ANESTHESIA

XXXIV. Chemical Constitution of Hydrocarbons and Cardiac Automaticity[1]

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In a former communication (1) the authors demonstrated that eleven cyclic and acyclic hydrocarbons, when inhaled, sensitized the dog's myocardium to epinephrine. On the other hand, in twelve animals ethylene failed to produce sensitization under varying experimental conditions. Thus it appears that ethylene is unique, in this regard, among the hydrocarbons studied by us and also by Chenoweth (2).

It is known that the aliphatic ethers as a class of anesthetic agents do not produce this type of myocardial sensitization. However, the unsaturated hydrocarbon, ethylene, appears to behave in this respect similar to the aliphatic ethers and dissimilar to the hydrocarbons. It is the purpose of this investigation to pursue further the relationship between chemical constitution and myocardial sensitization to epinephrine.

Compounds studied. Consideration was given first to inner oxides of hydrocarbons; such molecules as ethylene oxide and propylene oxide have structural properties common to the hydrocarbons and the ethers. Certain rare cyclic hydrocarbons, such as methyl cyclobutane, were included. Spiropentane, owing to its relationship to cyclopropane, was studied. In addition, acetylene was tested to determine whether or not it behaved like its more saturated analog, ethylene.

Experimental procedure. Electrocardiograms, Lead II, were recorded from the unanesthetized dogs. Epinephrine hydrochloride solution, 1:100,000 (preserved with sodium bisulfite), was injected intravenously, 0.01 mgm./kgm. The injection was made during a period of 25 to 40 seconds. At the end of the injection (usually the beginning of the effect) another tracing was made.

Subsequently each animal was permitted to breathe a mixture of the hydrocarbon in varying concentrations mixed with oxygen. With the liquid hydrocarbons the concentrations were between 10 and 25 per cent. With the gaseous compounds concentrations from 15 to 90 per cent were used. The closed circuit procedure was employed. When the inhalation had continued for from 10 to 20 minutes the foregoing experimental procedures were again carried out.

Results. The various compounds studied and the results observed are shown in table 1.

Discussion of results. In the dog, prior to the inhalation of the compound,

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epinephrine produced slowing of the cardiac rate, accentuation of the T-wav
and an occasional inversion of the QRS-complex. Under the influence of th
hydrocarbons producing sensitization, however, multifocal ventricular ectop
tachycardia occurred in nearly all experiments. In some animals this passed in
ventricular fibrillation and caused death.

From the data in table 1 it will be observed that acetylene was incapable o
producing sensitization similar to that produced by saturated hydrocarbons (2).
In these dogs, exposure to acetylene[3] was more comparable to exposure to ethyl
ene that to other hydrocarbons. In four of the twelve animals some sensitizatio
occurred, as evidenced by only a tachycardia with occasional arrhythmia an
not ventricular fibrillation. Three of the twelve dogs exposed to acetylene wer
exposed to cyclopropane on subsequent days. Not any of the three animal
showed arrhythmias with epinephrine under acetylene; all three showed mult
focal ventricular ectopic tachycardia with epinephrine under cyclopropane.

TABLE 1

NAME OF COMPOUND	NUMBER ANIMALS IN WHICH SENSITIZATION OF MYOCARDIUM OCCURRED AND NUMBER USED
Acetylene	4/12
Ethylene (cat)	0/8
Ethylene Oxide	0/2
Propylene Oxide	0/2
Spiropentane	2/4
Vinyl Chloride	3/7
Ethyl Chloride	5/6
Isopropenyl Chloride	1/3
Methyl Cyclobutane	2/2

It appears that among the hydrocarbons, unsaturation reduces the incidence
of myocardial sensitization. Thus exposure to ethylene (1) in our experience di
not sensitize the dog's myocardium to epinephrine. Nevertheless the introduc
tion of a methyl group into the molecule with the formation of propylene, pro
duced marked cardiac sensitization when inhaled. Similarly, acetylene produced
only mild cardiac sensitization in certain animals with epinephrine. In three ani
mals the inhalation of methyl acetylene produced marked arrhythmias and some
fibrillation without the injection of epinephrine. By examination of the data in
table 1 it is observed further that sensitization with ethyl chloride was produced
more often than with vinyl chloride in the eight animals studied.

Garb and Chenoweth (3) conducted their studies on the papillary muscles of
the cat's heart. We considered it of interest to study the cat's heart under ethyl
ene anesthesia in order to include another species. Accordingly, we anesthetized
eight cats (eleven experiments) with ethylene-oxygen mixtures and subjected
them to the experiment. Like the dog, they did not show sensitization.

[3] "Airco" acetylene was purified by washing with water, concentrated sulfuric acid and
20 per cent sodium hydroxide solution, respectively.

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Carb and Chenoweth (3) have suggested the hypothesis that different concentrations of the hydrocarbon reduce myocardial irritability in various portions of the ventricles. This gives rise to small temporary blocks in the presence of certain sympathomimetic amines. Our findings indicate that the changes in myocardial irritability are much less marked with unsaturated hydrocarbons than with saturated compounds. Indeed we have failed to produce the classical effects of sensitization in any of twelve dogs or eight cats with ethylene. However, with acetylene, sensitization of a minor degree was produced in four of twelve dogs when this hydrocarbon was inhaled.

It appears therefore that sensitization of the myocardium is disfavored by double and triple bonds between the carbon atoms in the inhaled hydrocarbon. However, failure to sensitize seems to be a matter of degree and not the absolute absence of some incipient effect. We have not been able to correlate these observations with various differences in the physical properties of saturated and unsaturated hydrocarbons. Nevertheless a distinct diminution in the degree of myocardial sensitization does appear to be associated with the presence of unsaturation in the molecule.

CONCLUSIONS

1. The capacity of acetylene to sensitize the dog's myocardium to epinephrine appears to be intermediate between ethylene and saturated hydrocarbons.
2. Ethylene failed to sensitize the heart of the cat to epinephrine.
3. It appears that vinyl chloride produces sensitization of the myocardium less frequently than does its saturated analog, ethyl chloride.

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