The treatment of skin conditions such as impetigo, seborrhoeic dermatitis, and secondarily infected tinea led to the greatest number of reactions:

Dermatoses	62.66%
Otitis externa	4.00%
Wounds	13.00%
Grazes and minor injuries	14.33%
Burns	4.00%
Other diseases (e.g., tonsillitis, appendicitis)	2.00%

It seems impossible to determine what percentage of people treated by sulphonamides locally develop sensitization, but it is interesting to note the experience of other dermatologists in treating skin infections with these drugs. For instance, Pillsbury *et al.* (1941) treated 190 varied cases with no evidence of absorption and no local or general reaction; Kalz and Prinz (1942) treated 130 patients with no systemic effects and no mention of dermatitis; York (1942) had one case of contact dermatitis in 96 cases; the Robinsons (1941), in a series of 48 cases of impetigo, had two cases of contact dermatitis; Glicklich (1942) saw no toxic effects in 42 cases; Ingels (1943) had 10 cases of sensitivity in 300 cases; with microcrystalline sulphathiazole Bigger and Hodgson (1944) had one case of sensitivity in 50 cases treated; of 196 patients treated by Costello *et al.* (1942) 21 had skin reactions—i.e., of 1,052 cases treated 3.5% became sulphonamide-sensitive. Before I abandoned the local application of these drugs, out of 400 cases treated with 5% sulphathiazole paste or cream I observed 4 which developed photosensitization, either mild or severe.

There seems to be little doubt that sulphonamides can be applied to the skin, as Pillsbury (1944) says, with little risk of causing sensitization if the process is not an eczematous one and the drug is used for not longer than 5 days in the form of a thick paste or water-miscible cream; but as diseases such as impetigo can be treated satisfactorily by other methods, it appears that sulphonamides should no longer be used as a topical application.

In 1943 I performed various tests on men with the light eruption. Patch tests gave erratic results, as they were invariably positive on areas previously affected by the rash—i.e., the parts exposed to light—and usually negative on other parts of the skin. Scratch and intradermal tests were rarely used, as they tended to cause (as often happens with these tests) an exacerbation of the original condition.

Complexion had, it appeared, little or no significance in this series of cases—in fact, the rufous type seemed less prone to severe reactions, while the worst cases were seen in men with dark hair and skin. Photosensitization was seen in Indians, Gurkhas, Sinhalese, and men of negro stock.

The incidence of sulphonamide reactions in the U.S. Forces seemed to be much lower than in United Kingdom, Dominion, or Empire troops: light eruptions were rarely seen, but occasionally the other types occurred. Two busy American dermatologists practising during the twelve months of 1944 in the same theatre of war saw in their own group of patients only 4 cases each that were definitely due to the sulphonamide series. Several reasons for this extraordinary difference may be suggested, but the most important are that the commonest way of using sulphonamides locally in the U.S. Medical Corps was in the form of 5% sulphadiazine in a water-miscible cream, and that acriflavine was seldom employed. Not unnaturally, American colleagues were sceptical of the high incidence in British troops until they were absolutely convinced by the numbers of cases shown them.

Summary

From Feb., 1943, to Dec., 1944, over 650 cases of cutaneous sensitivity to sulphonamides have been seen in North Africa and Italy; of these, 500 are reported and classified into 16 various types.

These reactions were due to the treatment of many different conditions, from major wounds and burns to slight grazes, impetigo, and chancroid.

Only 3 of the types described are liable to cause a grave or prolonged illness—i.e., the pemphigoid, the sulphonamide-light eruption, and the sulphonamide contact dermatitis.

Sulphonamide-light dermatitis accounted for 72.2%, and contact dermatitis and its complications for 17.2%—i.e., 90% of the total.

Most cases of reaction were due to the use of sulphanilamide in powder form; the safest drugs appeared to be sulphadiazine and sulphaguanidine.

Acriflavine can reactivate a sulphonamide-light or contact dermatitis just as may cocaine.

No race is exempt from this sensitization—skin colour and texture make little or no difference.

Sulphonamide reactions are uncommon in U.S. troops compared with British.

The local application of sulphonamides is contraindicated in skin diseases, though there is little risk if the drugs are used with certain precautions.

Intramuscular penicillin appears to be the treatment of choice in two types—the pemphigoid and the severe light dermatitis.

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PREVENTION OF SEA-SICKNESS IN ASSAULT CRAFT

A REPORT OF EXPERIMENTS UNDER TROPICAL CONDITIONS

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Assault landings in combined operations entail the transport of large numbers of men in small craft over seas which may be rough. Previous experience in operations (such as the invasion of Sicily) and in training has shown how disabling sea-sickness can be to troops taking part in such landings. In many countries a number of remedies have been tested in the search for a means of preventing or mitigating sea-sickness without impairment of the fighting efficiency of troops when disembarked on the beaches.

From the reports of previous workers it appears that the most efficient remedy is hyoscine (Holling, McArdle, and Trotter, 1944; Holling and Trotter, 1944); other members of the atropine series are less effective. Amphetamine (benzedrine) had been claimed by Hill (quoted by Jowett, 1943) to reduce the sickness rate dramatically, but was found by Jowett and Thomson (1943) to be ineffective. A combination of hyoscine with amphetamine has been claimed (Jowett, 1943; Jowett and Thomson, 1943) to be highly effective. Chlorbutol has been found of little value (Holling and Trotter, 1944).

