CHLOROQUINE SULPHATE IN TREATMENT OF CHRONIC DISCOID LUPUS ERYTHEMATOSUS

BY

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For some years mepacrine has been used in the treatment of chronic discoid lupus erythematosus (Prokoptchouk, 1940; Popoff and Kutinscheff, 1943; Page, 1951). From 1952 to May, 1954, a group of cases have been treated with chloroquine sulphate in this department. This drug has the advantage of being less toxic than mepacrine and does not lead to yellow discoloration of the skin.

Since the course of the disease is variable, with seasonal exacerbations, the patients were followed through the four seasons before coming to any conclusion. Routine investigations carried out included: (a) Hb, R.B.C., W.B.C. differential count, E.S.R.; (b) plasma proteins; (c) chest x-ray examination.

The following complications, as noted by Alving *et al.* (1948), were looked for: pruritus, anorexia, vertigo, tinnitus, visual disturbance, diarrhoea, malaise, urticaria. The possibility of agranulocytosis was kept constantly in mind and patients were warned to report any untoward symptoms, such as lassitude and sore throat.

Dosage.—The dosage of chloroquine sulphate used initially was 0.1 g. thrice daily by mouth (tablet, not base dose). If the clinical response was rapid the dosage was dropped to 0.1 g. twice daily.

Results

Eighteen cases have been under treatment (see Table). Ten showed clinical cure (scaling disappeared and the skin was either normal in appearance or atrophic); five improved—slight scaling remained; one (B) was subjectively improved; one (A) was unchanged; and in one (O) the condition continued to spread. No complications occurred.

The following points were noted with three of the 10 clinical cures while under treatment. Case K relapsed under treatment. The relapse occurred after the patient had stood in the sun without protection. There was also a relationship between the E.S.R. and clinical response, there being no response to treatment when the rate was raised. Case M

Results of Treatment

Case	Age	Sex	Duration when Therapy Started	Distribution	Previous Treatment	E.S.R.	Biopsy	Weeks of Treatment	Dosage	Months of Observation	Result	Comparison with Previous Therapy
A	87	F	4 months	Scalp; palate	Mepacrine	Raised	No	24	0.1 g. t.d.s. (50.4 g.)	11	Unchanged	—
B	32	M	10 years	Lip	Quinine, Bi, gold, CO ₂	Normal	"	24 16 28	0.1 g. t.d.s. (50.4 g.) No treatment 0.1 g. t.d.s. (59.2 g.)	17	Subjective improvement	Best
C	51	M	11 "	Face; ears	CO ₂ , sulphonamide, sulphapyridine, Bi, mepacrine	"	"	28	0.1 g. t.d.s. (59.2 g.)	12	Lesions cleared. Residual scarring	"
D	56	F	16 "	Face; nose	Calciferol, mepacrine	"	"	8 3 8	0.1 g. t.d.s. (16.8 g.) No treatment 0.1 g. t.d.s. (16.8 g.)	10	Lesions cleared, but relapsed on stopping chloroquine. Lesions cleared	"
E	56	F	7 "	Nose; temple	?	"	"	16 8	0.1 g. t.d.s. (33.6 g.) 0.1 g. daily (5.6 g.)	16	Skin cleared	"
F	36	M	1 year	Face; nose; lip	Calciferol	"	"	3 12 9	0.1 g. b.d. (4.2 g.) 0.1 g. t.d.s. (33.6 g.) 0.1 g. daily (6.3 g.)	11	Cleared	—
G	29	F	1 "	Face	—	"	"	16	0.1 g. t.d.s. (33.6 g.)	4	Improved	—
H	43	F	19 years	Face; ear	Gold, Bi, sulphonamide	"	"	3 28 4	0.1 g. t.d.s. (6.3 g.) No treatment; relapse following cold 0.1 g. t.d.s. (8.4 g.)	12	Cleared. Relapsed. Cleared	Best
K	35	F	1 year	Face	Mepacrine, gold	Raised at first	"	12 2 12	0.1 g. t.d.s. (25.2 g.) Went into sun; no treatment 0.1 g. t.d.s. (25.2 g.)	12	Improved. Relapsed. Clinically clear	"
L	37	F	8 months	"	Mepacrine	Normal	"	4	0.1 g. t.d.s. (8.4 g.)	1	Improved	—
M	56	M	2 years	"	"	"	Yes	8 4 8	0.1 g. t.d.s. (16.8 g.) Indigestion—no treatment 0.1 g. t.d.s. (16.8 g.)	10	Relapsed	Best
N	54	M	2 "	"	"	"	"	4 8 4	0.1 g. t.d.s. (8.4 g.) 0.1 g. b.d. (13.2 g.) 0.1 g. daily (2.8 g.)	6	Clinically clear Improved	"
O	32	M	1 year	"	Nil	"	No	12	0.1 g. t.d.s. (25.2 g.)	—	No change	Now on B
P	24	M	4 years	"	Mepacrine	"	Yes	3 8 4	0.1 g. t.d.s. (6.3 g.) 0.1 g. daily (5.6 g.) 0.1 g. t.d.s. (8.4 g.)	4	One small lesion appeared during course. Cleared with CO ₂	As good, but slower
Q	41	M	15 "	Face; ear	CO ₂ ; Bi	"	No	12 4	0.1 g. t.d.s. (25.2 g.) 0.1 g. b.d. (5.6 g.)	6	Scarring. No activity	Best
R	45	F	15 "	Nose	CO ₂	"	"	24	0.1 g. t.d.s. (50.4 g.)	16	Improved. Single lesion treated with CO ₂	Best
S	46	F	2 "	Face	Mepacrine, gold	"	Yes	14	0.1 g. t.d.s. (29.4 g.)	4	Improved	Best
T	64	M	19 "	Face; nose; ears	?	"	"	20	0.1 g. t.d.s. (42.0 g.)	11	Good result. Residual scarring	Best for 10 years

