to a guinea pig, animal dead in 21 hours; one tick from No. 22 to No. 29, animal dead in 23 hours.

Line B. 6 pairs of ticks on No. 19; flaccid paralysis 8 a.m. day 5, dead before noon; ticks removed 9 a.m. *First transfer:* 2 pairs to each of Nos. 25-27; flaccid paralysis, No. 25 in 54 hours (sacrificed when moribund), No. 26 in 18 hours (recovered 7 hours after removal of ticks), No. 27 in 11 hours (dead 2 hours later). *Second transfer:* Ticks from Nos. 26 and 27 completed engorgement on 2 young beagle dogs in 2 to 3 days, no effect.

Another series with wild-caught B.C. ticks illustrates susceptibility of hamsters recovered up to 67 days after original severe attacks:

Hamster 202 (recovered 45 days) developed typical signs 5 days after 4 pairs of ticks attached, but again recovered after early transfer of ticks to No. 260. Latter (recovered 28 days) paralyzed in 24 hours; again recovered after early transfer of ticks to No. 123. Last (recovered 67 days) became paralyzed in 10 hours but was fully recovered after ticks had finished feeding in less than 24 hours.

Hamsters have also been used to test our laboratory tick stocks of *D. andersoni, D. variabilis, Rhipicephalus sanguineus* (Egyptian strain), as well as wild-caught *D. occidentalis* from Oregon, without becoming paralyzed, though 3 of 10 tests of *R. sanguineus* were equivocal.

Conclusions. It is hoped that a means has now been provided, through use of hamsters, to study more intensively the incitant of this disease and to determine its possible relationship to the toxic principle reported by Steinhaus(4) in *D. andersoni* eggs. Ecologic and/or genetic factors may be influential, but it is pertinent that reared progeny of paralysis-producing ticks have now induced experimental disease. In spite of successful transmission by partially fed ticks from paralyzed animals in many of the above experiments, individual female ticks that produced paralysis in 3 child patients of Drs. Barmeyer and Adlerson of Missoula completed engorgement and mated on 2 dogs and 1 hamster, respectively, in 2 to 4 days without reproducing paralytic signs in these hosts. These observations indicate that hamsters are the animals of choice for the study of tick paralysis.

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Polydipsia and Polyuria During Chronic Administration of Levorphanol to Rats.* (24336)

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This paper is a report of preliminary experiments on observations of polydipsia and polyuria in rats treated chronically with levorphanol (Levo-Dromoran Tartrate). Interest in these observations arises from the fact that effects described are in apparent direct antithesis to the generally reported antidiuretic action of levorphanol. Also, close chemical and pharmacological similarity of levorphanol with morphine indicates that these observations may be of pertinence in relation to the action of morphine.

Materials and methods. To measure water intake and urine excretion, rats were placed in individual metabolism cages. The metallic funnel shaped floor of cage was coated with

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paraffin to decrease retention of urine on metal floor. A wire screen retained the feces. Water intake was measured by change in water volume read directly from 100 ml drinking tubes graduated in ml. Volume of the urine collected in Erlenmeyer flasks was measured with 100 ml graduated cylinder. Measurement of urine volume and water intake was performed at 9 a.m. and 9 p.m. The rats had access to food only at night. Control readings were taken for 2 days before injections were started. Results were the same as obtained with untreated controls tested throughout experiment. For chronic treatment 6 Sprague-Dawley male rats weighing 200-275 g were used. Levorphanol (Levo-Dromoran Tartrate) was given subcutaneously every 12 hours on the following schedule. Day 0-5: 10 mg/kg; day 5-9: 20 mg/kg; day 9-13: 30 mg/kg; day 13-18: 40 mg/kg and 50 mg/kg thereafter up to 26 days depending upon day of sacrifice. On 26th day 2 rats were given 20 mg/kg levallorphan tartrate (Lorphan) instead of levorphanol and sacrificed one-half hour later. Two were sacrificed 72 hours after the last dose of levorphanol given on day 26. The remaining 2 were sacrificed one hour after the usual 50 mg/kg dose of levorphanol on day 26. Brains of these animals were prepared for potassium and sodium determination by flame photometry using the procedure of Walker and Wilde (1). A Perkin Elmer flame photometer was used.

Results. At the initial dose of 10 mg/kg levorphanol the rats were sedated for about 2 hours. Water intake and urine excretion, shown in Fig. 1, were 5-10 ml/rat in daylight hours and 10-30 ml during night hours. With 20 mg/kg a few rats showed periods of sedation interspersed with excitement. Intake and excretion remained at control levels. With 30 mg/kg the rats showed longer periods of excitement and little sedation. Excitement was manifested by a general increase in movement as well as jumping around in the cages and gnawing on the wire walls. Muscle rigidity (possibly catatonia) was present along with exophthalmus. Similar results were obtained at higher doses, and tolerance to these effects did not seem to develop.

