16. When rats weighing more than this standard are employed reduce the results to the 140-Gm. standard by the use of the formula,

$$\text{Rat Units per cc.} = \frac{W}{140\,Q}$$

in which W is the weight of the rat in Gm. and Q is the volume in cc. of the minimum dosage required to cause *typical oestrus* in 2 out of 3 rats given the same dosage.

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THE STABILITY OF ANÆSTHETIC ETHER.*

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The causes responsible for the development of traces of peroxide in anæsthetic or U. S. P. ether have long been the subject of scientific research. Of recent years, added stimulus has been given to this work by reports appearing in the medical press indicating that respiratory and nervous complications observed in certain cases after ether anæsthesia occurred simultaneously with the presence of peroxides in ether. While it is manifestly difficult to demonstrate by clinical experiment or physiological test that the trace of peroxides often present in ordinary anæsthetic ether is responsible for the adverse reactions reported, the evidence is such as to make freedom from peroxides in anæsthetic ether a highly desirable condition.

During the last five years, a number of articles have appeared in the scientific press discussing methods of measuring the quantity of peroxides present and suggesting means for their removal as well as giving methods for treating ether to prevent their formation. None of these methods, however, have proved of value in eliminating peroxides or even controlling their formation. The problem of isolating ether peroxides is not simple, because of their highly explosive character in pure form, hence their constitution is not fully determined at present. While an explanation of the causes and nature of the reactions involved in peroxide formation is yet to be formulated, intensive work has revealed that peroxides form in pure anæsthetic ether more readily than was formerly believed. In fact, peroxides can be shown to develop in practically 100% of all containers of anæsthetic ether

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if the ordinary container is used and contents are examined at sufficiently frequent intervals. They do, however, disappear again in time, so that in very old ether they are likely to be absent. Aldehydes may appear while the peroxides are disappearing, but these, too, ultimately vanish, leaving a trace of an organic acid as the end-product of the reaction. The time required for the development of foreign substances and their subsequent change into acids is rather variable. In general, however, most anæsthetic ether will form peroxides within six months after manufacture and in all probability they will remain in the ether for one or more years before disappearing. One often finds wide variations in examining containers of ether from the same lot, indicating that the container has considerable influence on changes occurring in ether during storage. The conditions of storage and the degree of freedom from mechanical impurities, such as dirt, flux, etc., also have similar influence. Exposure to light and heat stimulates peroxide formation, while storage in the dark and in the cold retards it. In general, impure or contaminated ether will develop peroxides less readily than clean ether of high quality. So far as we know all ether suitable for anæsthetic purposes will develop peroxides when stored in the regular tin or glass containers, which, in the past, have been in commercial use.

Exhaustive studies on the stability of ether with special reference to the effect of the container and what might be termed the effect of catalysts and anticatalysts on the reaction responsible for deterioration of ether, lead to the discovery that the presence of copper prevented peroxide formation. Early experiments, in which ether was stored, respectively, in contact with strips of copper, copper alloys, tarnished, oxidized and green copper, in amber bottles showed it to remain peroxide free while the control samples developed peroxides as indicated by the U. S. P. test. These results were confirmed by more carefully controlled experiments in which ether in contact with copper and copper compounds was compared with ether stored in contact with pure tin and tin plate. Again the samples containing copper continually tested free from peroxides until the ether was exhausted, over two years later. The controls and containers containing tin plate showed traces of peroxides simultaneously on four months' storage, while those containing pure tin developed peroxides within eight months.

Since ether is marketed in tin containers, the work was repeated, using tins instead of bottles as containers. Copper was introduced into the tin containers so as to expose varying amounts of copper surface. Such cans were kept under observation and were also subjected to a heat at 54° C. in order to hasten peroxide development. The results proved conclusively that copper exerted a marked inhibiting action on the formation of peroxides, the action being greatest in those containers having the largest amount of copper surface exposed.

In general, ether in glass or tins usually showed traces of peroxides in from one to eight months, most containers giving a positive test in four months. The same containers of ether, when exposed to heat and pressure, developed peroxides in one hour. With an adequate surface of copper, or copper compound, exposed to the ether, no peroxides developed under storage of several years, and under heat and pressure treatment continued over sixty hours.

Ether containing peroxides was placed in copper containers and kept under observation by periodic tests. It was found that apparently peroxides do not

disappear from ether any more rapidly when stored in such containers than when stored in ordinary tins or glass, indicating that copper prevents peroxide formation rather than removing it after it has formed. Complete chemical and physical examination at monthly intervals on hundreds of cans of ether stored in copper-plated and other containers has shown that only storage in the presence of copper will keep ether, unchanged in every particular, over long periods and under temperature variations such as one must expect to encounter under ordinary conditions of commerce.

In conclusion, we can make the following generalizations:

1. U. S. P. or anæsthetic ether is free from peroxides when first prepared, but changes occur therein on storage in the usual containers, one of which is the development and later disappearance of peroxides.

2. These changes occur in 100% of the containers, if ether meeting U. S. P. specifications is stored in any of the ordinary containers, which in the past have been in commercial use, such as tins or glass bottles.

3. The formation of peroxides can be prevented by packaging ether in containers, the interior of which presents an adequate surface of copper or copper compound.

4. Contact with an adequate surface of copper in some form, preserves anæsthetic ether in its original pure condition.

5. Metallic copper does not remove peroxides from ether.

While our studies to date have not lead to a complete understanding of the reactions which underlie peroxide formation and their subsequent disappearance, there is a good deal of satisfaction to be derived from the knowledge that the marketing of ether in copper or copper-plated containers eliminates, so far as we know to-day, a difficulty that has been universally encountered by ether manufacturers. This discovery gives the anæsthetist the opportunity of obtaining anæsthetic ether which he may be reasonably sure to be peroxide free regardless of how long or short a time it may have been kept in stock, or under what conditions it may have been stored.

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CAUSTIC SODA FOUND TO STRENGTHEN WOOD INTENDED FOR GLUING.

The pharmacist is called upon for information relative to a great many things and, therefore, mention is made of the investigation by the Forest Products Laboratory of the Department of Agriculture where it has been found by experimentation that a 10% solution of caustic soda (applied to joints of wood that are to be glued and allowed to dry for a period of ten or fifteen minutes prior to applying the glue) will strengthen the joints. The laboratory concludes its statement with the remark that this procedure is to be recommended only where equally good results are unobtainable with standard gluing practices.