
III+ Fo	14	187	44	5	250 100%	15	290	28	5	338 100%	10	224	58	3	295 100%	39 4.4%	701 79.4%	130 14.7%	13 1.5%	883 100%
III+ F+	6	73	6	1	86 100.1%	5	78	14		97 100%	7	86	16		109 100%	18 6.2%	237 81.2%	36 12.3%	1 0.3%	292 100%
III++	1	26	16	3	46 100%		35	27		62 100%		28	29	3	60 99.9%	1 0.6%	89 53.0%	72 42.9%	6 3.6%	168 100.1%
III+++							1			1 100%		1			1 100%		2 100%			2 100%
Total III	21 5.5%	286 74.9%	66 17.3%	9 2.4%	382 100.1%	20 4.0%	404 81.1%	69 13.9%	5 1.0%	498 100%	17 3.7%	339 72.9%	103 22.2%	6 1.3%	465 100.1%	58 4.3%	1 029 76.5%	238 17.7%	20 1.5%	1 345 99.9%

TABLE 16

MEKNÈS: RESULTS OF RE-EXAMINATION OF 1154 CASES DECLARED CURED, ONE YEAR AFTER END OF TREATMENT

Children treated by:	Examined	Trachoma III with follicles	Trachoma III without follicles
Schedule 1	294	5 1.7%	3 1.0%
Schedule 2	425	4 0.9%	3 0.7%
Schedule 3	435	2 0.5%	3 0.7%
TOTAL	1 154	11 1.0%	9 0.8%

In this part of the country secondary infections are more prevalent and general living conditions are on a lower level than in the northern towns.

Two groups of similar village schools were selected with about 600 children in each. Treatment schedules 2 and 3 were attributed at random to these groups.

Treatment was started in January 1957 and all children still found in school were re-examined in June and in November 1957, and again in June 1958.

RESULTS

Table 17 shows the results in both groups treated by different schedules.

As in Meknès, no difference can be detected between the respective cures and failures in the two groups.

The number of the treated children who could be re-examined after the follow-up period is not large enough to allow of a safe comparison of the results by age and by severity in each stage of the disease.

FOLLOW-UP EXAMINATION

At the end of June 1958, i.e., 12 months after the end of treatment, 346 children who were declared cured in November 1957 could be re-examined. In three out of this number trachoma follicles were found besides scars. In ten other cases papillary hypertrophy was present in a form which indicated that reactivation could not be excluded. The number of possible relapses or reinfections does not appear to be different in either of the two groups.

CONCLUSIONS REACHED FROM EXPERIMENTAL TRIALS IN THE SCHOOLS OF MARRAKECH, MEKNÈS AND TIZNIT

1. Trachoma in Morocco is susceptible to treatment with antibiotics. Treatment with chlortetracycline has resulted in the clinical cure of 57%-80% of trachoma in Moroccan schoolchildren, the rate depending on the evolutive stage and severity of the disease and on the living conditions of the communities involved. Experience has shown that even in the more resistant cases a very high proportion of cures is obtained after a second course of treatment.

2. A standardized system of recording and evaluation has been developed which permits comprehensive and accurate comparisons of the therapeutic trials.

TABLE 17
TIZNIT: CATEGORIES OF RESPONSE TO TREATMENT
Treatment Schedule 2

Stage	Severity	Cured				Not cured					Doubtful (Category X)	TOTAL
		A 1	A 2	Not determined	Total	B 1	B 2	B 3	Not determined	Total		
I	+	1	1		2							2 100%
	++											
	+++											
Total I												
II	+	24	6	3	33 97.1%		1			1 2.9%		34 100%
	++	11	13	5	29 65.3%	2	5	3		10 22.7%	5 11.4%	44 100%
	+++		7		7 41.2%	3		2		5 29.4%	5 29.4%	17 100%
Total II		35 36.8%	26 27.4%	8 8.4%	69 72.6%	5 5.3%	6 6.3%	5 5.3%		16 16.8%	10 10.5%	95 100%
III+	Fo	46	7	6	59 92.2%		3			3 4.7%	2 3.1%	64 100%
	F+	45	11	8	64 85.3%	1	2	1		4 5.3%	4 9.3%	75 100%
III	++	17	12	3	32 54.2%	3	3	4		10 16.9%	17 28.8%	59 100%
	+++		1		1							1 100%
Total III		108 54.3%	31 15.6%	17 8.5%	156 78.4%	4 2.0%	8 4.0%	5 2.5%		17 8.5%	26 13.1%	199 100%
TOTAL		144 48.6%	58 19.6%	25 8.4%	227 76.7%	9 3.0%	14 4.7%	10 3.4%		33 11.1%	36 13.3%	296 100%