The possibility of side-effects being produced by hyoscine has been the subject of much research. The reduction in salivation, with consequent dryness of the mouth, is merely inconvenient. But the effects on the eye might, if severe, interfere with efficient shooting, observation, etc.; the sedative action might produce drowsiness; and, most important of all in tropical climates, the reduction in sweating might prove dangerous from interference with heat-loss. Both in Britain and in India tests with this drug have been carried out to determine whether these effects are pronounced enough to detract from its beneficial action in sea-sickness. Its effects on the stamina of troops and on their ability to perform complicated mechanical operations (stripping and reassembly of Bren guns, etc.) have been studied, and the performances of treated and untreated groups of men on the rifle range compared. Ophthalmological investigation of possible effects on accommodation and fine eye movements has been carried out (Wilson, quoted by Holling and Trotter, 1944). All reports agree that no undesirable effects are produced by the drug in the doses advocated for the relief of sea-sickness.

Studies have been made on two individuals working in a hot chamber reproducing tropical conditions, but no large-scale tests have so far been reported.

The experiments described in the present paper were carried out to determine the influence of this and other drugs on the incidence of sea-sickness among troops of various nationalities, and on the possible production of undesirable side-effects, under tropical conditions.

Material.—A group of over 5,000 men in training was used for the tests. The racial composition of the men was as follows: British troops, 1,667; Indian troops, 3,673; mixed (composition not recorded), 400. The various sects and races of Indian troops observed were: Punjabi Mussulmans, 637; Dogras, 206; Pathans, 316; Gurkhas, 1,586; mixed (Ajmirs, Brahmins, Ahirs, Moslems, Mundas, and Hoes), 928.

Meteorological Conditions.—The experiments were carried out on the west coast of India in latitude 19° N. during the month of May, approximately one month before the monsoon. Climatic conditions were average for place and season (see Table VII). Briefly, temperature and humidity were such as to favour the development of heat-stroke or heat-exhaustion in individuals performing strenuous exercise; sea conditions were never rough enough to produce more than 15 to 25% of sickness among unseasoned troops sailing in small craft.

Methods

During the investigation the troops were engaged on a full scheme of training, and experiments had to be designed so as not to interfere with this programme. In general it was impracticable to send parties of men to sea for the sole purpose of testing sea-sickness. Each experimental observation had to be fitted into the scheme of an assault exercise, planned and unalterable. This was usually possible, while still observing the essential conditions of the experiment—viz.: (1) the simultaneous observation under identical conditions of large numbers of men sailing at the same time in similar craft from the same starting-point to the same destination; and (2) their division into two or more groups of comparable size, one such group receiving inactive tablets (controls), while the other group or groups received tablets of the substance under test. Tablets were distributed one hour before embarkation to the selected groups of men, either by R.A.M.C. orderlies attached for duty in these experiments or by company commanders under the guidance of the unit medical officer. Particular care was taken to ensure that every man swallowed his prescribed pill. In all experiments the men in test and control groups alike were given paper vomit-bags, a supply of sweets, biscuits, and chewing-gum, and were instructed in the simple measures found by previous workers to reduce sickness among men crowded in small craft (i.e., keeping the deck clean by using bags for vomiting; eating a biscuit or a few sweets if slight nausea occurred). The chewing-gum was intended to reduce the unpleasant dryness of the mouth with hyoscine, but was given to all, irrespective of what drug they received.

The principles on which an experiment was planned may best be understood by consideration of an example.

Experiment V.—2/Blankshires; May 8/9, 1944

Three assault companies of a battalion, sailing in nine "Landing Craft Assault" (L.C.A.s) at 22.30 hours from the same point, were due to land on a beach at 02.00 hours and carry out an assault. Each L.C.A. carries 35 men, and the personnel allocated to each craft was given a serial number. Three serials or boat-loads were allotted to each company: Nos. 1–3, 4–6, and 7–9 respectively to the first, second, and third companies. Serial 10 was composed of Headquarters staff. Serials 11, 12, and 13 were made up of various auxiliary troops sailing in 3 L.C.A.s; serials 14, 15, and 16 carried the three platoons of the reserve company in 3 L.C.A.s. Serials 11–13 sailed at 22.30 hours and disembarked at 02.20 hours on the same beach as serials 1–9; serials 14–16 sailed at 23.40 hours and disembarked at 02.45 hours on the same assault beach. In addition several "Landing Craft Mechanized" (L.C.M.s) were employed, carrying few men in addition to their vehicle loads, and three larger craft—one "Landing Craft Infantry (Large)" (L.C.I.(L.)), and two "Landing Craft Tank" (L.C.T.s). The former carried 185 men of various units, sailing at 17.00 hours the afternoon before the assault, and landing at 03.45 hours. The L.C.T.s carried respectively 66 and 81 men, sailing at 21.45 hours and 19.30 hours respectively from a different jetty, and landing their troops at 04.00 and 05.15 hours respectively.

In planning the experiment the first nine serials carrying the three assault companies were treated as a group. The remedies to be tested and the control tablets were distributed as follows:

Serial No.	Remedy	
1	Sod. bicarb.	each 1 platoon of 1st Coy.
2	Hyoscine	
3	Ergotamine	
4	Sod. bicarb.	each 1 platoon of 2nd Coy.
5	Hyoscine	
6	Ergotamine	
7	Sod. bicarb.	each 1 platoon of 3rd Coy.
8	Hyoscine	
9	Ergotamine	

The other six L.C.A.s (omitting HQ. in serial 10) were also treated as a group, and remedies distributed as follows:

Serial No.	Remedy	
11	Hyoscine	mixed troops
12	Hyoscine plus ergotamine	
13	Sod. bicarb.	
14	Hyoscine	each 1 platoon of reserve company
15	Hyoscine plus ergotamine	
16	Sod. bicarb.	

