

by the foregoing method, reserving a sample of each of the salts used.

Cocaine 0.6% solution } based on Experiments Nos. 1 and 2.<sup>1</sup>  
Procaine 7.0% solution }

*Second.*—Divide each solution into four portions, fill each portion into ampuls as follows:

- (A) Fill into sterile ampuls without sterilizing or Berkfeldting.
- (B) Add 0.3% Three Cresols, Berkfeldt and fill into sterile ampuls.
- (C) Fill into ampuls and Arnold-sterilize on three consecutive days.
- (D) Fill into ampuls and autoclave for 15 min. at 115° C.

*Third.*—Test each lot to determine effect of sterilization.

*Fourth.*—Test each lot every three months to determine rate of deterioration on storage.

*Fifth.*—At the end of six months make fresh solutions of the reserve salts and determine whether or not the salt deteriorates with age.

The results of the 18 experiments reported last year showed that the amount of solution of cocaine or procaine required to produce complete anaesthesia was exactly the same before and after the different forms of sterilization, thus indicating that *sterilization does not affect the activity of solutions of cocaine or procaine*.

It was also shown that the unsterilized solutions, the solutions sterilized with heat, and the solutions sterilized without heat, all possessed exactly the same activity after 3 months as immediately after being prepared.

Each lot of solution has again been tested 14 months after filling and sterilization. The results of this final test on each lot as compared with the two previous tests are as follows:

Experiments Nos. 3, 4 and 19.

COCAINE SOLUTION 0.6%.

Filled into sterile ampuls without sterilizing or Berkfeldting.

Results.

Dose.	Expt. No. 3. Immediately after filling.	Expt. No. 4. 3 mos. after filling.	Expt. No. 19. 14 mos. after filling.
0.7	Sensitive	Sensitive	Sensitive
0.8	Sensitive	Sensitive	Sensitive
0.9	Sensitive	Very slightly sensitive	Sensitive
0.9	Not sensitive	Not sensitive	Sensitive
1.0	*Not sensitive	*Not sensitive	Sensitive
1.0	*Not sensitive	*Not sensitive	Sensitive
1.1	Not sensitive	Not sensitive	*Not sensitive

<sup>1</sup> "The Biologic Standardization of Local Anaesthetics," JOUR. A. PH. A., Vol. X, October 1921.

Minimum amount required to produce complete local anaesthesia for Experiments Nos. 5, 6 and 20.

Experiments Nos. 7, 8 and 21.

COCAINE SOLUTION 0.6%.

0.3% Three Cresols, Berkefeldted and filled into sterile ampuls.

Results.

Dose.	Expt. No. 7. Immediately after filling.	Expt. No. 8. 3 mos. after filling.	Expt. No. 21. 14 mos. after filling.
0.8	Sensitive	Sensitive	Sensitive
0.9	Very slightly sensitive	Sensitive	Sensitive
0.9	Sensitive	Slightly sensitive	Sensitive
1.0	*Not sensitive	*Not sensitive	Sensitive
1.0	*Not sensitive	*Not sensitive	Slightly sensitive
1.1	Not sensitive	Not sensitive	*Not sensitive

Minimum amount required to produce complete local anaesthesia for both Experiments Nos. 7 and 8, and 1.1 cc for Experiment No. 21.

Experiments Nos. 9, 10 and 22.

PROCAINE SOLUTION 7%.

0.3% Three Cresols, Berkefeldted and filled into sterile ampuls.

Results.

Dose.	Expt. No. 9. Immediately after filling.	Expt. No. 10. 3 mos. after filling.	Expt. No. 22. 14 mos. after filling.
0.8	Sensitive	Sensitive	Sensitive
0.9	Sensitive	Sensitive	Sensitive
0.9	Sensitive	Sensitive	Sensitive
*1.0	Not sensitive	Not sensitive	Not sensitive
*1.0	Not sensitive	Not sensitive	Not sensitive
1.1	Not sensitive	Not sensitive	Not sensitive

Minimum amount required to produce complete local anaesthesia for Experiments Nos. 9, 10 and 22.

Experiments Nos. 11, 12 and 23.

COCAINE SOLUTION 0.6%.

Filled into ampuls and Arnold-sterilized on 3 consecutive days.

Results.

Dose.	Expt. No. 11. Immediately after filling.	Expt. No. 12. 3 mos. after filling.	Expt. No. 23. 14 mos. after filling.
0.8	Sensitive	Sensitive	Sensitive
0.9	Sensitive	Sensitive	Sensitive

Dose.	Immediately after sterilizing.	3 mos. after sterilizing.	14 mos. after sterilizing.
0.8	Sensitive	Sensitive	Sensitive
0.9	Sensitive	Sensitive	Sensitive
0.9	Sensitive	Sensitive	Sensitive
*1.0	Not sensitive	Not sensitive	Not sensitive
*1.0	Not sensitive	Not sensitive	Slightly sensitive
1.0	....	....	Not sensitive
1.1	Not sensitive	Not sensitive	Not sensitive

Minimum amount required to produce complete local anaesthesia is 1 for Experiments Nos. 13, 14 and 24.

