biliary excretion in the rat(8). It would appear that in the rat much intestinal morphine of biliary origin is subsequently reabsorbed.

Summary. 1. Therapeutic doses of morphine-N-methyl-C^{14} have been administered to 5 human subjects. The major portion of the radioactivity is excreted in 24 hours. Urinary excretion accounted for most of the recovered activity, and there was some correlation between urine volume and carbon-14 excretion when these volumes were abnormally high or low. 2. Fecal excretion accounted for 7 to 10% of the dose and the possibility that this material originates in the bile as "bound" morphine with subsequent hydrolysis in the intestine is discussed. Intestinal excretion is not as important in man as in rats. 3. Pulmonary excretion of $C^{14}O_2$ ranged from 3½ to 6% of the injected dose in 24 hours. There was no sex difference in excretion by this route, as has been observed in the rat. 4. The carbon-14 excretion pattern for the one addict was similar to the nontolerant subjects, except in the case of the feces. 5. It has been shown that it is feasible to do tracer studies in normal subjects using less than a microcurie of carbon-14.

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Effect of Restraint on Temperature Regulation in the Cat.* (20792)

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(Introduced by U. D. Register.)
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Hypothermia produced by restraint in mice has been previously reported(1), and a brief review of the literature dealing with this subject presented. To the authors' knowledge only the smaller thermolabile laboratory animals have been studied for this response. This group includes the rabbit with thermal instability commonly noted in routine work (2). In the present series, cats, generally thermostable animals, have been stressed by restraint and the effect on body temperature noted. It is known that stresses, which are partially emotional in nature, result in a loss of temperature regulation of smaller mammals, with a resultant body temperature drop when the animals are exposed to cold(1). If such a response to stress, either emotional or physical, existed in man, the lowering of body temperature in the cold would impose a serious handicap on such individuals as mili-

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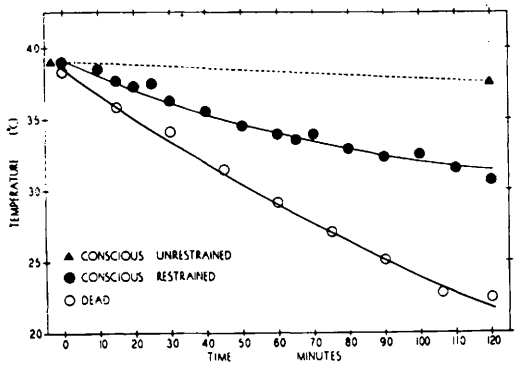

FIG. 1. Comparison of avg temperature drop of dead cats, restrained cats, and unrestrained cats (controls) in the cold (−15°C ± 2°).

tary personnel who must perform at peak efficiency. Thus the necessity of studying this problem in a large thermostable animal.

Methods and materials. Forty adult mongrel cats of either sex were used. They were divided into 14 controls, 13 restrained, and 13 dead animals. The control animals were housed individually in large cages in a cold room (−15°C ± 2°C). Deep rectal temperatures were taken with a thermometer at the beginning and end of the tests. The restrained animals were treated in one of two manners. Some had their legs, placed in normal positions. tied to 4 uprights; others, still in a normal position, had their hind legs tied to pegs while their neck was placed between uprights too close together for the head to be withdrawn. In both of these categories, the animals were placed in the cold room and body temperatures were taken intermittently with indwelling rectal thermometers inserted to a depth of 3 to 5 inches. The indwelling thermometer should be considered a part of the stressing technic. The third group of cats was killed by an overdose of sodium pentobarbital, placed in the cold room with indwelling rectal thermometers and temperatures taken intermittently throughout the duration of exposure.

Results. As shown in Fig. 1, the restrained animals lost body temperature (terminal temp. 31.5°C) while the control animals housed in large cages maintained an essentially normal body temperature (37.5°C). The body temperature of the restrained animals dropped in spite of continuous struggling which was maintained throughout the entire length of the exposure. A comparison of the curve for body temperature loss in the restrained cats with that for the dead cats shows that the restrained cats lost body temperature much more slowly than the dead animals (terminal temp. 22°C).

