TECHNICAL PAPERS

The Antitreponemal Effect of Oral Chloromycetin[1] in 32 Cases of Early Syphilis in Man—A Preliminary Report

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Chloromycetin (Chloramphenicol) was originally isolated from a soil organism, *Streptomyces venezuelae* (*1*). This antibiotic has been shown to have a wide range of therapeutic activity against many pathogenic organisms.

A systematic study of its use in the treatment of human syphilis has not yet been reported. However, it has been used by Smith and co-workers (*4*) in the treatment of experimental rabbit syphilis. These workers found that after dosages of 50 and 100 mg/kg of body wt the syphilitic lesions were cleared only temporarily of treponema.

Smadel and associates (*3*) reported that a single oral dose of chloromycetin would cure a high percentage of acute gonorrheal urethral infections. They suggested that chloromycetin might not have the effect of masking syphilitic infections and thus might be more desirable than penicillin for the treatment of gonorrhea.

Since the use of chloromycetin in the treatment of gonorrhea has been reported and since it seemed to have some antitreponemal activity in rabbit syphilis, we decided to study its effect upon the treponema of human syphilis.

Patients with lesions containing numerous *Treponema pallidum* were selected for this study. The first four cases received 120 mg/kg of chloromycetin per day. Two of these received an additional priming dose of 4 g. The next four patients received 60 mg/kg/day, and the remaining 24 received 30 mg/kg/day. Except in a few instances the antibiotic was administered orally in six equal doses at 4-hr intervals. Table 1 summarizes the treatment schedules and clinical and laboratory data of

TABLE 1

EFFECT OF CHLOROMYCETIN IN 25 CASES OF EARLY SYPHILIS IN MAN

No. of cases	Diagnosis	Chloromycetin mg/kg/day	Days treatment	Total dose in g	Dark-field negative in hr	Serologic titer				Remarks
						Before treatment	Months after treatment			
							1	2	3	
3	S*	120	6	56.0		1: 256	1: 4	NF‡	1:4	
	"			51.0	22–26	1: 128	1: 64	NF	NF	priming dose 4 g
	"			56.0		1: 128	2+	neg	NF	
3	S	60	6	44.5	23–24	1: 512	1: 64	1: 16	1:8	
	P†			18.0		neg	neg	neg	neg	
	"			27.0		neg	neg	neg	neg	
19	S	30	4, 6,	20.5		1:1024	1:128	1: 32	NF	
	"		or 8	10.5		1: 256	1: 64	NF	NF	
	"			18.5		1: 256	1: 16	NF	NF	
	"			10.5		1: 128	1: 32	1: 4	NF	pregnant
	"			16.0		1: 128	1: 64	NF	NF	
	"			12.0		1: 128	1: 16	1: 16	NF	
	"			12.0		1: 128	1:128	1:128	NF	
	"			12.0		1: 64	1: 32	1: 4	NF	
	"			12.0		1: 64	1: 16	1: 4	NF	
	"			12.0		1: 64	2+	neg	NF	
	P			27.5	22–28	3+	neg	NF	NF	12 g on 1st day
	"			12.0		neg	neg	neg	NF	
	"			22.0		neg	neg	neg	NF	15 g on 1st day
	"			22.0		neg	neg	neg	neg	12 g single dose on 1st day
	"			18.0		neg	neg	neg	neg	
	"			8.0		neg	NF	neg	NF	
	"			12.0		neg	neg	neg	NF	pregnant
	"			8.0		neg	neg	neg	neg	
	"			8.0		neg	neg	NF	NF	
25	(total)									

* Secondary syphilis.
† Primary syphilis.
‡ NF indicates no follow up.

[1] The chloromycetin (Chloramphenicol) used in this study was obtained through the courtesy of Parke, Davis & Company, Detroit, Michigan.

25 of the patients treated. Seven additional patients were treated but could not be followed up.

Treponema were not found in the lesions of the first four cases 22–26 hr after treatment was started. The treponemal disappearance time in the next four patients was 23 hr. Two cases given 30 mg/kg/day were negative in darkfield microscopic examination in 26 hr.