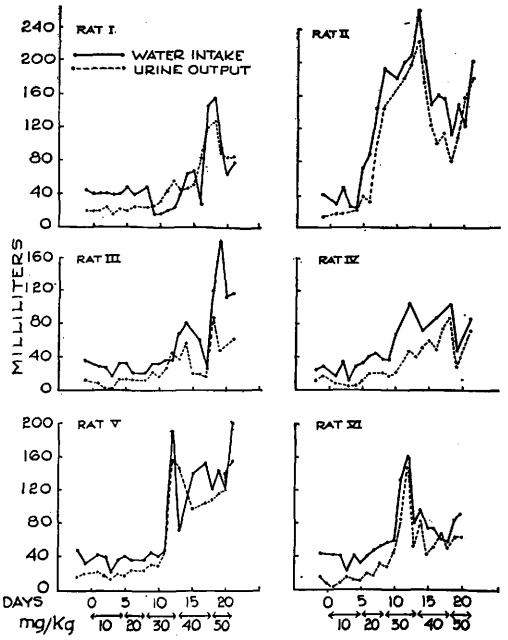

FIG. 1. Occurrence of polydipsia and polyuria in rats treated chronically with levorphanol.

One major point of interest is polydypsia and polyuria which occurred after maintenance on higher doses for longer than 7 days. The polydipsic response was observable in the following general sequence. In 5 to 10 minutes after injection of the levorphanol, the rats would begin drinking water vigorously. In many cases they would stop for several seconds and walk around the cage. However, they would quickly return to their water drinking. In this manner they would in some cases consume 50-75 ml of water in 4 hours. Urine output correspondingly increased. These results are seen in Fig. 1. There is some variation in onset of these effects, and also degree of peak effect varies considerably. For example, maximum effects were obtained for rat No. 2 on day 13 when for a 24 hour period his water intake was 280 ml and urine excretion 230 ml, whereas for rat 4 the corresponding figures were 108 and 92 ml on day 18. The fairly consistent difference between intake and output may be due to factors such as spillage, retention in cage, evaporation and insensible water loss.

On autopsy the 2 rats receiving levorphanol one hour before sacrifice had greatly distended urinary bladders, one containing 6.5, and the

other 5.5 ml of urine. Presence of urine retention complicates interpretation of the observation that the rats started to drink water before any micturition occurred in that polyuria could have preceded polydipsia. Adrenal hypertrophy was also noted.

A few experiments with possible bearing on the mechanisms of production of polydipsia were carried out. In view of the report that potassium depletion in rats leads to polyuria and polydipsia(2), the effects of levorphanol, levorphanol withdrawal, and levallorphan substitution on the sodium and potassium content of rats' brains were compared to controls. No difference was found in Na^+ and K^+ content of brains in the 4 groups, or any 2 of the 4 groups. Also no difference was found in sodium and potassium concentration of the plasmas. Polydipsia and polyuria found in levorphanol treated rats are more profound than those reported for the potassium depletion experiments(2).

An apparent contradiction in results exists between the diuretic effect of levorphanol noted here and reported in the literature(3). Could levorphanol have different effects in chronic experiments performed here as compared to the more acute experiments generally reported for antidiuretic experiments? Also, the doses of levorphanol in our experiments are rather large. Reports on morphine, a compound closely related to levorphanol, similarly point to an antidiuretic action for morphine(3). One early report does mention the occurrence of polydipsia and polyuria with morphine in rats(4). Further publications elucidating and extending the findings have not been found. Further studies using larger groups of animals on levorphanol are warranted since admittedly the number of animals used in the present report is small.

Conclusion. Chronic treatment of rats with levorphanol produced profound polydipsia and polyuria. These observations are of interest since levorphanol and its close relative, morphine, are known to produce antidiuretic responses on acute administration.

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Interaction of Methionine and Indoleacetic Acid in the Control of Abscission in *Nicotiana*. (24337)

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The role of indoleacetic acid (IAA) in retarding abscission in many species has been reported several times since Laibach(1) in 1933 first noted its effect by applying orchid pollen to an exposed petiole following removal of the blade of the leaf. An additional substance in control of abscission is indicated by experiments of several investigators. A substance produced by senescent leaves of several species has been shown to accelerate abscission in bean explants by Osborne(2). Van Overbeek, Blondeau, and Horne(3) reported that application of various maleimides (sulfhydryl blocking reagents) promotes leaf abscission in peach. Hotta and Ota(4) have reported other experiments with the abscission of bean cotyledons which indicate that iodoacetic acid also has an effect upon abscission presumably through effects on sulfhydryl groups. The striking effect of methionine (and some other amino acids) in accelerating floral abscission in tobacco has been reported earlier by the authors(5). This report of the effect of methionine as a specific entity in abscission makes a consideration of its intreaction with IAA in the overall control of abscission of spe