The men on the larger craft (serials 21, 22, and 23, sailing in the L.C.I.(L.) and L.C.T.s) were divided into roughly equal groups on each ship. To one party was given hyoscine, to the other sodium bicarbonate. It will be noted that in these craft controls and test groups were mingled, while in the smaller L.C.A.s carrying 30 to 35 men all individuals in one craft had the same pill—active or dummy, as the case might be. The small number of men carried in the L.C.M.s were omitted from the experiment.

Trained nursing orderlies, R.A.M.C., detailed for this duty, sailed in each craft as observers, one to each L.C.A., six in the L.C.I.(L.), and two to each L.C.T. They were provided with forms on which to record the names of all seen to vomit or noted to suffer from nausea. Details of actual times of sailing and disembarking, of entering and leaving rough waters, of lying "hove-to," and the code letter of the remedy administered to troops on board had to be entered in the spaces provided on the form. The orderlies followed the troops for half an hour after disembarkation to note any sign of illness or incapacity among the men. Arrangements had been made to deal with heat-stroke cases, should such occur.

It was considered that opinions regarding the military efficiency of the men would have most value if expressed by their own officers. Familiar with their men's usual behaviour, and with the particular situation as it developed on the beaches, they could be relied on to detect any abnormal reactions.

Figures from the analysis of the results of this experiment will be found in the Tables and the discussion below. It will be noted that in assessing the efficiency of a remedy due regard is paid to comparison with the control group sailing in identical craft over the same course at the same time.

Of 17 experiments, Nos. V, VI, and VII were of this type. Experiments I, II, and III were similar, except that in these the exercise was carried out by companies of infantry without ancillary troops; all serials sailed in L.C.A.s. Experiment VIII was an observation of a group selected out of over 5,000 men taking part in a large-scale exercise; it is discussed in detail below.

In several experiments (Nos. IX, X, XIV, XVI, and XVII) parties of men were sent to sea for a six-hour trip in "country-craft." These were 170-ton ocean-going dhows, all exactly similar. In each experiment a party of 150 men was divided into two groups of 75, each sailing in one dhow; to one group was given the remedy under test, to the other an inactive pill. So far as was possible the craft sailed together, under identical

conditions, and remained at sea for the same time. R.A.M.C. observers sailed on each to record the incidence of sea-sickness. These trips were all by day; no exertion was demanded of the troops on disembarkation.

In another series of experiments parties of 120 to 200 men with R.A.M.C. observers sailed on an L.C.I.(L.) for a six-hour trip (Expts. XI, XII, and XIII). The men on board were divided into three groups without selection. To one group (controls) the inactive pills were given; to each of the other groups was given one of the remedies under test. No exertion was demanded of the troops on landing.

Remedies Tested.—Since hyoscine had already proved in other countries to be the drug of choice, and since data were required on its action in Indian troops and under tropical conditions, this remedy in a dose of 1/100 gr. was chosen for special study. In view of the preference expressed by other workers for a combination of hyoscine (1/100 gr.) with amphetamine (5 mg.) a number of experiments were made in order to compare the efficiency of this combination with that of hyoscine alone. Ergotamine (0.5 mg.) was also tested, alone and in combination with hyoscine (1/100 gr.), because of its known power to relieve the nausea, etc., of migraine and the possible benefit to sea-sick subjects of the "sympathicotonic" type. Chlorbutol in doses of 10 gr. was compared with hyoscine (1/100 gr.) under controlled conditions.

Heat-stroke Precautions.—The season and climate in which the experiments were carried out rendered heat casualties likely among large bodies of troops engaged in strenuous work. In view of the possible effect of hyoscine in suppression of sweating, preparations were made for the treatment of heat casualties on a large scale should they occur.

Results and Discussion

1. Action in Prevention of Sea-sickness

In the course of 17 experiments a total of 5,740 men were subjected to tests. Among these were 2,206 men to whom inert "placebo" tablets of chalk or sodium bicarbonate had been given, and who acted as controls for the groups receiving the active drugs. Owing to various causes a large number of results had to be discarded as useless for analysis.

Because of calm seas, the sickness rates in the control groups in eight experiments averaged only 2.3%. Such experiments are useless for estimating the potency of remedies, and were discarded. Again, on two occasions after men had taken their remedies as issued the sailing of the craft was cancelled for naval reasons. In a third group the men on a L.C.I.(L.) were at sea for 21 hours; they had been issued with their remedies 13 hours after embarking and 8 hours before landing. A number were ill before the remedies were given, and a number of others more than six hours later, when the period of expected action of the drugs was over. The effect of the remedies during their period of likely action could not therefore be accurately assessed, and the experiment was discarded.

The total number of observations discarded was 2,102; the observations remaining for analysis total 3,638.

A consolidated summary of all valid experiments is given in Table I. The average incidence of vomiting recorded in 1,385 control subjects was 12.4%; an additional 3.6% were nauseated. The total personnel affected in the control group was thus 16%, Rough comparisons only are permissible from this table in considering the figures for sickness incidence with various remedies, since the aggregate figures for many experiments are being compared rather than the figure for each remedy contrasted with its twin control group.