Experiments Nos. 15, 16 and 25.

**COCAINE SOLUTION 0.6%.**

Filled into ampuls and autoclaved for 15 min. at 115° C.

Dose.	Results.		
	Expt. No. 15. Immediately after sterilizing.	Expt. No. 16. 3 mos. after sterilizing.	Expt. No. 25. 14 mos. after sterilizing.
0.8	Sensitive	Sensitive	Sensitive
0.9	Slightly sensitive	Sensitive	Sensitive
0.9	Not sensitive	Sensitive	Sensitive
*1.0	Not sensitive	Not sensitive	Not sensitive
*1.0	Not sensitive	Not sensitive	Not sensitive
1.1	Not sensitive	Not sensitive	Not sensitive

Minimum amount required to produce complete local anaesthesia is 1 for Experiments Nos. 15, 16 and 25.

Experiments Nos. 17, 18 and 26.

**PROCAINE SOLUTION 7%.**

Filled into ampuls, autoclaved for 15 min. at 115° C.

Dose.	Results.		
	Expt. No. 17. Immediately after sterilizing.	Expt. No. 18. 3 mos. after sterilizing.	Expt. No. 26. 14 mos. after sterilizing.
0.8	Sensitive	Sensitive	Sensitive
0.9	Slightly sensitive	Slightly sensitive	Sensitive
0.9	Sensitive	Sensitive	Sensitive
*1.0	Not sensitive	Not sensitive	Not sensitive
*1.0	Not sensitive	Not sensitive	Not sensitive
1.1	Not sensitive	Not sensitive	Not sensitive

Minimum amount required to produce complete local anaesthesia is 1 for Experiments Nos. 17, 18 and 26.

*1.0	Not sensitive	Not sensitive
*1.0	Not sensitive	Not sensitive
1.1	Not sensitive	Not sensitive

Minimum amount required to produce complete local anaesthesia is for both Experiments Nos. 3 and 27, showing that no deterioration takes cocaine during a period of 14 months.

Experiment No. 28.

PROCAINE SOLUTION 7%.

Made from reserve salt 14 months after solution tested under Experiment No.

Results.

Dose.	Expt. No. 5.	Expt. No. 28.
0.8	Sensitive	Sensitive
0.9	Slightly sensitive	Slightly sensitive
0.9	Slightly sensitive	Slightly sensitive
*1.0	Not sensitive	Not sensitive
*1.0	Not sensitive	Not sensitive
1.1	Not sensitive	Not sensitive

Minimum amount required to produce complete local anaesthesia is both Experiments Nos. 5 and 28 showing that no deterioration takes place cocaine during a period of 14 months.

EFFECTS OF REPEATED STERILIZATION.

In the discussion of last year's paper it was stated that in some operations surgeons use solutions of cocaine as high as 20% in strength and that owing to the general opinion that resterilization destroyed its activity, in most hospitals unused portions of such solutions were discarded.

Therefore, in order to determine the effects of resterilization upon the activity of solutions of cocaine and procaine, I prepared a 20% solution of cocaine and a 20% solution of procaine, and filled each into ampuls. One ampul of each lot was tested to the proper strength and tested on dogs. The remaining ampuls were then autoclaved at 115° C. for 15 minutes. Another ampul of each lot was then tested to the proper strength and tested. The remaining ampuls were again autoclaved at 115° C. for 15 minutes and another ampul tested. This procedure was repeated until each lot was sterilized and tested five times.

The results of these experiments follow:

After 3rd sterilization	1.0 cc (7.0%)	Clear, amber
After 4th sterilization	1.0 cc (7.0%)	Clear, amber
After 5th sterilization	1.0 cc (7.0%)	Clear, amber

These results show that five successive sterilizations produced no apparent effect upon the activity of the above solutions of cocaine and procaine.

It will also be noted that sterilization at 115° C. changes the procaine solution from colorless to an amber color, and that this change is not accompanied by change in activity.

#### CONCLUSION.

The activity of local anaesthetics can be quantitatively determined by the method proposed.

The activity of solutions of cocaine and procaine is not affected by the addition of 0.3% Three Cresols or by sterilization by means of the Arnold sterilizer or autoclave at 115° C. for 15 minutes.

Unsterilized solutions of cocaine and procaine, solutions sterilized without heat and solutions sterilized with heat apparently lose no activity during a period of 3 months.

Unsterilized solutions of cocaine and solutions of cocaine sterilized with heat apparently lose about 10% of their activity during a period of 14 months.

Solutions of cocaine which have been Arnold-sterilized apparently lose about 5% of their activity during a period of 14 months.

Solutions of cocaine which have been autoclaved for 15 minutes at 115° C. apparently lose no activity during a period of 14 months.

Unsterilized solutions of procaine, solutions sterilized without heat and solutions sterilized with heat, lose no activity during a period of 14 months.

Cocaine and procaine in the dry form are apparently stable and show no loss of activity during 14 months.

Concentrated solutions of cocaine or procaine can be sterilized five successive times at 115° C. without any apparent loss of activity.

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