TABLE 17 (concluded)
Treatment Schedule 3

Stage	Severity	Cured				Not cured					Doubtful (Category X)	TOTAL
		A 1	A 2	Not determined	Total	B 1	B 2	B 3	Not determined	Total		
I	+											
	++											
	+++											
Total I												
II	+	18	2		20 95.2%					1 4.8%		21 100%
	++	15	8	1	24 82.8%	1	4			5 17.2%		29 100%
	+++		4		4 30.8%	2	1	3		6 46.2%	3 23.1%	13 100%
Total II		33 52.4%	14 22.2%	1 1.6%	48 76.2%	3 4.8%	5 7.9%	4 6.3%		12 19.0%	3 4.8%	63 100%
III+	Fo	56	18	7	81 94.2%						5 5.8%	86 100%
	F+	61	15	11	87 83.7%	1	6	1		8 7.7%	9 8.7%	104 100%
III	++	26	28	3	57 68.7%	4	6	3		13 15.7%	13 15.7%	83 100%
	+++		2		2 40.0%	1			1	2 40.0%	1 20.0%	5 100%
Total III		143 51.4%	63 21.7%	21 7.6%	227 81.7%	6 2.2%	12 4.3%	4 1.4%	1 0.4%	23 8.3%	28 10.1%	278 100%
TOTAL		176 51.6%	77 22.6%	22 6.5%	275 80.6%	9 2.6%	17 5.0%	8 2.3%	1 0.3%	35 10.3%	31 9.1%	341 100%

In an attempt to develop a rational and economically feasible method of collective treatment it was agreed to adopt and to work to an " acceptable limit of failure " on the basis that it is more economical, both in supplies and personnel, to re-treat a slightly larger percentage of relapses than to subject all cases to an unnecessarily long and expensive course of treatment in the first instance. This approach has proved successful.

3. This method of treatment cured the trachoma in more than 98% of the schoolchildren kept under control for a period of two years.

4. It would appear that relapse and reinfection rates are relatively low in schoolchildren, at least in the urban districts of Morocco. Out of a total of 1564 trachomatous schoolchildren in Marrakech pronounced cured after the standard six months post-treatment follow-up, it was possible to re-examine 914 one year later, i.e., 18 months after the termination of treatment. Of these, 11 cases (1.2%) showed signs of active trachoma. This goes to confirm the validity of the present criteria of clinical cure. It also supports the view that, since children of school age are less susceptible to seasonal conjunctivitis than the pre-school group, they are also less exposed to reinfection with trachoma.

5. Clinical evidence was collected that, after an appropriate treatment with antibiotics, fine papillary hypertrophy associated only with scars is not to be considered a sign of persistent activity of the trachoma.

6. The minimum effective course of treatment is, for the average type of case in Morocco, very considerably less than that originally recommended by the WHO Expert Committee on Trachoma (1952).

A series of carefully controlled trials in Meknès has shown:

(*a*) that the local application of 1% chlortetracycline ointment three times daily over 60 consecutive working days results in about 80% cures in the better-class urban schools;

(*b*) that under similar conditions the frequency of application can be reduced to twice a day without loss of efficacy;

(*c*) that equally good results follow intermittent short-term treatment over longer periods—e.g., application of chlortetracycline twice daily on three consecutive days every four weeks over a period of 20 weeks, i.e., six three-day cycles of treatment.

