PRELIMINARY AND SHORT REPORTS

SERUM CONCENTRATION FOLLOWING THE ORAL ADMINISTRATION OF CRYSTALLINE PROCAINE PENICILLIN G*

(Further Studies)

D. K. Kitchen, M.D., E. W. Thomas, M.D., and C. R. Rein, M.D.

In a previous publication (1), we described the serum penicillin concentration following the oral administration of crystalline procaine penicillin G in compressed tablet form. In addition, data were presented following the ingestion of crystalline sodium penicillin G in a similar unitage tablet. There was a marked difference in the serum concentration produced and maintained by the two penicillin salts. In that study, crystalline procaine penicillin G when administered in a single tablet containing 0.55 million units, produced a serum concentration at the first hour of approximately 0.06 units per cubic centimeter, rising to a height of approximately 0.08 units per cubic centimeter and thereafter falling gradually to 0.03 cubic centimeters on the average at about the sixth hour. The curve from the former report reappears herein as Curve B on Chart I and was compiled from data of a study of eleven patients. The tablets of crystalline procaine penicillin G in that experiment contained no binder and were *highly* compressed for fear of disintegration.

Subsequent experiments performed on 23 patients under the same conditions with crystalline procaine penicillin G tablets containing a binder and lightly compressed have revealed a striking difference in the serum concentration of penicillin produced to that originally reported. This appears as Curve A Chart I, which displays an average one-hour concentration of 1.6 units per cubic centimeter. This declined to 0.027 units per cubic centimeter on the average at about the eighth hour. This is comparable to our previous experiences (1) with crystalline sodium penicillin G when given in a similar amount, and under identical conditions. This reappears in Chart I as Curve C.

It is obvious that these differences were due to the degree of compression of the tablet of this penicillin salt and that the tablets utilized in the initial study were compressed to a point prohibiting proper disintegration producing subsequent faulty utilization.

Table I is self-explanatory and presents numerical data of the investigation. All tablets were administered in the morning one hour before the first meal of the day. Blood samples were drawn from each patient before the administration of the tablet (indicated by 0) and at the indicated intervals under "Hours". During the first hour after ingestion, no food or water were taken by the patient. Following this no restrictions were placed on water, food, or drug administration, other than antibiotics. All assays were performed by a cup-plate procedure utilizing Sarcina lutea as the test organism.

SUMMARY

Data are presented on the serum penicillin concentration produced by the oral administration of tablets of crystalline procaine penicillin G. These data differ widely from those obtained originally under the same conditions but with the exception that a tablet of *much*

* From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman) and the service of Dermatology and Syphilology of Bellevue Hospital (Dr. F. C. Combes, Chief of Service).

Bristol Laboratories, Inc., New York, N. Y., furnished the procaine penicillin tablets.

Mr. W. E. Crutchfield, Jr. Bristol Laboratories, made the statistical analyses of these data.

Received for publication December 15, 1949.

