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The Use of B 663 (Clofazimine) in the Treatment of Chinese Leprosy Patients with Chronic Reaction

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This report confirms earlier impressions of the usefulness of B 663 in the treatment of chronic reaction in Chinese leprosy patients and gives the results of investigations made over a 2-year period. (This paper should be read with reference to Dr. Warren's previous paper in *Leprosy Review* (1968) Vol. 30, No. 2, p. 61.)

INTRODUCTION

The report of the interim findings at 6 months in a trial of the use of B 663 in the treatment of Chinese leprosy patients with chronic reaction (Warren, 1968) is completed by this supplementary report. The trial concerned 30 patients and details of their selection and of procedure are given in the original report.

RESULTS

The initial patient (MW, F/25) continued to make good progress on a maximum dose of 600 mg of B 663 (clofazimine) per week, which was later reduced slowly until she was reaction-free on 200 mg per week. She requested the withdrawal of B 663 after 21 months of treatment when her bacterial index (BI) was 1.5, and the resumption of treatment with DDS. This was agreed to, as she had been free of reaction for 6 months, and DDS was recommenced. On a dosage of DDS ranging from 25 mg to 50 mg per week, however, she gradually developed increasing amounts of erythema nodosum leprosum (ENL), and eventually in the sixth month after stopping B 663 she developed arthritis, neuritis, and many attacks of ulcerated ENL. She then requested that treatment with B 663 be resumed. Her skin coloured had faded considerably at this time. After about 6 weeks on B 663 at 600 mg per week she was again almost reaction free and well enough to return to work. She has continued taking B 663 for a further 12 months and her BI had fallen to 0.7. She has been totally free of reaction for 4 months on 300 mg of B 663 per week.

This experience warned us of the dangers of stopping B 663 in a patient with a relatively high BI, who previously had been reaction-prone even when not receiving any antileprotic drugs. A similar return of lepra reaction has been seen in a number of patients who stopped B 663 too early.

Group A

The 4 patients previously receiving prednisolone have not required further prednisolone.

Patient No. 1 (*F*/30) continued to require 1200 mg of B 663 weekly; any reduction in this dosage allowed reaction to return, but her BI has now fallen satisfactorily, if slowly, from 3.3 to 2.2 in 2 years and her general physical condition is much improved.

Patient No. 2 (*F*/46) continued to be reaction-free on 900 mg of B 663 per week, but a reduction to 600 mg per week was accompanied by a return of reaction, with ulceration, so the dose of B 663 was increased to 1200 mg per week and maintained there for 6 months, when she was definitely free of reaction. However, as her BI did not fall, she became very depressed and requested addition of IMI sulphetrone; this was granted in the twentieth month of B 663 treat-

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TABLE 1

Progress of Group B patients receiving B 663

Patient No.	*Sex, age in 1967*	*At commencement weight (lb.)*	*BI*	*At 12 months weight (lb.)*	*BI*	*At 2 years weight (lb.)*	*BI*	*Max. dose given per week (mg)*	*Estimated optimum dose per week (mg)*	*Remarks*
6	M/50	105	2.7	121	1.5	113	1.0	900	300	On 300 mg no reaction, but reaction recurred on 200 mg per week.
7	F/35	92	1.5	103	0.5	103	0.2	300	200	Reaction settled at once.
8	F/60	88	3.7	98	2.7	100	2.5	300	300	Good control of reaction.
9	F/43	105	2.7	113	1.3	Refused		600	400	Good control of reaction.
10	M/21	108	3.3	128	1.0	132	0.2	1200	600	ENL recurred as dose reduced.
11	M/27	109	2.0	118	1.0	116	0.5	1200	600	Reaction rapidly controlled, but returned when dose reduced.
12	M/35	106	3.5	106	2.5	113	2.2	600	500	Reaction rapidly controlled.
13	M/49	125	1.5	129	0.2	133 on DDS	Neg. 8 mths	600	400	Reaction rapidly controlled.
14	M/44	111	2.5	122	1.0	124	0.2	900	300	Rapidly controlled on 600 mg per week.
15	F/28	95	3.5	102	2.2	Refused		600	400	Good control.
16	F/55	108	1.2	113	0.2 Stopped	Discharged on DDS	neg.	600	300	Very good control.
17	M/49	130 Oedema	4.0	125	3.3	125	2.3	1200	400	Very good control.
18	M/53	130	3.7	144	2.2	144	1.3	900	700	Very good control.
19	M/31	118	2.5	120	2.2	118	2.0	1800	1200	Persistent ENL and neuritis till prednisolone self medication disclosed.
20	M/38	120	3.0	124	1.7	128	1.0	900	600	Very good control of reaction.
21	M/38	88	3.0	98	1.7	96	0.8	1200	900	Good control of reaction when on 900 mg, but reaction returned on lower dosage.

