Modification of Method of Analysis of Methohexital in Human Plasma

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While the manuscript, "Physiological Disposition of Methohexital in Man" was in press,
1 a report appeared on the metabolism of methohexital (Brevital) in dogs and rats.2 In
the latter, a metabolite of methohexital was isolated from dog urine and identified as
1-methyl-5-(1-methyl-4-hydroxy-2-pentenyl) barbituric acid. We were subsequently able
to obtain 2 mg. of this metabolite.* When 100 µg. of this compound was analyzed by the
previously reported method for methohexital in plasma, 44 per cent of the amount added
was recovered. However, when the buffer wash (citrate-phosphate buffer, pH 4.4) pre-
viously described in the method for the estimation of methohexital in fat1 was applied,
the metabolite was quantitatively removed and did not appear in the final measurement.
This finding indicates that the hydroxy metabolite, if present at all in man following methohexital
administration, does not interfere with the analysis of methohexital in fat by the above
method.

In the initial study,1 the buffer wash was used only for tissue analyses and not for
plasma determinations. Consequently, if the metabolite were present in significant amounts
in plasma, it could contribute to the concentrations found. This problem was studied as follows:
three human subjects were given 1.4 to 1.7 g. of methohexital sodium as a 1 per
cent solution intravenously in 10 minutes. Blood samples were withdrawn at intervals.
Plasma levels of methohexital were determined with and without the buffer wash. The
results are shown in table 1. Within the limits of the method, essentially the same plasma
levels were obtained, regardless of whether the buffer wash was employed or omitted. (These
findings do not exclude the possibility of the metabolite occurring in trace amounts in
human plasma.)

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Table 1. Plasma Levels of Methohexital with and without a Buffer Wash

<table>
<thead>
<tr>
<th>Dose (gram)</th>
<th>Time (minutes)</th>
<th>With Buffer Wash (mg liter)</th>
<th>Without Buffer Wash (mg liter)</th>
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<tr>
<td>1.7</td>
<td>15</td>
<td>31.2</td>
<td>33.1</td>
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<td>17.9</td>
<td>19.5</td>
</tr>
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</table>

* As sodium salt.
† From beginning of infusion.
‡ As free acid.

During the present study it was observed that even though the buffer wash was not essential for plasma analyses, inclusion of this step did lower the plasma “blank” appreciably. The buffer wash has now been incorporated as an integral part of the method for estimation of drug concentrations in plasma as well as in fat.

Also, occasionally during the extraction procedure emulsions form between the NaOH and the organic phases. If the usable volume of NaOH extract remaining is insufficient to fill the semimicro-cuvets (or if semimicro-cuvets are not available), duplicate extracts should be pooled for the final reading in the spectrophotometer.

References


INTRAOCULAR PRESSURE In ophthalmologic operations endotracheal intubation was accomplished under Fluothane anesthesia with succinylcholine intravenous drip. Succinylcholine caused a rise in intraocular pressure for 5 minutes even when the extraocular muscles had been cut. After 5 minutes the intraocular pressure decreased. Intubation also caused increased intraocular pressure. (Schlag, G.: Techniques and Problems of General Anaesthesia in Ophthalmologia, Klin. Mbl. Augenheilk. 142: 671 (May) 1963.)

HYPERGLYCEMIA Hyperglycemia which often occurs during laparotomy is usually attributed to surgical stress and associated adrenalin hypersecretion. Glycogenolysis in the liver is assumed to be the source of the glucose. Using rabbits the occurrence of hyperglycemia and associated reduction of liver glycogen was confirmed. Hyperglycemia occurred also in previously adrenalectomized animals and in those treated with dihydroergotamine. Hypophysectomy reduced the hyperglycemia but did not effect glycogenolysis. Cross-circulation experiments were done which indicate a glycogenolytic factor in portal vein blood, which is absent in peripheral blood. It is this factor which is responsible for the hyperglycemia during laparotomy. (Tillander, II.: Hyperglycemia in Abdominal Operations, Acta Chir. Scand. Suppl. 298 1962.)