The value of this short-term intermittent treatment in the case of trachomatous children in rural schools in southern Morocco has been confirmed by the Tiznit trials. Here, secondary infections are more prevalent and persistent, general living conditions being on a lower level than in the north.

7. The experiments have shown very clearly that there is no need to maintain the 60-day continuous treatment in the schools of Morocco, since the same results can be obtained by the much more economic intermittent treatment. The main advantages are the following:

(*a*) The consumption of ointment for a full course of treatment for one person is reduced from 18 g to 3-6 g;

(*b*) One instillator is able to treat 3-5 times as many children by the intermittent method;

(*c*) Intermittent treatment is readily accepted in the schools; daily applications for three consecutive days each month disturb school work very little. The simplicity of the schedule was welcomed by the teachers, who now willingly participate in its application, thus saving expense on personnel. Moreover, the simplicity of the scheme is the best propaganda for trachoma treatment itself.

8. Under certain conditions the school campaigns have helped to promote understanding of and active participation in measures against communicable eye diseases by families and the community as a whole.

9. These experiences have made it possible to plan the expansion of school treatment to all schools in the country.

In 1958 altogether 263 000 children were treated. The target number for 1959 is 350 000 and that for 1960 is 400 000. By that time treatment will cover all schools throughout the country.

SIMILAR EXPERIMENTS WITH INTERMITTENT TREATMENT IN OTHER COUNTRIES

It should be understood that some of the conclusions drawn from the experimental work in Morocco are not to be taken as fully valid for other countries. Factors such as the clinical type of the disease, its evolutive stage and duration, associated infections, the general environment, etc. vary considerably from one area to another and may affect response to treatment. It is therefore necessary for each country to determine by well-controlled trials the schedule of treatment most appropriate to the local problem of trachoma.

At the time of preparing this paper, however, some preliminary reports are available which confirm the efficacy of intermittent treatment with antibiotics.

In the Spanish village of La Mamola, 83% of the population of approximately 1200 were found to be trachomatous. Of these, 93.3% were cured after one six-months course of intermittent treatment with 1% oxytetracycline ointment (M. Calvo-Flores—personal communication, 1958). In other villages in Spain similar encouraging results have been recently observed (M. Mesquita-Lopez—personal communication, 1958). These results are better than those observed in Morocco, where the climatic and environmental conditions are, of course, much worse. From Yugoslavia, D. Savić (personal communication, 1958) reports that out of 101 cases with active trachoma treated with chlortetracycline ointment twice daily for five consecutive days each month over a period of six months, 56% were cured after a six-months follow-up period. It should be noted that owing to absenteeism nearly half of the patients of this group received less than 70% of the prescribed number of applications of the ointment.

In Turkey, out of 660 children with active trachoma in the provinces of Adana and Gasiantep, 65% were cured; in 13% the cure was doubtful and in 22% trachoma was still active at the end of the first course of intermittent treatment (K. Tosunoglu —personal communication, 1958).

From Algeria J. Ruff (personal communication, 1958) reports that at the end of the first course of treatment given to some 15 660 schoolchildren there appeared to be no difference between the results after continuous treatment for 60 days and those after application of the intermittent schedule. Further examinations and trials are needed for a proper evaluation of the method in Algeria.

J. Graham Scott [1] reports about 70% of cures in schoolchildren in South Africa after intermittent treatment with chloramphenicol (two daily applications for three consecutive days each month over a period of one year).

P. Delon [2] reports that in Indonesia, although the over-all rate of cures of trachoma in schoolchildren was relatively low, there was no appreciable difference between the results of the continuous and intermittent schedules of treatment with chlortetracycline.

It is now believed that the minimum requisite treatment with antibiotics may vary from country to country, and that irregular attendance for treatment, frequent in some schools in certain countries, may impose a treatment cycle of more than three days. Further trials are also necessary to determine the optimum interval between cycles of treatment.

[1] In a communication, to be published, to the Annual Meeting (1958) of La Ligue contre le Trachome

[2] In an unpublished report on the WHO/UNICEF-assisted pilot project for the control of trachoma in Indonesia (1958)

MECHANISM OF INTERMITTENT TREATMENT

At the moment there is no direct way of explaining the mechanism of the intermittent antibiotic treatment of trachoma, which at first sight seems so inadequate.