ment. The dosage of the latter has been reduced slowly, and she is now receiving 300 mg of B 663 weekly and 3 g weekly of sulphetrone by injection. She has had no reaction for the past 12 months, her BI is 0.8, and her general condition is excellent.

Patient No. 3 (*M*/35) required a maximum of 900 mg of B 663 weekly to control reaction. The dosage was then reduced, but after 8 weeks on 400 mg weekly he developed multiple small pustular reactional lesions on the hands and feet, so an increased dose of 600 mg of B 663 weekly was resumed. The fall in the BI has been slow but fairly consistent. This patient realizes that he is physically better and his general outlook has improved immensely.

Patient No. 4 (*F*/35) required 8 months for total weaning off prednisolone. During this time her BI hardly altered, but then fell dramatically over the next 12 months. Reduction of the dose of B 663 to 300 mg per week caused no problems. Her BI fell from 2.8 to 0.8 in 2 years and she is now fully active, after being a bed patient for over 2 years.

The general impression is that patients who have been receiving prednisolone require a higher dosage of B 663 for longer periods than patients with other forms of reaction. We now

TABLE 2
Progress of Group C patients receiving B 663

Patient No.	*Sex, age in 1967*	*At commencement weight (lb.)*	*BI*	*At 12 months weight (lb.)*	*BI*	*At 2 years weight (lb.)*	*BI*	*Max. dose given per week (mg)*	*Estimated optimum dose per week (mg)*	*Remarks*
22	M/41	114	2.5	122	1.5	119	1.3	1800	900	Reaction returned after a few weeks on 600 mg per week, but keeps well on 900 mg per week.
23	M/41	109	2.3	118	1.7	106	1.3	1200	600	Neuritis and reaction rapidly controlled on 600 mg—tried high dose as no BI fall.
24	M/33	106	2.3	110	1.3	112	0.8	900	900	Neuritis rapidly returned when reduced below 900 mg. Problem patient. Prednisolone self-medication eventually disclosed.
25	F/36	96	1.5	116 then stopped B 663	0.3	Now discharged		900	900	Neuritis settled quickly and no return on reduced dose.
26	M/40	105	2.0	104	1.5	106	1.0	1200	600	Required 1200 mg to stop neuritis and no reaction after that.
27	M/26	102	3.5	104	2.8	102	2.2	1200	1200	Neuritis returns after 900 mg for a few weeks, but very well on 1200 mg. Nerve function is improving.
28	M/37	108	4.2	117	2.8	126	1.8	1200	400	Occasional ENL and slight neuritis on 300 to 400 mg per week, but general attitudes have improved. He now works.

recommend that they receive 1200 to 1800 mg of B 663 weekly at the commencement. Reduction of the dose of B 663 is usually proceeded with slowly, and probably should not go lower than 600 mg weekly while there is any suggestion of reaction. It is observed that the BI frequently does not fall to any extent while the patient is still on prednisolone.

Group B

This group comprised 16 patients with chronic reaction, and their progress is summarized in Table 1.

An attempt was made to estimate the optimum dose of B 663 for each patient, that is, the minimum dose that prevented the return of reaction.

