

blue was injected into the injured and normal forelimbs as described above. Two to 3 hours later the dye was seen to have penetrated to the regional lymphatics on the inflamed side as readily as under normal circumstances. The results reported in this communication are in agreement with previous observations and indicate that fixation at the site of a sterile inflammation induced by hot water is due to mechanical obstruction in the form of a fibrinous network, *i. e.*, coagulated plasma, and in part to the presence of a number of lymphatics that are occluded by fibrinous thrombi.

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**Configuration and Anesthetic Activity of Aromatic Alcohols.\***

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In general, local anesthetics are deficient in duration of action rather than potency. A striking demonstration of prolongation of effect as a result of a small change in structure of a drug-compound has recently been afforded. It is definitely established in the sympathomimetic amines that the transformation of the side chain so that the carbon bearing the nitrogen becomes a secondary carbon atom results in prolongation of effect.<sup>1</sup> To test the validity of this principle in another field, we are now studying for local anesthetic activity some derivatives of ephedrine in which the same peculiarity of structure exists. Of other series, procaine type compounds do not readily lend themselves for this study because of the difficulty of preparing the desired amino-alcohols. However, the aromatic alcohols with pertinent structure are easily obtained. Some of these have been studied before; in fact it has been stated,<sup>2</sup> on rather invalid evidence, that the change from primary to secondary to tertiary alcohol reduces the activity.

Anesthesia of the rabbit cornea and the frog sciatic nerve has been determined for a series of primary, secondary, and tertiary alcohols,

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<sup>1</sup> Alles, G. A., *J. Pharmacol. Exp. Therap.*, 1933, **47**, 339.

<sup>2</sup> Hirschfelder, A. D., and Bieter, R. N., *Physiol. Rev.*, 1932, **12**, 190.

TABLE I.  
 Anesthetic Effects of Certain Aromatic Alcohols.

Compound and Formula	Boiling Point °C/10 mm.	Duration Anes- thesia Rabbit Cornea with Saturated Sol. < 0.1M	Onset of Anesthe- sia Frog Sciatic Nerve with Con- centration:	
			0.05 M	0.04 M
Phenyl carbinol: $\text{C}_6\text{H}_5\text{CH}_2\text{OH}$	92	min. 2*	min. 14	min. 24
Methyl phenyl carbinol: $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{OH}$	93-4	4*	7	10
Ethyl phenyl carbinol: $\text{C}_6\text{H}_5\text{CH}(\text{C}_2\text{H}_5)\text{OH}$	102-4	10	5	6
Dimethyl phenyl carbinol: $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)_2\text{OH}$	89-91	8	9	10
Benzyl carbinol: $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OH}$	100	5	7	10
Methyl benzyl carbinol: $\text{C}_6\text{H}_5\text{CH}_2\text{CH}(\text{CH}_3)\text{OH}$	99-100	10		8
Dimethyl benzyl carbinol: $\text{C}_6\text{H}_5\text{CH}_2\text{C}(\text{CH}_3)_2\text{OH}$	96	2		16
Phenyl ethyl carbinol: $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$	117-8	5		11
Phenyl vinyl carbinol: $\text{C}_6\text{H}_5\text{CH}=\text{CHCH}_2\text{OH}$	134	2		13

\* 0.1 Molar.

all of which were redistilled before use. The results from local application of aqueous solutions at the concentrations noted are seen in the table in which the figures indicate average duration of anesthesia in minutes for the cornea in 3 different rabbits for each drug, and average time in minutes for the production of sensory block of the sciatic nerve in at least 4 different frogs in each instance. Tests were made at minute intervals and the respective findings usually agreed within 2 minutes. The data indicate the relative merits of the compounds both with regard to duration of anesthesia and speed with which it may be induced.

It appears that increase in the length of the straight carbon chain and/or the transformation to secondary and tertiary alcohol may increase the activity. The presence of unsaturation seems undesirable. The expectation is fulfilled that the secondary alcohols are more active than the primary.