Discussion. Although several investigators (1-4) in working with rats, mice, or rabbits, have reported restraint-induced hypothermia, there has, to the authors' knowledge, been no report of such a phenomenon in a large, thermostable laboratory animal such as the cat. Most of these investigators used a modification of the Hamilton technic(3) and stated the belief that emotionality was an important factor contributing to hypothermia. Ware *et al.*(5) have reported they were unable to obtain hypothermia by use of this method unless the restraining cage was tight enough to restrict breathing. This work raised serious questions concerning an "emotional" nature of the stress and caused many to doubt the reliability of the conclusions drawn by other investigators using this technic. The cats used in the present studies were not caged and therefore there was little possibility of restraint of breathing. Body temperature fell, nevertheless, thus indicating that hypothermia can be produced in the cat by restraint without restriction of breathing. As mentioned previously, the restrained animals, without exception, struggled vigorously during the exposure. For body temperature to fall under such conditions in an otherwise relatively thermostable organism, distinct physiological changes favoring heat dissipation must have occurred. The possibility of an emotional factor and the physiological mechanism involved are being studied. A comparison of the curves for body temperature drop in the dead and restrained animals indicates that the restrained cats maintained temperature regulation better than mice under similar conditions(1).

The fact that a stressful situation so dramatically interferes with temperature regulation in the cat suggests that a similar mechanism may exist in the human. Thus the problem of proper morale and indoctrination becomes more acute in light of the possible

effects of such an induced hypothermia upon personnel exposed to a stressful situation in the cold.

Summary. Healthy adult male and female cats were restrained in essentially normal positions by binding of legs or head to stationary supports. The effect of exposure on the body temperature of these animals in a cold room (−15°C ± 2°C) was compared with that of dead animals and with controls which were housed individually in large cages. Temperatures were taken with indwelling rectal thermometers in the dead and restrained animals and at the beginning and end of the tests in the case of the control cats. Body temperatures of the restrained animals over a 2-hour exposure fell markedly (5.6°C) as compared to the control group (1.2°C). The temperature fall of the dead animals was the greatest (10.2°C). Since the animals were not caged, the hypothermia which resulted must be attributed to factors other than restricted breathing, perhaps partially to emotional stress.

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Effect of Fluoroacetate Upon Poliomyelitis in Monkeys.* (20793)

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Recent studies from this laboratory have demonstrated that the intraperitoneal administration of sodium fluoroacetate inhibits the growth of influenza virus in the lungs of mice (1) and that it suppresses the growth of the Lansing strain of poliomyelitis virus in the brains of mice(2). In the latter report it was shown that this compound also effected an increase in the incubation period of disease. These experiments as well as others employing tissue cultures(3) demonstrated that fluoroacetate does not destroy the virus upon simple contact but rather that its effect is obtained by interrupting the Krebs cycle so as to interfere with the utilization of citric acid. The accumulation of citric acid in large quantities in animal tissues following fluoroacetate administration has been adequately demonstrated(4-7) and its continued synthesis without further metabolism appears to be due to inactivation of the enzyme system necessary for the oxidation of citrate. The present report describes the effect of intravenously inoculated fluoroacetate upon cynomolgus monkeys and their infection with poliomyelitis virus.

Methods. Cynomolgus monkeys (*Macaca irus*) weighing between 1.5 and 3.5 kg were used throughout this study. A solution of sodium fluoroacetate was freshly prepared in distilled water and inoculated intravenously in measured quantities to give exactly the desired mg per kilo of body weight. Toxicity tests determined that a dosage of 5 mg per kilo was very near the maximum tolerated dose but was well tolerated by the animals except for occasional and temporary weakness, irritability, and anorexia. The citrate content of the brain tissue in 3 monkeys following administration of this dose of the drug was determined by the pentabromoacetone method(7). The values in γ/g wet tissue were found to be 33, 29, and 36, respectively. Normal values of 40, 41, and 42 obtained with untreated monkeys demonstrate that the brain is not the site of citrate accumulation. The significance of this finding will be considered in the discussion. In the experiments to be

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