For comparison of the preventive effect of various remedies a "protective index" is advocated by Holling *et al.* (1944). This is obtained from the formula

$$\text{P.I.} = \frac{\%\ \text{Sick in control group} - \%\ \text{Sick in test group}}{\%\ \text{Sick in control group}} \times 100$$

This expression "shows the percentage of the sick in the control group who presumably would not have been affected if they had been in the test group" (quoted from the statistician's report on our experiments). This index for each experiment is given in the analytical tables. The indices in Table I show that ergotamine used alone fails to protect an appreciable percentage of susceptible individuals, while hyoscine alone or in combination with amphetamine protects over 70% of those liable to sea-sickness.

More exact analyses of these figures are given in Tables II to IV, in which figures for each remedy are compared with those from exactly comparable control groups. For example, in Table II (a) figures for hyoscine-treated individuals and controls, all sailing in L.C.A.s under exactly comparable conditions, are contrasted; and so for other series.

TABLE I.—*Incidence of Sea-sickness with Various Drugs: Consolidated Results*

Expt. No.	Total Men Observed	Control Group			Hyoscine			Hyoscine plus Amphetamine			Hyoscine plus Ergotamine			Chlorbutol			Ergotamine		
		No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea
I	305	104	9	5	100	1	0	101	4	2	—	—	—	—	—	—	—	—	—
II	413	137	20	14	138	6	4	138	12	1	—	—	—	—	—	—	—	—	—
III	395	128	33	2	129	3	1	138	2	3	—	—	—	—	—	—	—	—	—
V	752	305	20	1	313	1	0	—	—	—	52	2	0	—	—	—	82	10	3
VI*	516	173	12	0	175	9	0	—	—	—	64	0	0	—	—	—	104	12	0
VIII	544	282	34	12	262	7	0	—	—	—	—	—	—	—	—	—	—	—	—
IX	152	76	24	0	—	—	—	—	—	—	—	—	—	76	9	0	—	—	—
XV	411	105	10	6	103	0	1	105	0	0	—	—	—	98	9	1	—	—	—
XVI	150	75	9	10	—	—	—	—	—	—	—	—	—	75	3	0	—	—	—
Totals	3,638	1,385	171	50	1,220	27	6	482	18	6	116	2	0	249	21	1	186	22	3
Vomited			12·4%			2·2%			3·7%			1·7%			8·4%			11·8%	
Nauseated			3·6%			0·5%			1·2%			0			0·4%			1·6%	
Total Affected			16·0%			2·7%			4·9%			1·7%			8·8%			13·4%	
Protective Index: Vomiting						82·3%			71·8%			86·3%			32·2%			4·8%	
Protective Index: Total Affected						83·1%			69·4%			89·4%			45·0%			16·2%	

* Figures from large craft (1 L.C.I.(L.); 2 L.C.T.s) are omitted from analysis because sickness incidence in these was insignificant in both control and test groups.

TABLE II.—*Effect of Hyoscine on Sea-sickness*

Type of Craft	Expt. No.	Control Group			Hyoscine Group			Protective Index	
		No. in Group	No. Vomiting	No. with Nausea	No. in Group	No. Vomiting	No. with Nausea	For Vomiting	For Total Affected
(a) L.C.A.s	I	104	9	5	100	1	0		
	II	137	20	14	138	6	4		
	III	128	33	2	129	3	1		
	V (a)	89	8	0	93	0	0		
	V (b)	52	8	0	52	0	0		
	VI	103	11	0	104	7	0		
	VIII (a)	104	18	12	105	4	0		
	VIII (b)	102	4	4	105	3	5		
	XV	105	10	6	103	0	1		
Totals		924	121	43	929	24	11		
Percentages			13·1%	4·7%		2·6%	1·2%	80·1%	98·7%
(b) L.C.I.(L.)	V	100	2	1	85	0	0		
L.C.T.s	V	64	2	0	83	1	0		
L.C.M.s	VIII	31	5	2	24	0	0		
L.C.M.s	VIII	45	8	4	23	0	0		
Totals		240	17	7	215	1	0		
Percentages			7·1%	2·9%		0·5%	0	93·0%	95·0%

TABLE III.—*Effects of Hyoscine plus Amphetamine, of Hyoscine plus Ergotamine, and of Hyoscine on Sea-sickness*

Type of Craft	Expt. No.	Control Group			Hyoscine and Amphetamine			Hyoscine and Ergotamine			Hyoscine Only			Protective Indices					
														Vomiting			Total Affected		
		No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea	No. in Grp.	No. Vomiting	No. with Nausea	H. & A.	H. & E.	H.	H. & A.	H. & E.	H.
(a) L.C.A.s	I	104	9	5	101	4	2	—	—	—	100	1	0						
	II	137	20	14	138	12	1	—	—	—	138	6	4						
	III	128	33	2	138	2	3	—	—	—	129	3	1						
Totals ..	..	369	62	21	377	18	6	—	—	—	367	10	5						
Percentages	..		18·8%	5·7%		4·8%	1·6%	—	—	—		2·7%	1·35%	71·4%	—	83·9%	71·6%	—	82·0%
(b) L.C.A.s	V	52	8	0	—	—	—	52	2	0	52	0	0						
Percentages	..		15·4%	0	—	—	—		3·8%	0		Nil		—	75·3%	100·0%	—	75·3%	100·0%