complained of indigestion, but, on questioning, he said he was "a martyr to attacks of indigestion." Case T found that his rheumatic pains, for which he had had many medical remedies, cleared "miraculously" while he was under treatment, but they returned as soon as the treatment was stopped.

The patients who were under observation for less than six months were asked to communicate with us should there be a relapse, but as yet we have had no response.

Two cases of subacute disseminated lupus erythematosus were also treated with chloroquine sulphate with no satisfactory clinical response.

Summary and Conclusions

Eighteen cases of chronic discoid lupus erythematosus were treated with chloroquine sulphate by mouth. The results are tabulated and discussed.

It is considered that chloroquine sulphate is as efficient a form of palliative therapy as any previously used, though not as yet the answer for the chronic disease. There is still a place for CO₂ snow treatment where there is a single discoid lesion.

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REFERENCES

- Alving, A. S., *et al.* (1948). *J. clin. Invest.*, 27, Suppl. p. 60.
Page, F. (1951). *Lancet*, 2, 755.
Popoff, L., and Kutinscheff, M. (1943). *Derm. Wschr.*, 116, 186.
Prokoptchouk, A. J. (1940). *Vestn. Vener. Derm.*, No. 2-3, p. 23. (Cited *Book of Dermatology and Syphilology*, 1952, p. 92.)

CHRISTMAS DISEASE ASSOCIATED WITH FACTOR VII DEFICIENCY CASE REPORT WITH FAMILY SURVEY

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Reports of congenital deficiencies of isolated blood coagulation factors have become common. Instances of more than one such deficiency occurring simultaneously in the same individual have been much less frequently reported. Koller (1954) has drawn attention to this possibility by describing a case of combined haemophilia and Factor V deficiency. Soulier and Larrieu (1953) have reported a case of combined haemophilia and Christmas disease, the diagnosis being based on the failure of the patient's plasma to correct the clotting defect of either haemophilia or Christmas disease. To our knowledge, no association of Factor VII deficiency with Christmas disease has previously been reported. Such a combination has recently come to our notice in a family, some of whose members suffer from haemorrhagic manifestations.