One factor which may be of value in this schedule is that the treatment is continued intermittently for a longer period than the duration of the continuous schedule, i.e., 5-6 as against 2-3 months.

It is a common observation that in many cases clinical cure is not completed until weeks or months after the end of the prescribed course of antibiotic treatment. In the Meknès trials the following observations were made:

Of all cases found clinically cured at the end of a six-months' follow-up period, the following per-

centages had been considered cured at the moment the treatment was terminated:

Cases treated three times daily for 60 days (schedule 1)	48.6%
Cases treated twice daily for 60 days, (schedule 2)	44.8%
Cases treated twice daily for three consecutive days each month during five months (schedule 3)	80.2%

In the rest of the cases more time was necessary for resolution and cicatrization.

The fact that a high proportion of cases reached clinical cure during the course of intermittent treatment suggests that even the early cycles of treatment have a marked inhibiting effect on the virus.

We know, however, from observations made on children who have not received the full course that one or only a few three-day cycles are not enough to give satisfactory results. Our feeling today is that five or six cycles constitute the minimum effective course of treatment for the average case.

An advantage of the five-month's period of intermittent treatment over the two or three months' continuous treatment may be that the conjunctival sac is kept relatively free from bacterial infection for a longer period. Few really believe, however, that the absence of bacteria alone could lead to the cure of trachoma in so large a percentage of cases in such a relatively short-time. That certain antibiotics, including chlortetracycline, have a direct and specific action on the trachoma virus has been shown (Thygeson & Nataf, 1958; T'ang et al., 1957; Collier & Sowa, 1958).

It has been suggested that the trachoma virus has a certain life-cycle during which its morphology, metabolism, staining properties, etc. change. Its multiplication is supposed to occur in one specific phase of the cycle. There is yet little definitely known about the length of the complete cycle, or its components, but it is believed that the virus may persist for long periods in an inactive, non-multiplying form.

The frequent observation that "reactivated" trachoma is easier to cure with antibiotics than that of low clinical activity suggests that the virus is more susceptible to antibiotics when it is in an "active" phase. Theoretically it is possible that the virus is most susceptible during or soon after the phase of multiplication. In that case the three-day cycle of treatment may perhaps be sufficient to eliminate all virus particles which are at that time in such a susceptible phase. The same antibiotic may have little or no effect on virus particles which, at the time of application, are in an inactive state.

If, by the time of the next three-day treatment cycle, some of the residual "inactive" virus has passed into the "susceptible active" phase, this portion may again be eliminated. Thus, if the intervals between the three-day treatment cycles happened to be suitable, little or no multiplication could take place and finally all the virus would be eliminated. If this be so, continuous treatment with the same antibiotic would not be any more effective. This explanation of the very similar results obtained with the continuous and intermittent schedules of treatment does not seem to be in conflict with the recent laboratory findings of T'ang and co-workers (1957) and of Collier & Sowa (1958) or the clinical experience of Bietti & Pannarali (1955). Nor does it contradict the ideas recently expressed by Bietti, Thygeson and Nataf on how antibiotics act in general on the trachoma virus.

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RÉSUMÉ

Au Maroc, une forte proportion des cas de trachome réagissent favorablement au traitement à la chlortétracycline. Le dépistage systématique et le traitement collectif dans les écoles permettent de réduire efficacement la maladie chez les enfants. Les cas précoces guérissent avec des cicatrices très légères et, par conséquent, sans grand risque de complications cicatricielles ultérieures. D'autre part, les réinfections après guérison sont rares chez les enfants d'âge scolaire.

En 1953/54, la première campagne organisée en grand dans les écoles s'est étendue à tous les établissements de Marrakech. Le schéma de traitement appliqué aux

enfants trachomateux s'inspirait des recommandations du Comité OMS d'experts du Trachome (premier rapport, 1953): une application locale de pommade à la chlortétracycline à 1% trois fois par jour pendant 60 jours ouvrables consécutifs (cinq jours par semaine). Les résultats, observés sept mois après la fin du traitement sur un groupe de 3800 enfants trachomateux, ont été les suivants: 56,9% étaient cliniquement guéris; 33,6% accusaient une amélioration appréciable et étaient probablement guéris (ces cas ont été classés provisoirement comme « Cas x » en attendant les résultats des contrôles ultérieurs); 9,5% présentaient encore des signes de trachome évolutif.