Two patients refused to continue taking B 663, giving the resulting skin discoloration as the reason. One of them (Patient No. 15) had shown a dramatic fall in the BI initially while on B 663, but refused to continue taking the drug because of this discoloration. She was therefore given DDS by mouth, the starting dosage being 50 mg weekly and gradually increasing. However, after 5 months, when receiving 100 mg of DDS weekly, she developed severe neuritis, especially of both median nerves at the wrist, the right being more severe than the left. She agreed to recommence B 663 at 600 mg per week while continuing the DDS, but later assented to stop DDS completely. A surgical decompression of the right median nerve was performed, with rapid relief of pain and re-

covery of function. She has agreed to remain on B 663 alone at present. A further 2 patients became negative and stopped B 663 treatment, but the others all completed 2 years' treatment and some are continuing for a third year. One patient (No. 19) was found to be medicating himself with prednisolone, but it is unlikely that the others in Group B did so.

Group C

This group consisted of 7 patients with neuritis as the main complication; all were controlled, but the average dose of B 663 was somewhat higher than in Group B. The neuritis was well controlled, but the level was often critical, and missing even 2 or 3 doses, each of 100 mg, in one week has precipitated neuritis in several of them. Their progress is summarized in Table 2.

In this group of patients nerve function was evaluated by a light-touch test, the areas of anaesthesia being entered on a chart, and also by voluntary-muscle tests to estimate the power of the muscles of the hands and feet. During the 2 years on B 663 a number of patients have shown improvement in muscle power. Increased sensory perception is not so obvious but has occurred in some patients.

Patient No. 24 developed an acute foot-drop on 10 October, 1967, that is 14 weeks after commencing treatment with B 663, but before the dose was increased to the level that was later found to be necessary to control his reaction and neuritis. By the end of the 2 years almost full muscle power had returned and improvement was still occurring. At the end of the 2 years this patient reported that he had been treating himself with prednisolone as an analgesic since before commencing B 663. His clinical condition and the response to sudden cessation of prednisolone do not support his story but it must be considered in examining his response to B 663.

Patient No. 25 had shown considerable weakness of the small hand muscles, increasing with each of many recurrent bouts of neuritis, before she commenced B 663. Within 9 months of starting on B 663 her voluntary-muscle tests had markedly improved and were virtually normal.

Patient No. 27 remained prone to neuritis even when on 900 mg of B 663 per week, and neuritis returned whenever he missed taking a few capsules. In June, 1969, he developed acute right median neuritis with gross enlargement and marked tenderness of the nerve, associated with muscle weakness and fibrillation. He had generalized neuritis at the time, and his dose of B 663 was increased again to 1200 mg weekly. A surgical decompression of the right median nerve was performed, and 3 months later he showed return of apparently normal power and sensation perception.

It would appear that neuritis will occur in some patients on B 663 even after many months of treatment, but at a suitably high dosage level neuritis does not occur and recovery of function may occur without further permanent neurological deficit.

Group D

Mr. G., aged 65, died after a coronary occlusion in the eighth month of B 663 treatment, but his general condition was much improved prior to his death.

Mr. K., aged 46, has continued to progress very well, his BI falling from 3.3 to 1.5 in 2 years. His diabetes is now completely controlled without drugs, and reduction of the dose of B 663 from 600 mg to 300 mg has been completed without trouble.

Group E

Relapsed patient (M/35) showed an initial good fall in his BI but this then became stationary and neuritis and reaction developed on a dosage of 900 mg weekly. In December, 1964, he had developed a right foot-drop, but this had gradually recovered until he had full power in the dorsiflexors of the foot in January, 1968. In April, 1969, 9 months after commencement of B 663, he developed an acute weakness of the dorsiflexors of the left foot. This was at a time when we were attempting to reduce his dosage of B 663 and he was receiving only 600 mg weekly. The dosage was therefore