TABLE IV.—*Effects of Ergotamine and of Chlorbutol in Sea-sickness*

Type of Craft	Expt. No.	Control Group			Ergotamine Group			Chlorbutol Group			Protective Index	
		No. in Group	No. Vomiting	No. with Nausea	No. in Group	No. Vomiting	No. with Nausea	No. in Group	No. Vomiting	No. with Nausea	For Vomiting	For Total Affected
(a) L.C.A.s	V	89	8	0	82	10	3	—	—	—		
L.C.A.s	VI	103	11	0	104	12	0	—	—	—		
Totals ..	..	192	19	0	186	22	3	—	—	—		
Percentages	..		9·9%	0		11·8%	1·6%	—	—	—	Less than zero	Less than zero
(b) Dhows	IX	76	24	0	—	—	—	76	9	0		
Dhows	XVI	75	9	10	—	—	—	75	3	0		
Totals ..	..	151	33	10	—	—	—	151	12	0		
Percentages	..		21·8%	6·6%	—	—	—		7·9%	0	63·6%	72·2%
(c) L.C.A.s	XV	105	10	6	—	—	—	98	9	1		
Percentages			9·5%	5·7%	—	—	—		9·2%	1·0%	3·2%	32·9%

The individual hyoscine experiments of Table II were analysed, evaluating the protective index in each experiment, to determine (*a*) the range of value, and (*b*) whether the index varies significantly with the sickness incidence in the control group. The results of this analysis are given in Table V.

TABLE V.—*Analysis of Protective Indices in Individual Experiments : Remedy, Hyoscine; Craft, L.C.A.s*

Expt. No.	Total Observed		Vomited		Total Affected		Protective Index	
	Controls	Test Group	Controls (%)	Test Group (%)	Controls (%)	Test Group (%)	Vomiting (%)	Total Affected (%)
I	104	100	8·6	1·0	13·4	1·0	88·3	92·5
II	137	138	14·6	4·4	24·8	7·3	69·8	70·6
III	128	129	25·3	2·3	27·3	3·0	90·9	89·0
V (a)	89	93	9·0	0	9·0	0	100·0	100·0
V (b)	52	52	15·4	0	15·4	0	100·0	100·0
VI	103	104	10·7	6·7	10·7	6·7	37·4	37·4
VIII (a)	104	105	17·3	3·8	28·8	3·8	78·0	86·8
VIII (b)	102	105	2·9	2·8	6·8	7·5	0·34	minus
XV	105	103	9·5	0	14·3	1·0	100·0	93·0

With two exceptions—Expts. VI and VIII (b)—the values of the protective index are all over 70%. The two strikingly low indices require further consideration.

Expt. VI.—In this experiment the remedies were administered to the troops as they boarded their craft, immediately before putting to sea. In other experiments of this series the remedies were given about one hour before sailing. There had not been sufficient time for absorption of the drug before the men were exposed to rough seas.

Expt. VIII (b).—In this case there is a discrepancy between the figures recorded by the R.A.M.C. observers and those reported by the men's company commander. The latter reported 7% of the test group sick, and 25% of the control group. The observers' figures have been retained to avoid any suspicion of manipulation of results. The protective index as calculated from the company commander's figures would indicate protection of the same order (72%) as in the other experiments in Table V.

Acclimatization.—Repeated exposure of the same individuals to the motion of the craft at sea was noted to produce some reduction in the incidence of sickness among the control (untreated) group in successive experiments. Possible fallacies in the experimental results due to this acclimatization were avoided through the method adopted of comparison of treated groups in all cases with a control group of similar individuals sailing under identical conditions.

Statistical Analysis of Results.—The results were reviewed by the Central Statistical Section, G.H.Q. (India). Values of χ^2 and of P calculated for each experiment are given in Table VI. The statistician's estimate of the reliability of each result is given in the final column of the table.

The results for hyoscine, with the exception of Expt. VI, are "reliable" or "highly reliable." The figures from Table II (a), derived from observations on 929 instances of hyoscine administration, have a probability of less than 1 in 100,000 that the observed effects were due to chance. The results for hyoscine plus amphetamine also are assessed as "highly reliable," with a probability of their being fortuitous of less than 1 in 10,000. The statistician considers, therefore, that the observed differ-

TABLE VI.—*Statistical Analysis of Tabulated Results*

(χ^2 = Measure of statistical reliability of the result. P = Probability that the result is independent of the use of the drug.)

No. of Table Analysed	Type of Craft	Drug Administered	Protective Index	Total Cover Index	χ^2	P	Reliability of Result	Remarks on Reliability
II (a)	L.C.A.s	Hyoscine	78·7%	96·2%	94·6	<0·00001	Highly reliable	Large sample; 929 men
II (b)	L.C.M.s L.C.T.s L.C.I.(L)	,,	95·0%	99·5%	19·5	<0·0001	Reliable	Good sample; 215 men
III (a)	L.C.A.s	,,	82·0%	96·0%	58·7	<0·0001	,,	Good sample; 367 men
	L.C.A.s	Hyoscine and amphetamine	72·0%	93·0%	35·8	<0·0001	,,	Good sample; 377 men
III (b)	L.C.A.s	Hyoscine	100·0%	100·0%	8·7	0·003	Not reliable	Sample too small for reliability
	L.C.A.s	Hyoscine and ergotamine	75·3%	96·2%	4·0	0·045	,,	Small sample; 52 men
IV (a)	L.C.A.s	Ergotamine	0	86·5%	0·92	0·337	* ,,	Good sample*; 186 men
IV (b)	Dhows	Chlorbutol	72·2%	92·1%	20·4	<0·0001	Reliable	Good sample; 151 men
IV (c)	L.C.A.s	,,	32·9%	89·8%	1·1	0·294	*Not reliable	Good sample*; 98 men

