THE EFFECTS OF CHLOROQUINE ON PATIENTS WITH SYMPTOMATIC PORPHYRIA*†

G. D. SWEENEY, M.B., CH.B.; M. LEVEY, B.SC.; E. B. DOWDLE, M.D., M.R.C.P.; and L. EALES, M.D., F.R.C.P.

CSIR/UCT Renal Metabolic Research Group, Department of Medicine, University of Cape Town, and Groote Schuur Hospital

The reputedly beneficial effect of chloroquine in the treatment of chronic discoid lupus erythematosus soon led to its use in other photosensitive states. Treatment with chloroquine or nivaquine has been reported in at least 17 patients with cutaneous porphyria. In 9 of these a transient adverse reaction has been observed. It manifests with fever, generalized myalgia, headache, malaise, and often abdominal pain with nausea and vomiting. Darkening of the urine is consistently present, but reports on porphyrin excretion are fragmentary, and further studies are obviously necessary.

This is a preliminary study of the effects of chloroquine in 5 patients with symptomatic porphyria (urocoproporphyria). The following features were present in all: florid cutaneous lesions, an excessive alcohol intake, no family history of the disorder, marked uroporphyrinuria, and a slight to moderate increase in faecal porphyrin (with the coproporphyrin fraction exceeding the protoporphyrin). Histological examination of aspiration liver-biopsy specimens showed some increase in periportal fibrous tissue and evidence of liver-cell regeneration (by courtesy of Dr. C. J. Uys), but the most consistent finding was a variable degree of siderosis. The porphyrin content was also measured.

The dose of chloroquine administered varied from 0·6 to 4+G. (Table I). The salient clinical features at the height of the reaction to the chloroquine are recorded in Table I.

*This work was supported in part by a grant, P.H.S. A-3997, from the National Institute of Health, Public Health Service, USA.

†Abstract of a paper presented at Research Forum, University of Cape Town, 15 March 1962.

TABLE I. DOSAGE OF CHLOROQUINE AND CLINICAL FEATURES OF THE REACTION

	Patient				
	W.L.	*D.S.*	*P.V.*	*G.S.*	*H.P.*
Chloroquine (G.)	2·5	1·0	0·63	2·0+	4·0+
Latent period (days)	3	3	2	2	8
Pyrexia, malaise ..	+	+	+	+	+
Headache	+	+	+	+	+
Red urine	+	+	+	−	+
Nausea	+	+	+	−	−
Abdominal pain ..	+	+	+	−	−
Urobilinogen ..	+	−	−	−	−

Associated with the pyrexia there was a massive uroporphyrinuria, one patient excreting 84 mg. of uroporphyrin at the peak of the fever. The increase in excretion of delta-aminolaevulinic acid and porphobilinogen in the urine was insignificant — in sharp contrast to the findings in acute genetic porphyria. Table II compares biochemical findings before and during the reactions in the 5 patients.

The abnormal bromsulphthalein excretion, the elevated serum glutamic oxaloacetic transaminase (SGOT) activity (by courtesy of Dr. G. M. Potgieter) and, in one instance, the appearance of urobilinogen in the urine, suggested that damage to liver cells accompanied the reaction.

Readministration of chloroquine to patient D.S. (initial dose 1·0 G.) was without any effect, while in P.V. an increase

TABLE II. BIOCHEMICAL FINDINGS BEFORE AND DURING THE REACTIONS TO CHLOROQUINE

	Patients									
	W.L.		*D.S.*		*P.V.*		*G.S.*		*H.P.*	
	Before	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*	*Before*	*During*
Uroporphyrin*	4·0	81·0	3·4	84·0	2·2	37·0	4·5	13·8	2·4	35
Coproporphyrin*	0·9	3·8	0·8	3·8	0·3	2·2	1·3	2·1	0·2	4·2
Aminolaevulinic acid*	2·8	0·6	6·4	2·8	1·8	2·1	4·9	1·1	2·2	2·1
Porphobilinogen*	0·3	0·4	1·8	3·0	1·6	8·6	1·9	0	2·1	4·7
Bromsulphthalein retained at 30 minutes			0	0	0	22%			0	Excess
Thymol turbidity	1	1	4	2	1	0·5	1		4	
Zinc turbidity	12	10	11	10	12	12	12		12	
Cephalin cholesterol		1	0	1	0	2	1		2	
Alkaline phosphatase (Bodansky units)	2·8	2·8	8·2	1·0	10·5		3·7		9·5	
SGOT (Karmen units)			15	1,113	23·5	230	26	117	31	252
Total bilirubin	0·5	1·3	0·4	1·5	0·2	1·1	1·4		1·2	
Conjugated bilirubin	0	0	0	0	0	0	0		0	

*In mg. per 24 hr.

in uroporphyrin output unaccompanied by clinical upset occurred. In this case only 0·625 G. of chloroquine had been given initially. In 2 cases the reaction subsided despite continued administration of the drug.

Follow-up studies have shown that chloroquine does not halt the porphyric process, whereas its use is associated with findings suggestive of liver damage. This appears to be reversible. The skin lesions of symptomatic porphyria invariably improve during hospitalization (and abstinence from alcohol). The impression is that the drug is of doubtful value in the therapy of cutaneous porphyria.

The mechanism of the reaction is unknown, but it is suggested that the liver cells of patients with symptomatic porphyria are peculiarly vulnerable to chloroquine. At a certain concentration destruction of porphyrin-containing liver cells occurs. The contained porphyrin is released into the circulation and excreted by the kidney while other products of cell lysis account for the clinical signs and symptoms and the elevated SGOT activity. Chloroquine is known to be concentrated by the cells of visceral organs, particularly the liver and kidney. Furthermore, the livers of patients with symptomatic porphyria contain large amounts of porphyrin, between 100 and 1,000 mg. per kg. wet liver. Much of this porphyrin is probably intracellular.

The sequence of a latent period before the onset of symptoms and a subsequent refractory state when readministration may fail to elicit a response is worth emphasizing. An analogy may be drawn with a similar sequence — that induced by certain drugs in individuals whose cells lack glucose-6-phosphate dehydrogenase. Furthermore, the rare occurrence of cutaneous porphyria in patients with alcoholic liver disease suggests an underlying defect which may be genetically determined, and it is not inconceivable that this defect may be coupled with chloroquine sensitivity.