

QUININE PROPHYLAXIS IN NORTHERN INDIA.

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(Continued from p. 267.)

In 1929 a total of 701 British and 3,560 Indian troops at Nowshera, Peshawar, Shagai and Landi Kotal in the Peshawar district, and Hangu and Thal in the Kohat district, were included in the test, which extended from September 1 to December 4—over three months. During this time quinine was only given for two periods each of three weeks. There was an interval of ten days between these periods. The last six weeks of the experiment served for observing whether any "suppression" of malaria had taken place as a result of the administration of quinine.

The procedure adopted was similar to that already described, with minor local modifications. In certain Indian units the quinine mixture was poured out of a gallipot into the open mouths of the sepoys as they squatted on the ground in rows, and in most stations, magnesium sulphate was added in the preparation of the quinine mixture already described.

The quinine group was numerically between two and three times the size of the control group.

Observation was kept to see whether the finding of parasites was more difficult in blood films from cases admitted from the quinine group, and whether the cure of the disease (as evidenced by the duration of stay in hospital) was delayed.

The effect of the experiment on two groups of soldiers was also watched. One group was composed of young soldiers fresh from the United Kingdom and not previously exposed to malarial infection, and the other of slightly older men who had spent one or more seasons in India and many of whom had suffered from malaria.

With a view to forestalling the suggestions (provided that the results turned out to be satisfactory) that quinine might simply have confused the diagnosis and caused malaria to be returned as some other disease, or that some enthusiastic protagonist of quinine prophylaxis might have assisted the production of good results by unconsciously misdiagnosing cases of malaria in the quinine groups, it was decided in all cases to record: "Total Admissions from All Causes" from both groups. Numbers of admissions from causes other than malaria could, therefore, be closely scrutinized and any material difference in the two groups investigated.

It should be clearly understood that during the whole period covered by the experiment, viz., four years, there was, of course, not the slightest relaxation in the other anti-malaria measures at our disposal which were everywhere prosecuted with the customary vigour and method.

Early in 1930 arrangements were made and details worked out for a final test covering all troops, British and Indian, in the two areas. It was thought that 30,000 men would be involved in the experiment and as events turned out this number would have been greatly exceeded. It was proposed to endeavour to determine, among other points, an optimum dosage and whether or not an interval between courses was really necessary or even advisable.

However, the experiment was forbidden by "higher authority" on the grounds that the case for quinine prophylaxis had been completely proved, and orders were received to issue 10 grains of quinine (acid solution) daily, five days a week, for a period of ten weeks, from the beginning of September to the middle of November to all troops in malarious stations. This was done and a questionnaire was submitted to all hospitals asking for information on the following points:—

(a) Opinions of Commanding and other officers and medical officers as to the efficacy of quinine prophylaxis as practised.

(b) Popularity with the men.

(c) Any defects noted in the method of administration, e.g., dose, time, frequency, duration, etc.

(d) Percentage of fever cases to total admissions during the period quinine has been administered this year and the two previous years.

(e) Proportion of benign tertian to malignant tertian cases during the period under review and during the corresponding period in previous years.

(f) Any evidence of quinine-fast parasites.

(g) Any evidence that quinine prophylaxis renders the recognition of malaria parasites in the blood stream more difficult.

(h) Any evidence that quinine prophylaxis "masks" malaria or that the cessation of quinine is followed by an outbreak of these "suppressed" cases (say within a month of the cessation of the course).

With a view to the further reduction of malaria in the districts, quinine was given daily for ten days to all arrivals in healthy stations from malarious stations.

In addition, all troops on the line of march were given quinine, and this was continued for ten days after the termination of the march.

RESULTS.

1926 (*vide Table I*).

Out of 210 troops who received quinine for three weeks from October 4 to 24 there were 17 cases of malaria during the whole of the month, corresponding to a ratio per thousand of 80·95. During the same period 68 cases occurred in the control group, 225 strong, representing a ratio per thousand of 302·22. The incidence of malaria, therefore, in the control group was almost four times that in the quinine group.

The numbers are too small to allow of a detailed analysis, but it would appear that the third unit shown (an R.A. Unit) did not re-act to the

treatment as well as the other units and that the infantry unit's response was considerably above the average. The interest shown by this infantry unit's Commanding Officer and the personal supervision given by him may afford the explanation of the difference.

TABLE I.—RESULTS OF QUININE PROPHYLAXIS, 1926.