* In these cases χ^2 is low although the samples are large enough to give a significant result. This suggests lack of efficiency of the drug used.

ences in protective indices for the two remedies are probably real. Further analysis by another method (standard deviations) confirmed this conclusion. This implies that the observed lower figures for protection by hyoscine plus amphetamine express an actual inferiority to hyoscine alone, under the conditions of the experiments.

The results for ergotamine, alone and combined with hyoscine, are assessed as "not reliable," since there are probabilities of from 337 in 1,000 to 45 in 1,000 that such results as were observed might be due to chance. In the footnote to Table VI it is pointed out that the unreliability of the results for ergotamine is not due to small samples. The low value for χ^2 is dependent on low observed differences between sickness rates in test and control groups. This statistically suggests that the drug (ergotamine) is not an effective remedy.

So, also, the results for chlorbutol in L.C.A.s are "not reliable," with a nearly 30% chance of error. The figures for chlorbutol derived from observations in dhows, however, are "reliable" and the chance that the results observed were unconnected with the remedy is less than 1 in 10,000. The wide disparity between the chlorbutol results in the two types of craft has not been explained. Further experiments would be required to define the efficacy of this drug.

Comparison of "Protective Index" and "Total Cover Index."—The protective index of Holling *et al.* has already been described. The "total cover index" is the percentage of men not affected in the test group, and includes those naturally immune plus those protected by the remedy given. From it the expectation of sickness with a given remedy is known. The values of both indices are given in Table VI.

Comparative Efficacy of Drugs.—Of the remedies tested in which the results are acceptable to the statisticians the degree of protection afforded by hyoscine is the highest, being throughout of the order of 80% as gauged by the protective index, and 96% as gauged by the total cover index. Hyoscine plus amphetamine gives somewhat lower figures, with a protective index of 72% and a total cover index of 93.6%. Chlorbutol in dhows shows protection of the same order (75% and 92% by the two indices).

2. Hyoscine and Heat-stroke

From Table VII it will be seen that during the investigation hyoscine was administered to a large number of men. The

TABLE VII.—*Meteorological Conditions during Hyoscine Experiments*

Expt. No.	Total Men Engaged	No. of Men c Hyoscine	Nature of Exercise	Time of Day	Meteor. Conditions				Observed Effects of Heat
					Cloud	Temp. Max.	Temp. Min.	Humidity	
I	305	201	Moderate	Dawn	9/10	90·7	79·2	83%	Nil
II	413	278	,,	,,	9/10	90·9	79·6	90%	,,
III	395	267	,,	,,	9/10	90·7	82·0	80%	,,
IV	41	20	Light	Day	5/10	92·8	81·0	88%	,,
V	752	365	Moderate	Night	—	92·8	81·0	88%	,,
VI	814	359	,,	,,	—	93·4	82·8	77%	,,
VII	625	248	,,	,,	—	90·3	81·2	78%	,,
VIII	5,461	424	Strenuous	Day and Night	2–4/10	92·3	81·0	81%	*2 treated: *1 death
X	150	75	Nil	Day	2/10	92·0	81·0	78%	Nil
XI	120	74	Moderate	,,	3/10	92·2	81·3	73%	,,
XII	200	132	Nil	,,	3/10	92·2	81·3	73%	,,
XIII	120	80	,,	,,	5/10	93·0	81·0	75%	,,
XV	411	208	,,	,,	5/10	92·2	82·1	81%	,,

* All among personnel *not* receiving hyoscine.

subjects were in part British troops (780) and in part Indian troops of many races and sects (1,951). Throughout the period of the experiments the climatic conditions were favourable for the development of heat-stroke and heat-exhaustion, as is shown by the meteorological data in the table. In the great majority of cases (2,213) the men who had had hyoscine underwent fairly strenuous exertion immediately after landing on assault beaches, comparable in degree to that demanded by actual battle conditions.

Throughout these experiments, in which over 2,700 men were given hyoscine, no case of heat-stroke occurred among those who had had the drug.

On one large-scale exercise (Expt. VIII) 424 men had hyoscine and carried out a very strenuous assault without incident. During this exercise one fatal case of heat-stroke occurred in a British soldier. This man was in the "control" company of a battalion that had had a pill of chalk at midnight on May 16–17. He disembarked with his unit at 09.00 hours on May 17, carried out strenuous military work all through a hot and brilliant day in an area where water was short, and developed symptoms of an urgent nature at about 18.00 hours. He died at 20.00 hours that evening. Post-mortem examination revealed no evidence of malaria or other infection. A most careful check was made, and there is no doubt that he had had a chalk pill. Of six other cases treated in medical units that day for "effects of heat," four proved to have infections (two coryza, one malaria, and one a superficial cutaneous infection); two were genuine cases of heat-exhaustion. One was a Sepoy, the other a British N.C.O.; neither of them had had any pill, active or inert.