CHART I

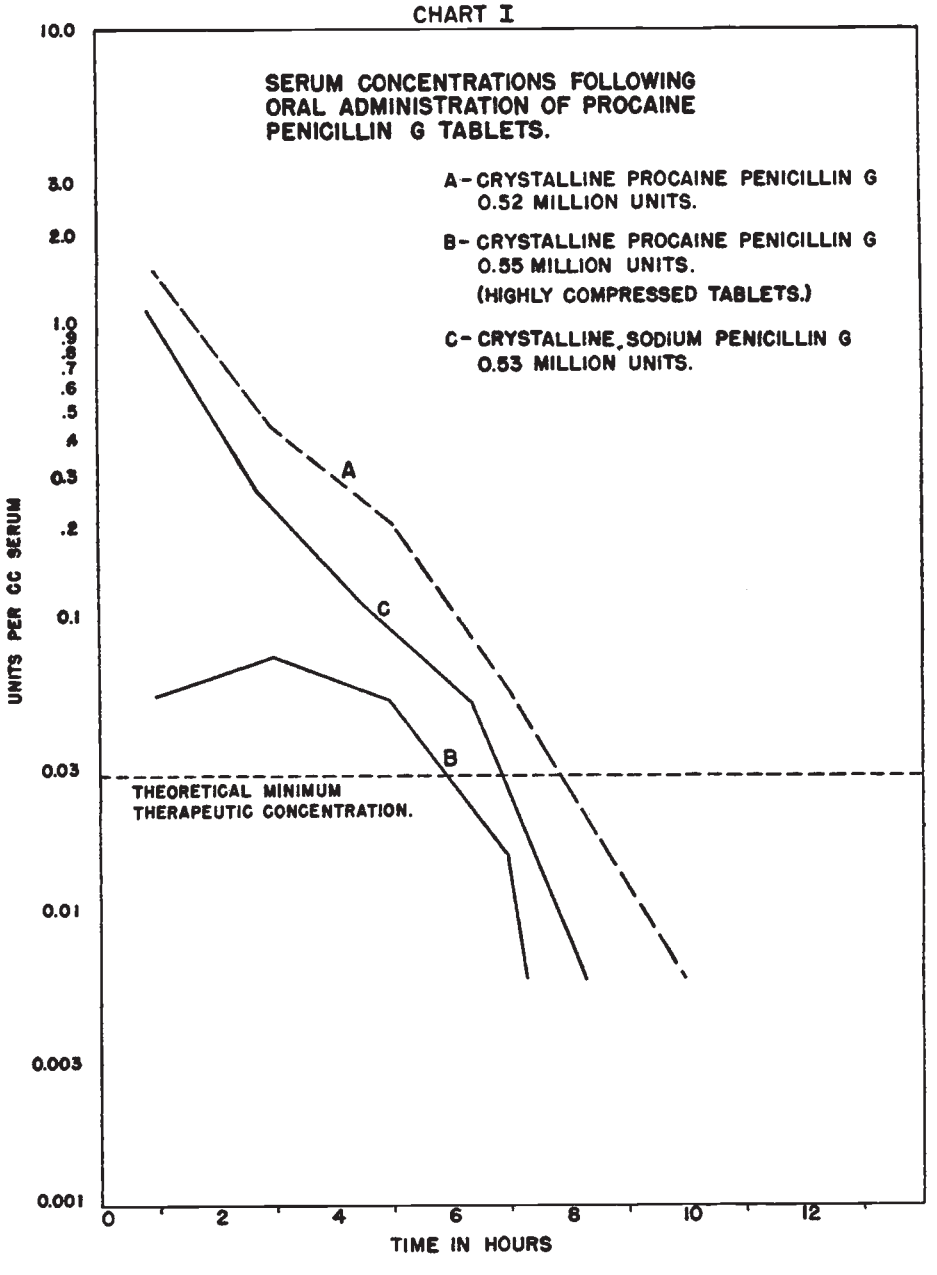
SERUM CONCENTRATIONS FOLLOWING ORAL ADMINISTRATION OF PROCAINE PENICILLIN G TABLETS.
A - CRYSTALLINE PROCAINE PENICILLIN G 0.52 MILLION UNITS.
B - CRYSTALLINE PROCAINE PENICILLIN G 0.55 MILLION UNITS. (HIGHLY COMPRESSED TABLETS.)
C - CRYSTALLINE SODIUM PENICILLIN G 0.53 MILLION UNITS.
UNITS PER CC SERUM
10.0
3.0
2.0
1.0
.9
.8
.7
.6
.5
.4
0.3
.2
0.1
0.03
0.01
0.003
0.001
A
B
C
THEORETICAL MINIMUM THERAPEUTIC CONCENTRATION.
0
2
4
6
8
10
12
TIME IN HOURS

TABLE I

HOURS	NO. OF PTS.	AVER. SERUM CONCEN.	% ABOVE 0.03 UNITS PER CC
0	23	0	0
1	23	1.60	100
3	23	.453	100
5	12	.220	100
7	23	.058	82.7
8	8	.027	62.6
10	23	.006	13.0

higher compression was used in the original study. Differences in these observations are attributable to the degree of compression of the tablet; the highly compressed tablets utilized in the original investigation in all probability did not disintegrate properly following their ingestion.

REFERENCE

1. KITCHEN, D. K., THOMAS, E. W., AND REIN, C. R.: Serum Concentration Following the Oral Administration of Crystalline Procaine Penicillin G and Crystalline Sodium Penicillin G, J. Invest. Dermat. **12:** 147–149, Mar. 1949.