TABLE 3
Response of patients changing from B 663 to dapsone

Patient No., sex and age	*Duration of B663 therapy*	*BI at change*	*Current dose of B 663 at date of change*	*Method of change*	*Commencing dose of DDS*	*Remarks*
M.W. (1) F/25	21 months, no reaction for 6 months	1.5	3/w	Change to	DDS 500 mg/w	Reaction slight within 3 weeks, but became severe. At 5 months she requested to restart B 663.
(2)	Further 13 months on B 663. No reactions for 3 months	0.7		Add DDS	25 mg/w	No reaction within 6 weeks. Increased DDS after 8 weeks.
2 F/46	15 months. No reaction for 6 months	1.3	12/w	Add IMI Sulph.	2 cc/w = 0.1 g Sulphetrone by injection	No reaction. IMI Sulphetrone increased to 6 cc weekly with B 663 at 3/w.
9 F/43	12 months. Had no reaction for 2-3 months	1.5	4/w	Sudden change to Refused more B 663	DDS 50 mg for 3 months then increased	Slight reaction only. Slow increase of DDS to 200 mg per week.
10 M/21	2 years	0.7	4/w	Add DDS	10-20 mg	ENL recurred within 3 weeks. Given B 663 alone again till BI 0.2.
11 M/27	2½ years	0.3	2/w	Add DDS	50 mg/w	No reaction for 4 weeks so stopped B 663.
14 M/44	2 years	0.3	3/w	Sudden	100 mg/w	No reaction.
15 F/29	9 months, refused more B 663 when no reaction for 3-4 months	1.2	5/w	Sudden change to	DDS 50 mg/w slowly increasing	Reaction returned at 100 mg (off B 663 under 6 months). Severe—see Case 15 details under Group B.
21 M/38	2 years	0.8	3/w	Sudden	50 mg/w	Reaction within 3 weeks. He requested to recommence B 663 alone.
	when restabilized		3/w	Add DDS	25 mg/w	Reaction in 2 weeks—so DDS stopped till BI lower.
22 M/41	18 months	1.5	18/w	Added IMI Sulph.	2 cc = 1 g/w	No reaction till B 663 dropped to 6/w then ENL recurred.
23 M/41	18 months	1.5	9/w	Add DDS	100 mg	No reaction—B 663 slowly reduced to 5/w. DDS increased to 150 mg/w then B 663 stopped.
31 M/45	13 months	2.7	12/w	Sudden change refused B 663	ASS ½ cc/w = 100 mg DDS	No real reaction for 3 months then recommenced ENL and neuritis with increasing severity.

increased and there has already been much recovery of muscle power, which is now nearly normal. He obviously required 1200 to 1500 mg of B 663 per week to remain free from reaction and neuritis, so the acute paresis occurred on a dosage that we now consider was too low for his needs.

A further 30 patients have been treated with B 663, some of them for reaction, with similar results, but usually with more rapid control due to the experience gained in this trial. This group of patients included a number with relapsed lepromatous leprosy who are apparently resistant to dapsone and/or to thiambutosine; it also included patients with borderline and atypical lepromatous leprosy.