Au cours de l'année scolaire suivante, les cas encore évolutifs reçurent un nouveau traitement: pommade à la chlortétracycline en application locale comme auparavant et trisulfamide par voie buccale. A la suite de ce second traitement, tous les enfants, sauf 1,6% d'entre eux, furent guéris. De même, il s'est confirmé que la grande majorité des « Cas x » avaient été guéris par le premier traitement.

En vue de mettre au point un traitement plus simple et plus économique, les trois schémas suivants ont été comparés au cours d'essais parallèles exécutés dans les écoles de Meknès pendant l'année scolaire 1955/56:

Schéma 1: Application d'une pommade à la chlortétracycline à 1% trois fois par jour pendant 60 jours ouvrables consécutifs (c'est-à-dire le schéma primitif).

Schéma 2: Application deux fois par jour pendant 60 jours ouvrables consécutifs.

Schéma 3: Application deux fois par jour pendant trois jours consécutifs, ce cycle étant répété chaque mois pendant six mois.

Trois groupes distincts, mais comparables, comptant au total 4136 enfants trachomateux ont été inclus dans ces essais. Les résultats des trois schémas ont été remarquablement voisins entre sujets analogues par *a*) le stade et la gravité de la maladie; *b*) l'âge; *c*) le milieu social et les conditions matérielles.

De même, il n'y a pas eu de différence appréciable entre les trois groupes en ce qui concerne: *d*) le degré de cicatrisation résiduelle après guérison; *e*) le taux de rechutes constaté un an après la fin du traitement.

Pendant l'année 1957/58, la méthode du traitement rapide intermittent a été de nouveau mise à l'essai, cette fois dans des écoles rurales de la province de Tisnit (partie sud du Maroc). Dans cette région, les infections bactériennes associées sont plus fréquentes et le niveau de vie est plus bas.

Les schémas de traitement 2 et 3 ont été appliqués à deux groupes comptant au total 1167 enfants trachomateux. Comme dans les essais de Meknès, on n'a pu constater aucune différence appréciable entre les résultats du traitement continu et ceux de la méthode intermittente.

Dans aucun de ces essais, les résultats n'ont été enregistrés avant l'expiration d'une période de contrôle variant entre 4 et 7 mois. En outre, des examens complémentaires ont été pratiqués 12-18 mois plus tard en vue de dépister les rechutes tardives ou les erreurs de diagnostic.

Sur la base des résultats ainsi obtenus, les auteurs estiment qu'une légère hypertrophie papillaire subsistant après l'antibiothérapie et constituant l'unique symptôme conjonctival autre que la cicatrisation, et en l'absence de toute lésion cornéenne évolutive, ne devrait pas être considérée comme le signe d'un trachome évolutif persistant.

Les auteurs proposent l'explication suivante de l'efficacité du traitement intermittent. C'est au stade de la multiplication active que le virus du trachome serait le plus sensible aux antibiotiques. Le cycle de traitement de trois jours peut suffire à éliminer toutes les particules virales qui ont atteint ce stade, mais non celles qui, au moment du traitement, sont dans une phase inactive. Des traitements brefs répétés à intervalles appropriés permettraient finalement d'éliminer tous les virus présents.

Quelle que soit l'explication, la méthode intermittente s'est révélée extrêmement efficace dans le traitement du trachome au Maroc. De même, les rapports préliminaires provenant de plusieurs autres pays confirment qu'il y a peu de différence entre les résultats de cette méthode et ceux de la méthode ancienne du traitement continu. Le schéma intermittent permet une grosse économie, non seulement d'antibiotiques, mais aussi de personnel et de moyens divers, ce qui rend possible une large expansion des programmes de traitement.

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