From the results of the experiments it is concluded that hyoscine in the dosage employed (1/100 gr.) does not predispose to heat-stroke or heat-exhaustion among British or Indian troops carrying out full duty in assault exercises under tropical conditions.

3. Hyoscine and Military Efficiency

After the first few experiments various instances were brought to our notice in which men had apparently failed to carry out their duties efficiently, and the question of drug action arose. In one case an officer attributed his display of gross inefficiency to a pill he had had some hours before; it was shown that in fact he had had sodium bicarbonate. In other cases officers and men complained of feeling sleepy on landing in the early hours of the morning; in some cases a hyoscine action could not be excluded, though in others the pill given had been inert. It was soon apparent that there was a tendency among troops to ascribe to drug action any shortcomings in their behaviour during the exercises. On discussion with the officer commanding the troops in training, it was decided to make a large-scale test of the effects of hyoscine on efficiency rather than, as had been intended, to undertake a large-scale test of sea-sickness prevention.

Expt. VIII.—In each assault battalion (one British, one Indian) it was arranged to give hyoscine to one company, an inert pill to a second, and no pill of any kind to a third. The reserve battalion (Indian troops) were similarly treated. A smaller number of personnel of various artillery units were similarly subdivided, groups receiving respectively hyoscine, an inert pill, and no remedy. A supply of tablets of chalk, in shape and size approximating as closely as possible to the hyoscine tablets used, was secured for this experiment. The nature of the pills issued to individuals, companies, etc., was not known to anyone but us two.

The usual observations on sea-sickness incidence were made by R.A.M.C. observers, while detailed reports on efficiency of troops were called for from company and troop commanders, and from officers commanding units.

In this exercise a full-scale assault had to be carried out on beaches, with penetration inland over difficult hill country with scrub and bush. Troops were engaged in as nearly as possible battle conditions for a period of 36 to 48 hours. The experiment thus afforded a good test of whether hyoscine predisposed to the development of ill effects from heat or had any other effect on military efficiency. The reports from individual commanding officers, etc., may be summarized as follows:

Force Commander.—Generally speaking, the men were not seriously affected by hyoscine; some complained of drowsiness—as often as not those who had had the dummy pill. But one company of Pathans appeared to have been sleepy and incapable of reasonable action for an hour after landing; these men had had hyoscine. This same company had also complained of drowsiness on a previous occasion, when only one-third had had hyoscine.

Officer Commanding a British Battalion.—No complaint of inefficiency noted.

Officer Commanding an Indian Battalion.—One company commander complained that his men appeared "doped" on landing, and carried out an unusual manœuvre after disembarkation, earning adverse criticism in consequence. These were the Pathans referred to by the Force Commander. (It was later learned that their unusual manœuvre had been planned some days before the assault!)

Officer Commanding another Indian Battalion.—Reported signs of "dopiness" among men of one company on landing, which "wore off quickly once ashore." This company, unknown to him, had had hyoscine. It is to be noted that this battalion disembarked on a very gently shelving beach, and that the men had to cross a wide water-gap in wading ashore. This was

considered by the umpires to have induced hesitation in disembarking.

Officer Commanding a Field Regiment and Anti-aircraft Battery (British Personnel).—No impairment of efficiency noted. In both these artillery units the experiment had been planned so as to include, in test and control groups alike, a number of individuals whose duties involved arduous physical labour or mental concentration.

The Commandant of the Training Centre stated that he personally did not consider that the remedies given interfered with the efficiency of the troops engaged. He stated that their performance compared very favourably with that of previous (and untreated) groups in training.

In considering the evidence it must be remembered that all the exercises in which excessive drowsiness was a source of complaint were carried out at night. Landings in general were at dawn, and the sea trips were made during the early hours of the morning after embarkation at or before midnight. Lack of sleep thus played a part in inducing drowsiness, as did the undoubted sleep-inducing effects of the motion of the craft. Further, such complaints as were received came from a relatively small section of the total subjects engaged, and the responsibility of the drug was not clearly established.

The balance of opinion, including that of senior officers observing the troops at work, was that untoward effects on military efficiency were not produced.

Summary

Experiments on the prevention of sea-sickness were carried out in the Tropics during the training of troops under conditions closely approximating those of battle. British (1,667) and Indian (3,673) troops were used for tests.

In all experiments, vomit-bags, sweets, biscuits, and chewing-gum were issued to all men taking part, and men were allowed to stand up in the craft if they so desired.

Assault craft of various types (L.C.A.s, L.C.M.s, L.C.T.s, L.C.I.(L.)s) were used for all but a few experiments in which 170-ton dhows were employed.

In all experiments control groups receiving inert pills were observed under conditions identical to those of the test group(s). Usually control and test groups were each of approximately 100 men.

The drugs tested and the number of observations on each were: hyoscine (1,990); hyoscine plus amphetamine (625); hyoscine plus ergotamine (116); chlorbutol (619); ergotamine (116).

After rejection of 2,102 observations rendered valueless by calm seas, etc., 3,638 remained for analysis. The validity of the results has been statistically assessed. A high degree of reliability is shown for those for hyoscine, hyoscine plus amphetamine, and for some chlorbutol experiments.

Of the remedies tested, hyoscine 1/100 gr. proved most effective. The degree of protection was of the order of four-fifths of those susceptible. This degree of protection was observed in relatively calm seas, when the sickness rate in controls was 16%.

