# THE EFFECT OF DIFFERENT ETHERS ON THE BLOOD-SUGAR LEVEL.

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With 2 Figures in the text.

(Received for publication 20th April 1948.)

In a previous publication (HAJDU, M. BEZNÁK, RÁDY, 1947) we described experiments dealing with the mechanism of the hyperglycaemia which follows coronary ligature in cats anaesthetised with ether. We showed that this hyperglycaemia did not take place if we denervated the heart previous to coronary ligature, thus proving that the stimuli which result in blood sugar elevation reach the centrum via nervous channels. In control experiments we found no hyperglycaemia in ether anaesthesia lasting 6—8 hours, a finding contrary to the data in the literature. The discrepancy was explained by the hypothesis that the absence of hyperglycaemia in our case was due to the anaesthesia being — in consequence of artificial respiration — very superficial and even.

Our experiments were resumed again primarily to decide what substance or substances accumulated locally in the heart when a branch of the coronary artery is ligatured, to cause an elevation of the blood sugar. In preliminary experiments we immediately found — contrary to our previous findings — a marked hyperglycaemia due to ether anaesthesia. This hyperglycaemia was of such an extent that it was impossible to decide whether a further blood sugar elevation, resulting from the ligature of the coronary artery, had or had not taken place.

Our present experiments aimed to ascertain the cause of the difference between our earlier and our present findings. After many unsuccessful attempts it occurred to us that the difference in the ethers

used for anaesthesia might be responsible for the different effects on the blood sugar level. This assumption seemed the more correct as simple commercial ether, which we succeeded in obtaining shortly after the war, was used in our experiments of 1946, while our present experiments were begun with Swedish aether ad narcosim. At the same time we thought that perhaps seasonal changes might influence the hyperglycaemia caused by ether anaesthesia. Our experiments were, therefore, spread over a whole year.

## METHODS.

The experiments were carried out on 71 cats of both sexes, weighing $2.5 \pm 0.6$ kg. The animals fasted 24 hours before the experiment. Artificial respiration was used, primarily to ensure an even and easily adjustable anaesthesia for 7 hours. It was necessary, for the cat's chest was opened, both mammary arteries ligatured, the pericardium cut open and the chest closed with clamps. This procedure was adopted, as in the beginning these experiments were meant to be controls to show that other interferences accompanying the ligature of the coronary artery had no influence on the blood-sugar level. Blood pressure was not measured. For the blood-sugar determinations blood was taken from a side branch of the right femoral artery 3 times at 20 minute intervals. After the chest was opened blood was taken 4 times every ½ hour, and 4 times every hour, for altogether 6 hours after the opening of the chest. Blood sugar estimation was carried out by the modified Hagedorn-Jensen method (FUJITA-IWATAKI, 1931). Three kinds of ether were used for anaesthesia: a) Swedish aether ad narcosim* (Syntes. Nol. Sweden), b) So-called aether sulphuricus**, that is, the ether from which the Chinoin Pharmaceutical Mfg. Co. prepares ether for narcotic purposes, c) simple commercial ether, called aether depuratus. The experiments were carried out from February, 1947, to February, 1948, using a few cats each month.

## EXPERIMENTAL RESULTS.

Of the 71 cats, the data on 63 were used. The remaining 8 cats died at the beginning of the experiment or suffered from some illness which might have complicated the results (such as severe adhesive pericarditis,

* The Swedish aether ad narcosim was a gift from Profs. Y. ZOTTERMANN and H. THEORELL of Stockholm, for which we have pleasure in expressing our gratitude.

** Our thanks are also due to the CHINOIN Pharmaceutical Mfg. Co. for providing us with the necessary aether sulphuricus.

etc.). No difference was found in the ether hyperglycaemia in the course of a year, so we did not tabulate our results in respect to seasons. 32 cats were anaesthetised with Swedish aether ad narcos., 20 with aether sulphuricus and 11 with aether depuratus. Our results are summarised in Figure 1. The vertical lines drawn to the different