Unit	Barrack room No.	Average strength during October	No. who received prophylactic quinine 4.10.26 to 24.10.26	No. who received no prophylactic quinine	Malaria admissions during October		Malaria admissions during November	
					No. who received prophylactic quinine	No. who received no prophylactic quinine	No. who received prophylactic quinine	No. who received no prophylactic quinine
-- Field Bty. R.A.	15 } 16 }	114	50	64	5 (a)	21	7	4
-- Field Bty. R.A.	1 } 2 }	109	56	53	2	12	14	11
-- Field Bty. R.A.	11 } 12 }	100	39	61	7 (b)	16	7	14
-- F.A.C., R.A. . .	19	40	26	14	1 (c)	3	—	—
-- "A" Coy., Highlanders	6 } 7 } 8 }	72	39	33	2 (d)	16	6	3
Total		435	210	225	17 (80.95 %/∞)	68 (302.22 %/∞)	34 (161.9 %/∞)	160 (302.22 %/∞)

Note.—(a) One of these cases was admitted after the completion of the three weeks' course.

(b) Four of these cases were admitted after the completion of the three weeks' course.

(c) This case was admitted after the completion of the course (in this instance the course only lasted seven days as the unit moved to Akora Training Camp).

(d) One case was admitted on the second day of the course and the other a week after completion of the course.

It will also be noted that of the total of seventeen cases from the quinine group six occurred in the week immediately following the termination of the quinine course. This suggests a temporary suppression of malaria during the exhibition of the quinine. That such suppression, if it did occur, was of no material significance is evidenced by the fact that during the following month, i.e., November, the incidence of malaria in the two groups was practically identical, viz., 161.9 per mille in the quinine group and 160 per mille in the control group.

The value of carrying out the acid Tanret test on admission to hospital was nil, for it was practically always negative, many hours usually having elapsed since the last dose of quinine.

During 1927 I was present in the station during the whole period of the experiment, and was therefore in a position to give direct personal supervision and to carry out the statistical and other work involved.

1927 (*vide Tables II, III and IV*).

Quinine was given during September from the 5th to the 25th inclusive and during October from the 6th to the 26th inclusive to 194 British troops and 443 Indian.

TABLE II.—RESULTS OF QUININE PROPHYLAXIS. BRITISH UNITS, 1927.

Unit	Average strength September	Average strength October	No. who received prophylactic quinine Sept. 5 to Oct. 6 to 26	No. of controls Sept. Oct.	Malaria admissions during September						Malaria admissions during October					
					Recipients of prophylactic quinine		Control		Total cases in Unit		Recipients of prophylactic quinine		Control		Total cases in Unit	
					Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000
— Fd. Bty. R.A.	103	131	40	$\frac{63}{91}$	1 (a)		6		7				9		9	
— Fd. Bty. R.A.	101	134	41	$\frac{60}{93}$	1 (b)		8		9				10		10	
— Fd. Bty. R.A.	114	132	54	$\frac{60}{78}$	3 (c)		7		10				10		11	
— Bde. F.A.C. ...	40	43	15	$\frac{25}{28}$	—		1		1				2		3	
“B” Coy. 2nd Bn. Fusiliers	106	107	44	$\frac{62}{73}$	1 (d)		4		5				6		7	
	464	547	194	$\frac{270}{353}$	6	30.93 ‰	26	96.29 ‰	32	68.96 ‰		15.46 ‰	37	104.81 ‰	40	73.13 ‰

- (a) One case admitted hospital on 1st day of 1st course
 (b) “ “ “ “ 2nd “ “ “
 (c) “ “ “ “ 3rd “ “ “
 (—) “ “ “ “ 6th “ “ “
 (—) “ “ “ “ 8th “ “ “
 (d) “ “ “ “ 3rd “ “ “
 (e) “ “ “ “ 3rd “ 2nd “
 (f) “ “ “ “ 8th “ “ “
 (g) “ “ “ “ 12th “ “ “

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TABLE III.—RESULTS OF QUININE PROPHYLAXIS (INDIAN UNITS), 1927.