No case of heat-stroke or heat-exhaustion occurred among 2,731 men who were given hyoscine. The average maximum and minimum temperatures during the experiments were 91.9° and 82.1° F., with an average relative humidity of 80%. Considerable physical exertion was performed by 1,789 of the treated men on assault exercises; a further 424 carried out a very strenuous assault during an exercise in which one fatal case of heat-stroke and two cases of heat-exhaustion occurred among 5,000 untreated troops.

The conditions of the tests were such as to reveal any impairment of military efficiency. Drowsiness in landing-craft was general in all experiments, in untreated as well as treated groups. Only on two occasions (and these involving the same men) was there a possibility that one company might have been adversely affected by hyoscine. Executive officers did not attribute shortcomings of the troops during exercises to the effect of any drug.

We are indebted to Lieut.-Gen. Gordon Wilson, C.B.E., *M.C.*, Director of Medical Services, General Headquarters, India, for permission to publish these results. It is a pleasure to record our appreciation of the co-operation and assistance so willingly given us by the Central Statistical Section of G.H.Q., India. Our thanks are also due to the officers commanding the training centre and the troops in training, as well as to their staffs, for the generous facilities afforded us and for the interest they displayed in the work.

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HUMAN CREEPING MYIASIS

REPORT OF A CASE

BY

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Very few cases of human creeping myiasis have been reported and none described very fully, so that the following case may be of interest to both physicians and parasitologists.

Clinical History

The patient (K. C., W.857), a boy aged 14, was admitted on Jan. 21, 1944, to University College Hospital. He lived in South London, and had the normal activities of a boy of his age. He had never been abroad, and had left home only for holidays at Brighton or Shoreham, where he used to visit the harbour; but he had not done this during the previous two years. He often used to go on Epsom Downs to fly model aeroplanes. He had no allergic personal or family history, but was sometimes bitten by insects and he whealed markedly as a result. His general health was good. Twelve months before admission he began having prickly pains over the shoulders and chest—"like a needle pricking the skin"—associated with aching pains in the shoulders and legs. These continued, without causing much inconvenience, in bouts about twice monthly for six months and then stopped. In July, 1943, he first noticed a swelling in the skin, not reddened, about 3 cm. in diameter, giving rise to a pricking pain on pressure but otherwise painless. It lasted two days and then disappeared. From then on he had many similar swellings, usually single, occurring at various sites (left calf, right popliteal area, left shoulder, back, and the back of the head and neck). They were 1 to 5 cm. in diameter and raised 0.5 to 1 cm. above the skin. They were red or skin-coloured, and caused a pricking pain on being touched, but did not throb. They usually remained for a few days and then disappeared, but the boy had from time to time the sensation of something moving beneath the skin, and he thought that the lumps sometimes moved, going down at one place and coming up near by at another.

On Dec. 30, 1943, one of these swellings came up on the right thigh, and in a short time showed a black spot in the centre. It was fomented, and on Jan. 2 burst, discharging sero-sanguineous fluid. The cavity was syringed by a doctor, and a white maggot emerged. At that time the boy had a severe sore throat, which subsided uneventfully. He was shortly afterwards seen at the Hospital for Tropical Diseases and found to have an eosinophilia of 54%. He was then referred to U.C.H., where his course was as follows:

Jan. 21, 1944.—On admission there were no swellings and the skin was normal. The patient was a sensible uncomplaining boy in apparently good general health. T. 98.6°, P. 104, R. 20, B.P. 115/80. Blood count: R.B.C. 4,800,000, Hb 100%, W.B.C. 22,000 (neutrophils 35%, lymphocytes 19%, monocytes 2%, eosinophils 44%).

Jan. 24.—Left temporal region painful (throbbing, worse on palpation), no swelling visible. During the night a swelling developed, and next day it involved all the left circumorbital tissues and the frontal region to the roots of the hair, extending just over the midline; it was tender, showed capillary pulsation, was oedematous, and pitted readily on pressure. The skin was reddened, with no circumscribed margin. The palatal fauces were reddened. Soft glands were palpable in left axilla and on right side of neck. Attempts to obtain fluid from the swelling were unsuccessful. T. 103.6°, P. 108, R. 24, in the evening. Blood culture negative. Radiograph of chest negative.

Jan. 27.—Oedema spreading; left eye practically closed. Adrenaline (0.25 c.cm. of 1: 1,000) given subcutaneously with doubtful effect. The oedema then gradually subsided and was gone by Feb. 1, as was also an irregular spiking temperature, present since admission. Urine normal. Stools negative for ova and parasites.

Feb. 6.—In the night the patient developed tenderness over the 7th left rib in the mid-axillary line. At 7 a.m. there was in this situation a small red non-indurated slightly tender raised area, 2 by 1 cm., with a central clear yellowish linear bleb. This was incised, and from immediately below the skin a white segmented maggot, very slightly motile, 1 by 0.3 cm. in size, was shelled out. Temperature 97.4°. The maggot was taken to the London School of Hygiene and Tropical Medicine, and identified by Dr. John Smart of the British Museum (Natural History) as the larva of the warble-fly (*Hypoderma bovis*) in the spineless stage (first instar, according to Knipling's (1935) description).

Feb. 8.—A similar swelling, but with a small dark spot in the centre, was present on the right medial malleolus. It was fomented; but by 8 p.m. the dark spot had disappeared, the swelling being otherwise unchanged. During the day four pink papules, 4 by 1 mm. in size, appeared in a straight line on the front of the left side of the chest, as though distributed along the 4th intercostal space. One