TABLE 4

Serial haemoglobin and erythrocyte sedimentation rates for the whole group

Patient No.		*Haemoglobin (g%)*					*Erythrocyte sedimentation rates (mm/1st hour)*				
		Initial Value	*At 3 months*	*At 6 months*	*At 12 months*	*At 2 years*	*Initial Value*	*At 3 months*	*At 6 months*	*At 12 months*	*At 2 years*
1	F/30	10.2	10.2	9.9	10.2	10.5	80	68	45	65	50
2	F/46	10.5	10.2	11.4	12.0	11.4	72	52	27	28	45
3	M/35	10.2	11.4	10.7	11.4	12.8	72	45	52	70	60
4	F/35	10.7	9.2	10.2	11.4	12.3	73	102	22	36	40
6	M/50	11.4	9.5	11.0	11.7	9.9	110	80	50	55	75
7	F/35	8.8	11.0	12.4	12.1	12.0	109	63	34	68	
8	F/60	10.2	10.2	11.0	11.4	10.2	65	90	60	67	75
9	F/43	12.4	11.4	10.7	11.4	11.1	52	55	47	52	
10	M/21	10.2	9.9	10.5	12.0	13.7	108	60	55	43	37
11	M/27	11.0	11.4	11.0	12.1	13.1	105	73	65	40	5
12	M/35	11.4	11.7	10.2	11.4	12.3	48	36	76	30	31
13	M/49	12.8	11.4	11.7	12.4	13.4	81	45	35	32	
14	M/44	12.4	13.1	10.7	12.1	12.6	80	47	45	45	45
15	F/28	12.1	13.9	12.4	11.7	11.4	23	20	28	26	15
16	F/55	12.1	11.7	11.4	12.0		45	27	30	10	
17	M/49	9.9	9.9	11.0	11.7	13.4	82	40	38	15	8
18	M/53	11.4	11.0	11.0	12.1	14.3	120	65	33	30	12
19	M/31	10.2	10.2	10.2	11.4	12.3	108	110	78	76	25
20	M/38	10.2	11.0	10.5	11.7	13.6	106	113	70	56	61
21	M/38	8.8	9.9	11.7	12.4	14.0	70	23	20	33	15
22	M/41	9.9	9.9	9.9	11.0	12.3	94	58	37	52	48
23	M/41	11.7	11.4	10.2	11.4	12.0	92	72	84	52	18
24	M/33	9.9	9.9	9.9	10.2	10.8	74	75	70	35	34
25	F/36	10.7	9.5	10.5	11.4	11.7	108	53	20	38	
26	M/40	12.1	14.0	11.7	12.0	14.3	10	15	25	28	5
27	M/26	11.0	11.0	11.0	11.0	11.4	81	72	56	54	62
28	M/37	11.7	8.8	9.9	10.5	10.8	44	72	42	47	45
29	M/46	10.5	13.1	11.7	11.4	12.0	88	44	45	47	20
30	M/35	12.1	11.7	11.0	11.7	11.1	5	7	36	20	33

Normal values: male 13.5 to 18 g %; female 11.5 to 16.5 g %; male 0 to 15 mm/hour; female 0 to 20 mm/hour.

SIDE EFFECTS

Apart from the skin pigmentation no undesirable effects have been seen. Two female patients refused B 663 after 12 months' treatment because of skin discoloration, and several patients have refused to start taking the drug for the same reason.

DOSAGE LEVEL

We would now recommend for Chinese leprosy patients with reaction, the following dosage schedules:

(1) B 663 at 1200 mg weekly initially for patients with marked neuritis;
(2) B 663 at 1200 to 1800 mg weekly for patients dependent on prednisolone; and
(3) B 663 at 600 to 900 mg weekly for other forms of reaction.

If control of the reaction is not achieved within 6 weeks the dosage should be increased. The dose that controls reaction should be maintained for 3 months before any reduction is attempted, or, in the case of patients dependent on prednisolone, until the patient has been weaned from the latter for 3 months. The level of dosage does not appear to affect the rate of fall of the BI provided reaction is controlled.

CESSATION OF B 663 TREATMENT

Two patients in this trial requested the stopping of B 663 treatment while the BI was still high. Each of these patients developed increasing amounts of reaction until finally they asked for the resumption of B 663.

After this experience it was decided to vary the routine of change from B 663 to dapsone,