Unit	Average strength September	Average strength October	No. who received prophylactic quinine Sept. 5 to 25 and Oct. 6 to 26	No. of controls	Malaria admissions during September						Malaria admissions during October					
					Recipients of prophylactic quinine		Control		Total cases in Unit		Recipients of prophylactic quinine		Control		Total cases in Unit	
					Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000	Actual Nos.	Incidence per 1,000
-/- Punjab Regt.	395	416	99	98	—	—	—	—	13	—	—	—	1	—	12	—
-/- Punjab Regt.	456	513	116	120	—	—	2	—	5	—	—	—	1	—	2	—
-/- Sikh Regt. ...	862	675	98	98	—	—	1	—	24	—	—	—	1	—	12	—
-/- Sikh Prs. ...	489	508	80	87	—	—	—	—	—	—	—	—	1	—	1	—
-/- I.B.T. Coy. ...	304	303	50	38	—	—	1	—	3	—	—	—	1	—	1	—
Totals	2,506	2,415	448	441	—	—	4	9.07 ‰	45	17.96 ‰	—	—	5	11.34 ‰	28	10.71 ‰

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British.—During the whole of September the malaria admissions from the quinine group numbered 6, representing a ratio of 30·93 per mille, and there were 26 admissions from the 270 controls, a ratio of 96·29 per mille. During October there were 3 admissions from the quinine group (15·46 per mille) and 37 cases of malaria among 353 controls (104·81 per mille).

Indian Troops.—No cases of malaria occurred during September or October among the 443 Indian troops who received the quinine course. Among the 441 constituting the controls there were 4 cases (9·07 per mille) during September and 5 cases (11·34 per mille) during October.

While, therefore, no cases of malaria were recorded during the course of the experiment in the quinine group of Indian troops. Among British troops the incidence in September in the control group was over three times and in October nearly seven times that of the quinine group.

Examining the detailed figures by units it is seen that the R.A. units show better results in comparison with the infantry unit than was the case in 1926.

The question of suppression could not be investigated owing to the intervention in late October and November of training camps and manœuvres.

During August and September of 1928 I was absent from the station carrying on research work for a brother officer who was ill, and so the experiment was supervised in September by another officer. The scheme was, however, organized by me, was under my direct control in October, and the figures and results were collected and worked out by me.

1928 (*Table IV*).

At Nowshera quinine was given to 371 British and 1,142 Indian troops from September 24 to October 13, and again after an interval of ten days, from October 24 to October 31, when owing to training, etc., the experiment was terminated. But owing to the low incidence of malaria, the test was of very little value.

Two cases of malaria (5·39 per mille) occurred among the 371 quinine group (British groups) during the last week of September as against 2 (7·66 per mille) among the control group of 261. During October there were again 2 cases in the quinine group against 9 (31·14 per mille) among the control group of 289.

As regards the Indian troops there were no cases in either the quinine or control groups during the first part of the experiment. During October there were 6 cases in the quinine group of 1,142 representing a ratio per thousand of 5·26, and 11 cases in the controls 1,018 strong—a ratio of 10·81 per thousand.

Quinine was also given during the Chitral reliefs. On the outward journey 469 Indian troops received a dose for six to eight days, depending

TABLE IV.—SUMMARY OF RESULTS OF QUININE PROPHYLAXIS EXPERIMENT IN NORTHERN INDIA, 1926 TO 1929.

Place	Period of experiment	Received Prophylactic Quinine.		Received no Prophylactic Quinine.		Estimated saving of malaria admissions among quinine roll. (Estimate based on rate prevailing among controls)	Total number of unreported cases
		No. receiving quinine with dates	* No. of cases of malaria (incidence per ‰ in brackets)	No. receiving no quinine	* No. of cases of malaria (incidence per ‰ in brackets)		
BRITISH TROOPS.							
Nowshera ..	Oct., 1926 ..	210 (4.10.26 to 24.10.26)	17 (80.95‰)	225	68 (302.22‰)	47	35
do.	Nov., 1926 ..	194 (5.9.27 to 25.9.27)	34 (161.90‰)	—	36 (160.00‰)	—	—
	Sept., 1927 ..	194 (6.10.27 to 26.10.27)	6 (30.93‰)	270	26 (96.29‰)	13	14
	Oct., 1927 ..	194 (6.10.27 to 26.10.27)	3 (15.46‰)	353	37 (104.81‰)	17	17
do.	Sept. 24 to 30, 1928	371 (24.9.28 to 30.9.28)	2 (5.39‰)	261	2 (7.66‰)	1	2
	Oct., 1928 ..	371 (1.10.28 to 31.10.28)	2 (5.39‰)	289	9 (31.14‰)	10	10
Nowshera and Peshawar	Sept. 1, 1929 to Dec. 4, 1929	473 (1.9.29 to 22.10.29)	228 (482.03‰)	228	145 (635.96‰)	73	11
INDIAN TROOPS.							
Nowshera ..	Sept., 1927 ..	443 (5.9.27 to 25.9.27)	—	441	4 (9.07‰)	4	4
	Oct., 1927 ..	443 (6.10.27 to 26.10.27)	—	441	5 (11.34‰)	5	4
do.	Sept. 24 to 30, 1928	1,142 (24.9.28 to 30.9.28)	—	953	—	—	5
	Oct., 1928 ..	1,142 (1.10.28 to 31.10.28)	6 (5.26‰)	1,018	11 (10.81‰)	6	10
Chitral Relief Column	Outward journey, Sept., 1928	469 (6 to 8 days)	3 (6.39‰)	3,202	57 (17.80‰)	5	1
	Homeward journey, Oct., 1928	538 (6 to 8 days)	—	3,046	26 (8.53‰)	5	4
Nowshera, Peshawar, Shagal, Thal, Hangu, Landi	Sept. 1, 1929 to Dec. 4, 1929	2,455 (1.9.29 to 22.10.29)	854 (347.86‰)	1,105	591 (534.84‰)	459	10
Kotal							

