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FATAL POISONING FROM MOTION SICKNESS PREVENTIVE

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The Army has studied various preparations for the prevention of motion sickness. Motion sickness includes air sickness, train sickness, sea sickness and car sickness. A preparation was developed called "Motion Sickness Preventive, Army Development Type," which was shown to be effective in reducing the incidence of motion sickness under varying conditions. This preparation contains sodium amytal 1 grain (60 mg.), scopolamine hydrobromide 1/300 grain (0.2 mg.) and atropine sulfate 1/400 grain (0.15mg.). With expanding travel over land, sea and air it is to be expected that such a product will soon be available on the open market. To emphasize rigid control of the dispensation of such a product, a case of death from overdosage is reported.

REPORT OF CASE

A general prisoner in the stockade of a ship returning from England was found dead in his bunk. Two other prisoners were sufficiently narcotized to require hospitalization. Investigation disclosed that the prisoners had taken "motion sickness preventive tablets" for the "intoxicating" effect that followed. The deceased was believed to have taken at least six such tablets. One of the surviving prisoners, when admitted to the hospital, appeared "intoxicated." He was semistuporous; speech was slurred and incoherent and the gait was wobbly, "like a drunk." He denied having taken alcohol but admitted that he took motion sickness preventive tablets. No alcoholic breath odor was detected. Chemical examination of the urine was negative for alcohol or other volatile poisons. He had no complaints. Physical examination revealed dilated pupils, a positive Romberg sign, negative Babinski and an unsteady gait. Within twenty-four hours all symptoms and signs cleared up. The patient stated that he had taken six motion sickness preventive tablets.

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Postmortem examination of the prisoner who was found dead disclosed superficial erosions of the skin of the face from vomited gastric content, dilated pupils (7 mm. diameter) and congested conjunctivas. The lungs were edematous and exuded a frothy fluid on section. The heart showed no gross abnormalities. The liver was grossly normal. The spleen was slightly enlarged. The kidneys were congested. The stomach was grossly natural. Examination of the head revealed leptomeningeal congestion and a grossly normal brain. Microscopic examination displayed intra-alveolar capillary hemorrhages in the lungs, congestion of the splenic pulp and submucosal capillary and venous congestion of the stomach. Sections of the brain revealed subarachnoid edema and venous congestion, capillary congestion of the cortical gray matter, occasional perivascular small round cell "cuffing" in the medulla oblongata, congestion and slight edema of the medulla spinalis, and subarachnoid venous congestion of the cerebellum.

TOXICOLOGIC EXAMINATION

Brain, liver, stomach contents and urine are the materials of choice for the isolation and identification of barbiturates and alkaloids. Since the presence of volatile poisons such as methyl alcohol, ethyl alcohol or chloral hydrate had to be ruled out, a portion of brain was steam distilled. The distillate was tested for the various common volatile poisons, and these were found to be absent.

Three hundred Gm. portions of brain and liver, 200 cc. of stomach contents and 100 cc. of urine were analyzed separately for barbiturates and alkaloids. Urine is best suited for a rapid detection of barbiturates. The urine was first slightly acidulated with diluted hydrochloric acid and then successively extracted with several portions of 50 cc. of ether. The combined ether extracts were washed with a small portion of water and poured into a tared beaker. The ether was evaporated over a boiling water bath. A white and usually crystalline residue may indicate the presence of a barbiturate. This was later confirmed. The aqueous was saved for later analysis for alkaloids.

In the analysis of the tissues, the procedure is a little longer in that an alcoholic extraction precedes the ether extraction, as described in the classic Stas-Otto procedure.

The tissues were weighed, macerated in a Waring blender, transferred with a little water to an evaporating dish and acidulated with tartaric acid. An equal quantity of *95* per cent ethyl alcohol was added and the dish was placed on, a boiling water bath for two hours. Heat and alcohol will precipitate the proteins; barbiturates are soluble in hot alcohol. The hot alcoholic extract was filtered and the residue reextracted with alcohol as before. The combined alcoholic extracts were evapo-

rated to a syrup at low temperature. The residue was taken up in *50* cc. of dilute sulfuric acid (1:500), allowed to stand and then filtered into a separatory funnel. This was successively extracted with several 500 cc. portions of ether. The combined ether extracts were washed with a small portion of water and poured into a tared beaker. The ether was evaporated on a boiling water bath. A white and crystalline residue indicated the presence of a barbiturate. This was weighed and then later qualitatively confirmed. The aqueous layer from these ether extractions was saved for later analysis for alkaloids.