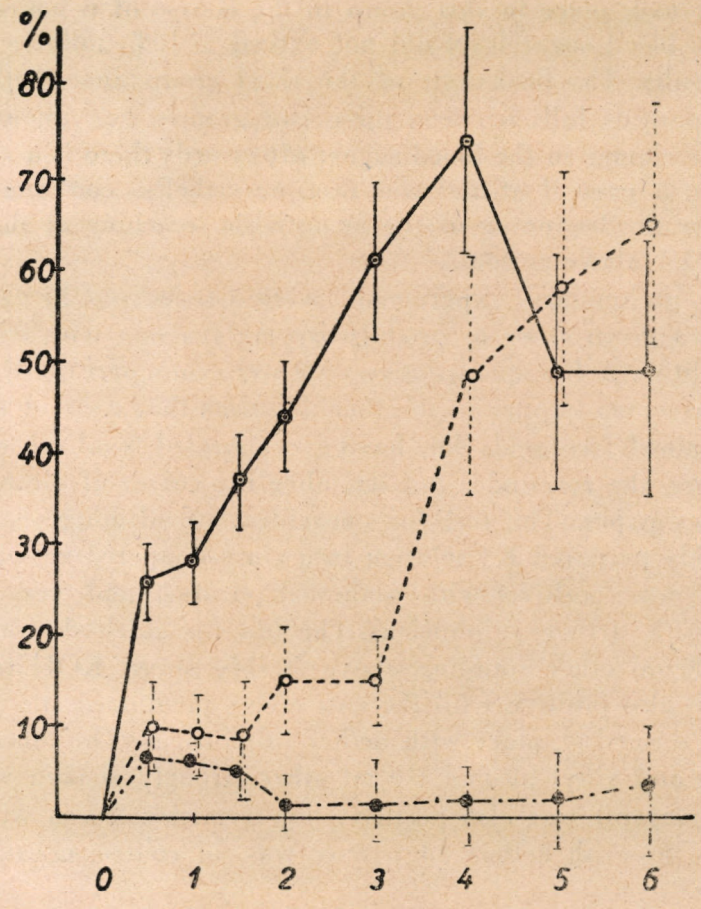


Figure 1. Blood sugar changes in cats anaesthetised with different ethers. Abscissa: Time in hours. Ordinate: Percentual change in blood-sugar as compared with the initial blood sugar level. —— : Swedish aether ad narcosim, - - - aether depuratus, —.—.— : aether sulphuricus.

lines show the standard deviation of the average at the time given. It can be seen from this Figure that the three kinds of ethers all behave differently. A very marked hyperglycaemia results in the group anaesthetised with the Swedish ether as compared with the other two

groups; the blood sugar elevation is already significant at the end of the first half hour. It shows a gradual increase in the first 4 hours, then seems to begin to fall but is still 50% above normal and the elevation is still significant at the end of the 6th hour as compared with the group where no change occurred in the blood sugar level. This latter group was anaesthetised with aether sulphuricus. No hyperglycaemia took place in this group in the course of 6 hours and the changes in blood sugar level did not exceed ± 10%, tallying with our earlier results. The behaviour of the third group anaesthetised with aether depuratus falls between these two groups. For almost 3 hours there is no change in the blood sugar; afterwards there is a sharp rise, and this rise, even if at a slower rate, nevertheless continues up to 6 hours after the beginning of the anaesthesia, reaching at that time a value of 65% above normal.

Some preliminary experiments were carried out to connect the ability of a given ether to produce hyperglycaemia with some of its other qualities. A few quantitative tests were thus performed to detect the most common impurities in ether. It seems that none of the ethers used contained free acids for, having evaporated 5 ml ether at room temperature, the remainder did not alter the colour of either red nor blue litmus paper. The test for peroxides (10 ml ether shaken with 1 ml freshly prepared KJ solution in a glass-stoppered vessel with air excluded) was positive with aether depuratus, and very strongly positive with aether sulphuricus. The test for aldehydes and vinyl alcohol (20 ml ether standing above freshly sliced KOH in a dark place) was also positive with the two ethers mentioned; the colour of the KOH seemed stronger with aether sulphuricus. The other test for aldehydes and vinyl alcohol (10 ml ether strongly shaken with 1 ml Nessler's reagent) was also positive, but seemed more so with aether depuratus. Swedish aether ad narcos. was, of course, negative in all these tests.

The toxicity of the three ethers used was also determined. These experiments were carried out on female white rats weighing 200 ± 20 g. Groups of 5 rats were put in closed vessels filled with air, containing different concentrations of ether. The concentrations of ether in which 0 — 100% of the rats died during 10 and 15 minutes anaesthesia were determined. These results are shown in Figure 2. It is to be seen that in 15 minutes the rats begin to die at an ether concentration of 0.09%, and when the concentration of ether in the air reaches 0.105%,

100% of the rats die. In 10 minutes the rats die between concentrations of 0.105—0.125%, these concentrations being the same for all the three ethers.