* These totals include all cases of malaria admitted, not merely during the period when quinine was being given, but during the whole period of experiment (*vide* column 2).

on the date of their arrival at Dargai, and 538 received a dose on the homeward journey for six to eight days depending on the date of their departure from Dargai.

The evidence, so far as Nowsbera is concerned, slender though it is, is quite decidedly in favour of quinine prophylaxis.

The figures for the Chitral Relief Column are, however, more convincing, and moreover it should be borne in mind that quinine was only given for a relatively short period of the whole march. On the outward journey the quinine roll of 469 had only 3 cases of malaria (incidence ratio per mille 6.39) whereas the control of 3,202 had 57 cases (incidence ratio per mille 17.80) i.e., the controls had nearly three times as much sickness due to malaria. On the homeward journey the 538 who were on quinine had no malaria. The control, 3,046 strong, had 26 cases representing a ratio of 8.53 per thousand.

During 1928 the experiment was under my administrative control only. Detailed instructions were issued on my initiative, and the working out of the scheme was left to medical officers on the spot.

1929 (*vide Tables IV, V and VI*).

In 1929 the scope of the experiment was greatly extended and included 701 British and 3,560 Indian troops in six different stations in Peshawar and Kohat Districts.

The experiment lasted for 95 days though quinine was only given for two periods of three weeks, viz., from September 1, 1929, to September 21, 1929, and again, after a ten-day interval, from October 2, 1929, to October 22, 1929. The test was thus divided into four distinct parts, viz. :—

- (1) First quinine course of twenty-one days (with one day's rest per week).
- (2) Interval of ten days.
- (3) Second quinine course of twenty-one days (with one day's rest per week).
- (4) Observation period of six weeks.

The detail of results is given by units and in the case of all important totals the ratio per mille has been worked out to aid comparison. Further, to facilitate comparison of the relative incidence in the different periods as indicated above the equivalent annual ratios of admissions for malaria and admissions from all causes during each period have been added at the bottom of Table V and Table VI for quinine and control rolls. In addition the last column of each of the tables referred to shows the estimated saving of admissions for malaria. This estimate is based on the malaria rate prevailing among the controls.

Following two good years, 1928 being a record good year, 1929 proved to be the worst year on record in the district for malaria.

Out of a total of 473 British troops on the quinine roll 228 contracted malaria during the whole period of 95 days, giving a ratio per mille of

TABLE V.—RESULTS OF QUININE PROPHYLAXIS EXPERIMENT. BRITISH TROOPS PESHAWAR DISTRICT. SEPTEMBER, OCTOBER AND NOVEMBER, 1929.

ADMISSIONS FROM QUININE ROLL.

