

**Title:** LONG TERM STERILITY OF DILUTED OR PRE-DRAWN SOLUTIONS OF SUCCINYLCHOLINE, EPHEDRINE, THIOPENTAL AND CURARE

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**Introduction.** Although it takes only 2 to 3 minutes to mix Pentothal Ready-to-Mix and draw up curare and succinylcholine, during a stat cesarean section, the anesthesiologist may not have the time to prepare these drugs and take care of the patient as well. Because of this, it is common practice to prepare for these cases by pre-mixing and pre-drawing these emergency drugs. In our Labor and Delivery Suite, most procedures are performed under regional anesthesia. For instance, in 1985, out of 2439 anesthetics, only 282 were performed under general anesthesia, while 1946 were carried out under epidural and 213 under spinal anesthesia. This means that, on the average, we have none or one general anesthetic a day. The cost of preparing and replacing pentothal, succinylcholine, curare, ephedrine and Anectine drip daily is approximately \$16,000 a year. If these drugs are replaced every 48 hours instead of every 24 hours, we can save an average of \$8000 a year.

Concern for the safety of this practice led to a literature search and correspondence with the drug manufacturers regarding stability and sterility studies on these drugs. Stability studies seem to be adequate (1) and show that these drugs remain stable for a week to a month. However, to the best of our knowledge, sterility studies on these drugs when drawn up in syringes or diluted in normal saline have not been adequately done (2). The purpose of this study was to determine if these drugs remain sterile if drawn up or pre-mixed for periods of 48 hours to one week.

**Methods. Part I:** Bags of succinylcholine 0.1% solution were prepared in the usual fashion by adding Anectine Flo-Pack<sup>R</sup>, 500 mg powder, to 500 mls of 0.9% Sodium Chloride IV solution and connected to a Venoset<sup>R</sup> and an 18G needle. The solution was labeled with date and time. The study bag was used on patients in the usual fashion. Just before replacing the IV tubing and needle between patients, one ml of solution was inoculated in Tryptic soy broth tube and incubated at 35°C for 48 hours. The study bag was used until its contents were consumed or until it was replaced at 48 hours. Another bag which was not used on patients served as control. Both study and control bags were inoculated at 48 hours. In addition, the control bag was cultured at the end of one week.

**Part II:** Ephedrine solutions were prepared by adding 9 mls of sterile, preservative-free saline to one ampule of ephedrine (Invenex<sup>R</sup>) to make a 5 mg/ml solution. The study syringe was used to treat hypotension in the usual fashion, sampled and inoculated between cases and at 48 hours. Control syringes were sampled at 48 hours. All samples were inoculated in Tryptic soy broth as above.

**Part III:** Pentothal Ready-To-Mix, 250 mg (Abbott), was pre-mixed and inoculated as above at the end of one week. Succinylcholine (Quelicin<sup>R</sup>), 20 mg/ml, and curare (Tubocurarine<sup>R</sup>), 3 mg/ml, were

drawn up in 6 and 3 ml syringes, respectively, and sampled at the end of one week.

**Part IV:** To verify the capability of the Tryptic Soy Broth to sustain bacterial growth despite the possible dilution effect of the added drug (1 ml of drug in 4 ml of broth),  $1 \times 10^3$  and  $1 \times 10^6$  colony forming units/ml of Escherichia coli ATCC 25922, Staphylococcus aureus ATCC 25923 and Bacillus subtilis ATCC 6633 were inoculated into tubes of the broth containing 1 ml of drug.

**Results.** Sterility checks (positive for growth = cloudy solution, negative for growth = clear solution) were made at 48 hrs and 1 week according to the study design. As seen in Table 1, the 16 samples from the succinylcholine drip study (Part I), 34 samples from the ephedrine study (Part II), 10 samples from pentothal, curare and succinylcholine syringes (Part III) were all negative (clear solutions).

	Part I		Part II		Thio-	Part III	
	Drip		Ephedrine		pental	Curare	Suc.
48 hrs	(C)	(S)	(C)	(S)	(C)	(C)	(C)
Neg.	7	9	13	21	--	--	--
Pos.	0	0	0	0	--	--	--
1 Week							
Neg.	4	--	--	--	10	10	10
Pos.	0	--	--	--	0	0	0

(C)=Control; (S)=Study.

Following incubation at 35°C for 24 hours, heavy growth was noted in all tubes inoculated with known organisms at the two inoculum densities for each drug/organism combination (Part IV).

**Discussion.** Review of the literature and correspondence with the manufacturers of Anectine Flo-Pack<sup>R</sup>, Quelicin<sup>R</sup>, Ephedrine Sulfate<sup>R</sup>, Tubocurarine Chloride<sup>R</sup> and Pentothal Ready-To-Mix<sup>R</sup> show that these drugs remain stable for prolonged periods of weeks to months (1), definitely within the 48 hour period that we have adopted as the time limit for replacing these drugs.

There are essentially four time periods when drug contamination can occur, namely, (a) drug manufacture and packaging; (b) drawing, mixing and dilution; (c) storage at room temperature; and (d) administration to patient. If the drug has been contaminated during (a) and (b), then storage at room temperature may increase the bacterial colony count to dangerous levels that can produce a significant clinical infection. However, unless such contamination has taken place, this study shows that these drugs remain sterile for periods of 48 hours to one week.

#### References

1. Kirschenbaum BE, Latiolais CJ: Am J Hosp Pharm 33:767-791, 1976.
2. Parker EA: Am J Hosp Pharm 26:653, 1969.