The entire residue of the suspected barbiturate was dissolved with exactly 2 cc. of chloroform. Ten drops of this chloroform extract were placed in a micro test tube. A drop of 1 per cent cobalt acetate in methyl alcohol was added, and the contents were mixed. Five drops of 5 per cent isopropyl amine in methyl alcohol were stratified over the mixture. A blue-violet color developed between the stratified layers. This indicated the presence of a barbiturate. For a quantitative estimation these were shaken and a distinct diffused violet solution resulted. Standards were Similarly prepared with pure amytal, representing 1 to 10 mg. The unknowns were matched with the standards. Further confirmation of the presence of barbiturates was made with Millon's reagent. These tests were positive.

Since we were confronted with the problem of identifying a specific barbiturate, further purification of the residue was necessary. Sublimation proved to be the simplest technique. Pure white crystals were obtained which had a melting point of 153.5 C., indicating amytal *(154* C.).

The quantitative estimations of the amount of amytal isolated per hundred grams of tissue were the average of the gravimetric and colorimetric procedures, which in each case checked fairly closely with each other. The urine yielded 8 mg. of amytal per hundred cubic centimeters, the stomach contents 14 mg. of amytal per hundred grams, the liver 5 mg. of amytal per hundred grams and the brain 5 mg. of amytal per hundred grams.

The various aqueous extracts following the first acid-ether extractions were made alkaline with the addition of dilute sodium hydroxide solution. These were each successively extracted with several 50 cc. portions of ether. The ether extracts were washed with a small portion of water and then evaporated on a steam bath. The residue was dissolved in 0.5 cc. of very dilute acetic acid (1:200). Several drops were placed on a small glass slide and the alkaloidal reagents (Mayers, Wagners, gold chloride, picric acid) were applied. The urine was very faintly positive for combined alkaloids, the stomach contents were faintly positive for combined alkaloids, the liver was negative for combined alkaloids and the brain was negative for combined alkaloids.

COMMENT

The fatal dose of amytal has been reported as 2 to 3 Gm.[1] (or approximately 30 to 47 one grain tablets). The patients who recovered had admittedly taken six tablets, which contained a total of 0.36 Gm. of sodium amytal or 0.32 Gm. of amytal. Gettler[2] reports the minimum lethal tissue and blood level of amytal as 1.5 mg. per hundred grams. Gettler states that "the barbiturates are more or less distributed in the blood, brain, liver, kidneys and muscles." Since we found a concentration of *5* mg. per hundred grams of liver and of brain, we may calculate approximately how many of the tablets were consumed by the deceased. Assuming that the striated muscles make up 40 per cent of the body weight[3] and that the blood makes up 7 per cent of the body weight, the combined number of grams of amytal in the brain, liver, kidneys, blood, muscles, urine and gastric contents amounts to 1.75 Gm., or approximately 27 grains. Converted to terms of sodium amytal, the patient evidently ingested at least thirty tablets. Thirty tablets would include approximately 1/10 grain, or 6 mg., of scopolamine hydrobromide and 1/13 grain, or 5 mg., of atropine' sulfate, or a total of 11 mg. of belladonna alkaloid. Although a death has been reported from as little as 7 mg. of atropine sulfate,[4] a case of recovery from as large a dose as 500 mg. of atropine sulfate is also on record.[5] Goodman and Gilman[6] state that the fatal dose of atropine is probably about 100 mg. for adults, which is far in excess of what the deceased had ingested. The conclusion is, then, that death was due to an overdose of sodium amytal rather than to the belladonna alkaloids; the question of a possible synergism may not be ruled out.

SUMMARY

A man died from an overdose of sodium amytal contained in a new preparation known, at present, as "Motion Sickness Preventive, Army Development Type." Improper, ungovernable use of this prqduct may augment the increasing number of fatalities incident to barbiturate poisonings.

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