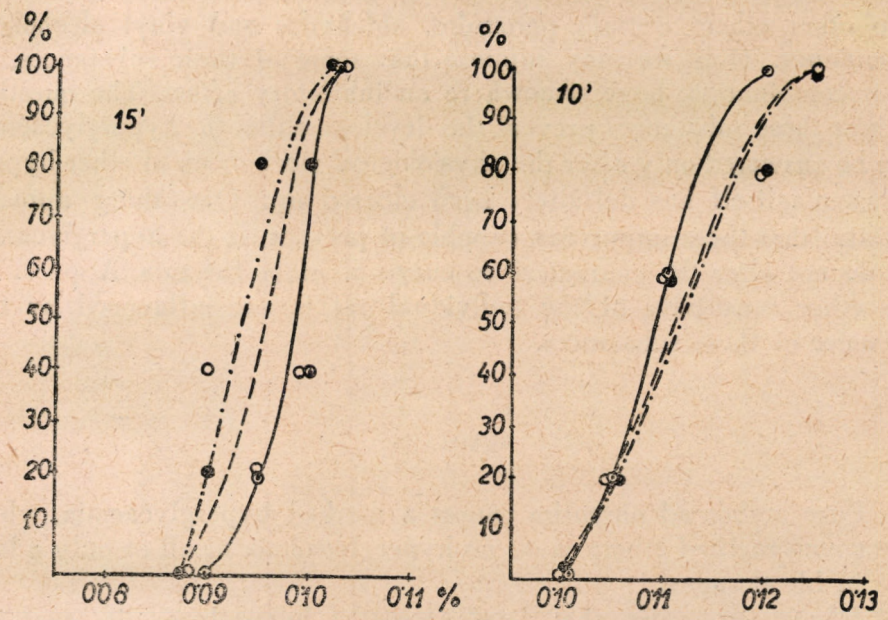


Figure 2. Characteristic curve (Trevan) of rats for different ethers. Abscissa: concentration of ether in air. Ordinate: Percentual mortality of rats in the course of 10 minutes (10′) and 15 minutes (15′). —— : Swedish aether ad narcosim, - - - aether depuratus, —.—.— : aether sulphuricus.

## DISCUSSION.

It is established that the absence of hyperglycaemia in our earlier experiments was not due — as was supposed at the time — to the anaesthesia being very superficial and even — but to the kind of ether used, which, like the aether sulphuricus of our present experiments, had no influence on the blood sugar level. It is thus easy to understand the contradiction between the literary data and our previous results, for authors describing ether hyperglycaemia doubtless used ether for narcotic purposes (from the use of which we were deterred only by the impossibility of obtaining it after the war). This ether, in our experiments too, caused a marked rise in blood sugar.

As regards the mechanism of the ether hyperglycaemia, or its absence, the likeliest hypothesis seems to be that ether in itself causes

hyperglycaemia through some unknown physiological mechanism, and the other ethers capable of preventing it, contain some impurities which inhibit hyperglycaemia. Indeed we found that, while the hyperglycaemia-producing ether does not contain any of the usual impurities, the two other ethers contain peroxides, aldehydes and vinyl alcohol in abundance. Thus we may suppose that some of these substances, or their combination, have somewhere an inhibitory effect. The question of how these substances prevent the development of the hyperglycaemia can be answered only after the physiological mechanism of ether hyperglycaemia itself has definitely been cleared up. One thing appears certain: that these impurities, capable of preventing the hyperglycaemia, do not alter the characteristic curve of ether for rats. Apparently the ether sensitivity of the individual rat is not influenced by the presence of these substances.

## SUMMARY.

Pure aether ad narcosim causes a marked hyperglycaemia, while other non-purified ethers cause no hyperglycaemia at all or only a late rise in blood sugar.

Ether preventing the development of hyperglycaemia contains peroxides, aldehydes and vinyl alcohol as impurities.

The characteristic curves (TREVAN, mortality % per ether concentration) of pure and impure ethers are identical.

There are no seasonal changes in the resulting ether hyperglycaemia.

We would like to thank PROF. A. B. L. BEZNÁK for his continuous interest throughout this work.

MRS. JEAN THOMPSON VASS kindly looked through the English of this paper, for which we here express our gratitude.

## LITERATURE.

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