TABLE 5

Changes in blood protein levels of patients on B 663

Patient No.	*Serum Protein*					*A/G ratio*				
	Initial Value	*At 3 months*	*At 6 months*	*At 9 months*	*At 12 months*	*Initial Value*	*At 3 months*	*At 6 months*	*At 9 months*	*At 12 months*
1	6.7	7.0	6.8	7.4	6.2	2.1/4.6	2.9/4.1	4.5/2.3	3.6/3.8	3.0/3.2
2	7.9	6.1	6.4	7.2	6.7	4.3/3.6	3.5/2.6	4.5/1.9	5.3/1.9	4.3/3.4
3	7.9	6.9	7.2	7.9	5.4	2.8/5.1	3.2/3.7	4.5/2.7	4.1/3.8	3.3/2.1
4	8.1	6.7	7.4	8.1	7.4	3.3/4.8	2.5/4.2	4.1/3.3	4.6/3.5	3.8/3.6
6	7.8	7.6	6.7	8.0	7.0	2.5/5.3	3.4/4.2	4.0/2.7	4.1/3.9	3.3/3.2
7	8.2	7.6	7.4	8.0	7.6	3.3/4.9	3.5/4.1	4.9/2.5	4.3/3.7	4.3/3.3
8	7.8	7.1	6.6	8.8	7.1	3.0/4.8	3.1/4.0	4.2/2.4	4.1/4.7	3.6/3.5
9	7.8	7.1	7.0	7.1	7.0	3.2/4.6	3.5/3.6	4.0/3.0	4.2/2.9	4.0/3.0
10	6.8	7.3	7.1	8.0	7.2	1.5/5.3	3.0/4.3	4.0/3.1	3.1/4.9	3.4/3.8
11	7.1	8.0	7.4	7.8	7.2	1.6/5.5	3.5/4.5	4.5/2.9	3.8/4.0	3.7/3.4
12	6.8	7.0	6.5	7.4	7.8	3.0/3.8	3.6/3.4	4.2/2.3	4.1/3.3	4.6/3.2
13	7.0	7.2	6.1	8.2	8.0	2.6/4.4	4.0/3.2	4.0/2.1	5.1/3.1	3.9/4.1
14	7.6	7.5	7.5	8.3	7.7	2.4/5.2	3.6/3.9	4.6/2.9	3.5/4.8	4.3/3.4
15	7.6	7.5	6.3	7.8	7.6	3.2/4.4	3.6/3.9	4.2/2.1	4.3/3.5	4.1/3.1
16	6.7	6.7	7.0	7.3	7.0	2.7/4.0	3.5/3.2	4.5/2.5	4.1/3.2	4.3/2.7
17	5.9	6.8	7.0	7.9	7.2	1.3/4.6	3.3/3.5	4.0/3.0	4.7/3.2	4.3/2.9
18	8.2	6.6	8.1	5.7	6.95	2.3/5.9	2.6/4.0	4.1/4.0	2.7/3.0	3.8/3.15
19	7.7	7.5	6.9	7.7	6.6	2.4/5.3	3.4/4.1	3.9/3.0	3.9/3.8	3.6/3.0
20	6.9	7.7	6.8	7.7	7.3	2.6/4.3	3.6/4.1	3.6/3.2	3.8/3.9	3.9/3.4
21	6.9	6.3	5.5	6.3	6.1	2.9/4.0	3.7/2.6	3.5/2.0	4.2/2.1	4.3/1.7
22	6.6	6.3	5.9	6.7	6.4	2.8/3.8	3.2/3.1	3.5/2.4	3.2/3.5	3.1/3.3
23	7.7	6.7	6.7	7.7	6.7	2.7/5.0	3.3/3.4	3.9/2.8	4.0/3.7	3.5/3.2
24	6.5	6.2	5.9	4.2	5.5	3.0/3.5	3.6/2.6	4.1/1.8	2.4/1.8	3.2/2.3
25	7.9	7.4	7.4	8.0	7.7	2.7/5.2	3.3/4.1	4.7/2.7	3.8/4.2	3.5/4.2
26	6.3	5.5	5.6	6.8	4.7	3.2/3.1	3.2/2.3	3.7/1.9	3.8/3.0	2.8/1.9
27	6.6	7.0	7.3	7.8	6.6	2.0/4.6	3.1/3.9	4.9/2.4	3.6/4.2	3.2/3.4
28	6.6	6.1	6.7	6.4	6.1	2.4/4.2	3.1/3.0	4.1/2.6	3.7/2.7	2.9/3.2
29	7.3	6.0	6.1	6.3		2.9/4.4	3.5/2.5	3.6/2.5	4.0/2.3	
30	7.4	6.3	6.4	6.6	6.4	3.5/3.9	3.5/2.8	3.9/2.5	3.8/2.8	3.7/2.7

Normal value: 6.5 to 7.9 g %; albumin 4.2 to 5.2 g %; globulin 1.5 to 3.0 g %.

but as far as possible to continue with B 663 until the BI was under 0.5 (or at least under 1.0) and the patient had not had reaction for at least 6 months.

The routines adopted were:

(1) Sudden cessation of B 663 therapy and commencement of low dose dapsone; or

(2) Reduction of B 663 dosage to 200—300 mg weekly, and then addition of a low dose of dapsone, while maintaining the B 663 until the dapsone was increased to 100 mg weekly.