Station and Unit	Strength	1st Course		Interval		2nd Course		Next 6 weeks		TOTAL		Estimated saving of malaria admissions among quinine roll. (Estimate based on rate prevailing among controls)
		Mal.	Total	Mal.	Total	Mal.	Total	Mal.	Total	Mal.	Total	
PESHAWAR.												
— (M) Bty. R.A.	30	—	4	2	3	3	4	8	10	13	23	
— Fd. Bty. R.A.	36	—	5	2	3	3	4	8	10	13	23	
Total Peshawar	66	Nil	9	4	6	5	7	14	20	23	43	
Ratio per mille Peshawar				60·6	6	75·76	7	212·12	20	348·48	635·96	
NOWSHERA.												
“B” Coy.	130	1	2	5	8	20	23	50	59	76	126	
2nd —												
Dett. Dist. Sig.	13	—	—	—	—	—	1	—	—	—	—	
— Fd. Bty. R.A.	93	—	4	4	5	16	19	—	—	—	—	
— Fd. Bty. R.A.	82	—	—	2	3	15	17	21	29	38	58	
— Fd. Bty. R.A.	72	—	—	2	4	9	13	22	26	33	53	
— Fd. Bde.	17	—	—	—	—	2	2	4	4	6	10	
— F.A.C.R.A.												
Total Nowshera	407	1	6	13	20	62	75	129	159	205	364	
Ratio per mille Nowshera		2·46		31·94	20	152·34	75	316·95	159	503·69	1238·22	
Total Peshawar and Nowshera	473	1	15	17	26	67	82	143	179	228	407	
Ratio per mille Peshawar and Nowshera		2·11	31·71	35·94	54·97	141·65	173·36	302·38	378·44	482·03	635·96	
Equivalent annual ratio per mille		36·7	551·1	1311·8	2006·3	2461·9	3013·2	2627·4	3288·8	18·17	2479	

* N.B.—This is the sum of the estimated savings of each unit and does not agree with

482·03. During the same period there were 145 cases of malaria among 228 controls—a ratio per mille of 635·96. The difference in favour of the quinine roll is 153·93 per mille. It is estimated that if the rate prevailing among the controls had prevailed among the quinine roll, i.e., if no quinine had been given, 85 more cases of malaria would have occurred. That is to say, there has been an estimated saving of 85 cases of malaria, calculated by units, or 27 per cent of the estimated total.

The total of admissions from all causes on the quinine roll was 302 (ratio per mille 638·48) and on the control roll 178 (ratio per mille 780·70), the admission ratio for all causes other than malaria being therefore 156·45 per mille in the case of the quinine roll and 144·64 per mille in the controls. It is evident, therefore, that no great “masking” occurred and that mis-

ADMISSIONS FROM CONTROL ROLL.

Station and Unit	Strength	1st Course		Interval		2nd Course		Next 6 weeks		TOTAL		Estimated saving of malaria admissions among quinine roll. (Estimate based on rate prevailing among controls)
		Mal.	Total	Mal.	Total	Mal.	Total	Mal.	Total	Mal.	Total	
PESHAWAR.												
— (M) Bty. R.A.	30	1	2	3	3	4	4	1	3	9	12	
— Fd. Bty. R.A.	36	—	6	3	4	11	11	7	9	23	30	
Total Peshawar	66	1	8	6	7	15	15	8	12	32	42	
Ratio per mille Peshawar		1·5	120·0	98·36	98·36	245·90	151·15	121·5	181·15	488·59	635·96	
NOWSHERA.												
“B” Coy.	130	1	2	6	6	10	12	31	36	48	56	
2nd —												
Dett. Dist. Sig.	13	—	—	—	—	1	1	1	1	2	2	
— Fd. Bty. R.A.	93	—	—	—	—	10	10	11	12	24	25	
— Fd. Bty. R.A.	82	—	—	2	3	6	7	7	9	16	26	
— Fd. Bty. R.A.	72	—	—	—	—	5	5	10	13	21	25	
— Fd. Bde.	17	—	—	—	—	1	1	1	1	2	2	
— F.A.C.R.A.												
Total Nowshera	407	1	2	13	14	33	36	61	72	113	136	
Ratio per mille Nowshera		2·46	15·2	31·94	32·14	79·61	88·45	147·65	176·27	276·65	364·22	
Total Peshawar and Nowshera	473	2	10	19	21	48	51	69	84	145	178	
Ratio per mille Peshawar and Nowshera		4·23	21·1	39·88	43·81	101·53	107·69	145·63	176·42	322·24	364·22	
Equivalent annual ratio per mille		36·7	551·1	1311·8	2006·3	2461·9	3013·2	2627·4	3288·8	18·17	2479	

the estimated saving worked out on the total incidence of malaria for the whole area.

diagnosis of malaria for other causes was at all events uncommon. There was a genuine reduction in the sick rate and it seems only reasonable to attribute this reduction to the quinine prophylaxis.

(To be continued.)

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