Since there was rapid disappearance of the treponemas from the local lesions on a relatively large dose it was decided to investigate the minimal effective dose of the antibiotic. A single oral dose of 250 mg was given to three cases, the lesions remained positive for treponema in darkfield examination even at 48 hr. Two cases were given 500 mg in a single oral dose; the lesions in one became negative in darkfield examination in 48 hr, and the other remained positive even at 96 hr. In these cases treatment was subsequently instituted on a 30 mg/kg/day schedule for 6 days with complete healing of the lesions.

In order to determine whether the treponemal disappearance time could be decreased, one case was given 2 g every 4 hr for six doses, a second case 2.5 g every 4 hr for six doses, and a third case 12 g as a single dose; the trepomenal disappearance time was 24, 26, and 24 hr, respectively. Apparently increasing the dose of chloromycetin does not appreciably shorten the treponemal disappearance time.

These findings suggested that an oral chloromycetin dosage of 30 mg/kg/day divided into six doses and given at 4-hr intervals might be effective in the treatment of early syphilis. Therefore, a total of 24 patients were treated with 30 mg/kg/day for 4, 6, or 8 days. The lesions in all cases showed evidence of initial healing within 24 hr and most of them showed complete healing by the end of therapy. Some delay in healing occurred in a few cases where the location of the lesion predisposed to a slower response. For example, a patient with a urethral chancre took 6 days to heal because of the constant flow of urine over the lesion.

Chloromycetin seems to us to promote healing by a different mechanism from penicillin. Penicillin produces initial healing at the periphery of a lesion, whereas healing with chloromycetin therapy seems to be initiated from the base of the lesion. This is particularly striking in the large ulcers of benign late syphilis of the skin.

Quantitative serologic tests using the Eagle Flocculation Test for syphilis were performed prior to therapy and at monthly intervals after treatment. It is noted in the table that there is a rapid decline in serologic titer in most cases at the end of one month following treatment.

Two of the patients who received 30 mg/kg/day were pregnant. The clinical and serological response until now has been satisfactory in both patients. One patient has delivered a live child. Although serologically positive at birth, clinical and serologic progress in this child have been excellent without further therapy. The second patient is still pregnant.

The only toxic or untoward reactions noticed with the dosages of chloromycetin utilized in this study were an occasional mild diarrhea and an occasional complaint of dryness of the mouth. The Jarisch-Herxheimer reaction in chloromycetin-treated patients is either less frequent than that observed in penicillin-treated cases or of such a mild nature that it is frequently missed. Only two patients were observed to have very mild reactions 48 hr after treatment was started. Several patients complained of a generalized aching sensation 48 hr after treatment began, but no fever or eruptions were noted. As these symptoms disappeared in 8–12 hr, despite further therapy, they may have been Jarisch-Herxheimer reactions.

Since relatively small doses of chloromycetin will cure acute gonorrhea, (*2, 3*) attention should be called to the possible danger of masking the diagnosis of syphilis.

Studies with the use of chloromycetin for the treatment of syphilis are continuing, and are being extended to include the late manifestations of syphilis. One patient with late syphilis manifested by extensive gummata of the leg is now under therapy with chloromycetin. This patient has had a dramatic healing response within 4 days after treatment was started.

References

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Effect of Pressure on Induction of Mutations by Nitrogen Mustard[1]

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An analysis of the mechanism of action of mutagenic agents depends, for the most part, upon indirect experimental methods (*1*). By studying changes in the mutation rate under varying experimental conditions, such as temperature and pH, it has been possible to obtain some idea as to the general stability of genes. Since nucleoproteins are apparently the most important components of the chromosome (*5*) (and presumably of the genes), it is likely that structural changes in these molecules underlie the basic alterations involved in gene mutation. Such structural changes might be of the order of magnitude observed by Johnson, Eyring, and collaborators in protein denaturation (*14*). Since pressure has been used successfully in the analysis of such equilibria or rate processes by these workers, it seemed to the authors that a similar study of the effect of pressure on the mutagenic action of the nitrogen mustards would aid materially in interpreting the results which have been obtained with these and similar agents. According to the general expressions which have been derived for a quantitative interpretation of the effect of pressure on biological processes (*8*), it should be possible to determine the magnitude of the volume change which occurs during the reaction that results in a gene mutation.

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