Table 3 summarizes the results of these treatment schedules. One patient who had been reaction-free for 6 months on 300 mg of B 663 per week was allowed to change over to dapsone when his BI was 0.2. Within 2 weeks, however, he had a recurrence of ENL and recommenced B 663 with resulting control of the reaction after 4 weeks.

Two patients whose BI was 0 when the B 663 was suddenly stopped had no trouble when changing from B 663 to DDS. Several other patients with a higher BI also had no recurrence of reaction associated with a sudden change from B 663 to DDS.

It was observed that it is very difficult to foresee how a particular patient will react, and whether a change from B 663 to DDS can be effected without a return of reaction. It is obviously desirable to have the patient completely free from reaction for some months on 200 to 300 mg of B 663 per week before trying to recommence DDS. We now usually give both drugs together for several months before stopping the B 663 completely.

LABORATORY INVESTIGATIONS

A series of laboratory and biochemical investigations were performed every 3 months for these 30 patients.

Table 4 summarizes the changes in the haemoglobin level and in the erythrocyte sedimentation rate (ESR). It will be observed that patients with anaemia at the start of B 663 treatment tended to show rising haemoglobin levels. The ESR was high in some patients at the beginning of B 663 therapy and tended to fall, though in many patients it did not reach normality (0 to 15 mm for males and 0 to 20 mm for females in the first hour) in the 2 years under observation.

Table 5 summarizes the changes in the serum protein levels and the albumin/globulin (A/G) ratio for the first 12 months of the trial. Unfortunately it was not possible to continue these estimations. It can be seen that there is definite reversal of the A/G ratio in many of the patients at the commencement of B 663 treatment but that this ratio had usually returned to near normal within 12 months.

DISCUSSION

The advent of B 663 has changed the whole outlook for our Chinese leprosy patients with reaction. Even the problem of the discoloration of the skin is usually outweighed by the obvious improvement of so many patients taking B 663, and also the fact that patients now know other patients in whom the colour has faded on cessation of the drug. The treated patients are also able to continue working and have spent much less time in hospital, so reducing the nursing care previously needed by many of them for long periods.

Over the years, in patients with borderline leprosy who develop acute paralysis we have come to expect a high degree of recovery of muscle power without the use of B 663. But those in the present series who have demonstrated returning function are patients with lepromatous and atypical lepromatous leprosy in whom we would not previously have expected a return of function. A longer study will be needed to ascertain how much permanent recovery has occurred or if increasing weakness occurs again when B 663 is stopped. This happened in one patient (No. 15) and recovery occurred again on resumption of B 663.

The laboratory findings support the impression that the patients generally show improved health after a period on B 663.

The use of dapsone together with B 663 did not have any obvious effect on the rate of fall of the BI, but did in a number of patients precipitate lepra reaction, which however settled again either on increased dosage of B 663 or on withdrawal of dapsone. In these cases the dapsone was added to the treatment only of a patient already stabilized on B 663, and who had not had reaction for some months. The dose of B 663 was not changed when the dapsone was started.

CONCLUSIONS

The rapid fall in the BI observed in the first 6 months was not maintained for the 2 years, but it is obvious that the fall in BI was on the average at least equal to that expected in similar but uncomplicated cases. In most patients the BI fall far exceeded that for the same patient in the previous 2 years.

The control of reaction was complete, and by adjusting the dose of B 663 other anti-reaction measures could be discontinued. The optimum dose of B 663 varies with the type of leprosy and with the severity of the reaction, and must be adjusted for each individual.

Patients showing an increasing nerve deficit before commencing B 663 showed some degree of, or complete, recovery of function of the affected nerve. There were some cases of new neuropathies developing in the first few months of treatment with B 663, but no nerve lesion that developed after 6 months on B 663 resulted in permanent marked loss of muscle power. The dose of B 663 can be adjusted so that neuritis does not occur even in patients who were previously neuritis-prone.

SUMMARY

Over a period of 2 years B 663 has successfully controlled chronic lepra reaction in its various forms in Chinese patients. At the same time it has obviously acted therapeutically, assisting in the elimination of the disease.

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