Case Report

A 29-year-old man was admitted to Addenbrooke's Hospital following a road accident in April, 1954, when he received a cut over the right eye which had continued to bleed intermittently for two weeks. He had had excessive bleeding from traumatic cuts since childhood, and recurrent haemarthroses of the elbows and knees had resulted in

partial flexion deformities of these joints. In 1951, following an appendicectomy, he had required 6 pints (3.4 litres) of blood, and the wound had healed by secondary intention (occasionally sutures had been sloughed out since then). In November, 1953, a dental extraction had required three weeks' hospitalization and 6 pints (3.4 litres) of blood. He had received 6 pints of blood at another hospital just before this latest admission in an attempt to control the bleeding from his forehead, with only moderate success.

General physical examination was unremarkable. Both wrists showed impairment of dorsiflexion, and there was 20 to 30 degrees limitation of extension in both knees and elbows. The cut in the forehead had been sutured, but a large subcutaneous haematoma had caused the wound edges to gape. Oozing from the wound was moderate. There was a nylon suture protruding from the appendicectomy wound in the abdominal wall, surrounded by a small area of granulation tissue. X-ray examination of the knees showed loss of articular cartilage, subarticular cyst formation, and sclerosis and osteophytes of both knees, particularly on the right side. The changes were regarded as compatible with those of repeated haemarthroses.

Laboratory investigation of the urine and routine haematological examination revealed nothing abnormal. Coagulation studies are shown in Table I.

TABLE I

Test	Method	Result	Normal Values
Clotting-time ..	Modified Lee-White	17.5 mins.	5-10 mins.
Platelet count ..	Rees-Ecker	670,000/c.mm.	2-400,000/c.mm.
Oil-suspended clot retraction	Budtz-Olsen (1951)	13% in 4 hr.	20% in 4 hr.
Prothrombin consumption	Quick <i>et al.</i> (1949)	22.9 sec. in 1 hr.	Over 30 sec. in 1 hr.
One-stage prothrombin time	Quick	22.3 sec. (40%)	80-100%
Factor V ..	Stefanini (1950)	95%	90-100%
Two-stage prothrombin	Biggs and Douglas (1953a)	104%	85-100%
Factor VII ..	Koller <i>et al.</i> (1951)	44%	90-100%
Thromboplastin generation test—fully corrected by normal serum but unchanged by normal plasma	Biggs and Douglas (1953b)	27%	100%

These tests indicated a defect in thromboplastin generation compatible with the diagnosis of Christmas disease, and a prolonged one-stage prothrombin time due to a marked reduction in Factor VII. By definition, Christmas disease is characterized by a normal one-stage prothrombin time (Biggs *et al.*, 1952), and Factor VII deficiency alone produces a defect in the thromboplastin generation test only if less than 10% of normal (Biggs and Marfarlane, 1953). Thus there appeared to be two separate deficiencies present in this patient. No evidence of liver disease existed to explain the reduced Factor VII level.

Clinical Course

He was given by intravenous drip 80 ml. of compatible 10-day-old serum, which reduced his clotting-time to 8.5 minutes, raised his prothrombin consumption to 26.2 seconds in one hour, shortened the one-stage prothrombin time to 17.2 seconds (58% of normal), and improved the clot retraction to 20% in four hours. Under cover of this treatment, the haematoma of the forehead was evacuated and re-sutured, and covered with a pressure bandage. At the same time the nylon suture was removed from the abdominal wound and a pressure bandage also applied. There was no excess haemorrhage as a result of these procedures. He was given a further 40 ml. of serum immediately post-operatively. His tests had returned to their pre-treatment level by 18 hours post-operatively. The sutures were removed without trouble 10 days later under cover of more serum intravenously. Traction to the right leg produced some improvement in the degree of flexion contracture. He was discharged after an uneventful convalescence.