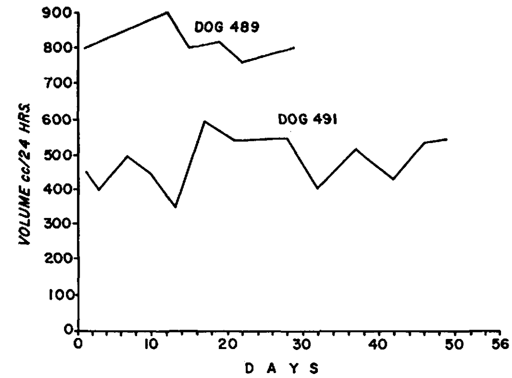

FIG. 2. Twenty-four-hr volumes of pancreatic juice from 2 dogs.

24-hour volumes of pancreatic juice of different dogs varied from 300-700 cc. However, the individual rate did not vary appreciably as the graph shows (Fig. 2).

At autopsy, there was no gross or histological evidence of duct dilatation or of pancreatitis.

Summary. This report describes a surgical procedure for preparing a pancreatico-duodenal fistula and shows the daily volume of secretion for 2 dogs.

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Antithyroid Effects of an Iodinated Hydroquinone Derivative.* (26820)

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A number of iodinated diphenyl ether derivatives have been evaluated with respect to their thyroid hormone-like or antithyroid properties(1). No simple iodinated hydroquinones or their derivatives have been evaluated however with respect to these characteristics. Since 2,6-diiodohydroquinone (DIH) has been suggested to be a potential degradation product of thyroxine(2) it was considered of interest to determine whether this simple hydroquinone or its derivatives possess hormonal or antihormonal characteristics. Preliminary studies of the effect of DIH on O_2 consumption in mice revealed that its toxicity interferred with an evaluation of its hormonal or antihormonal qualities. The diacetyl derivative of DIH (DDIH) however proved relatively non-toxic and exhibited antithyroid effects. This paper reports the extent and nature of these characteristics of DDIH.

Methods. The antithyroid characteristics of DDIH were measured through a study of its influence on the elevated O_2 consumption of mice injected with L-thyroxine or L-triiodothyronine. Methods and equipment used were essentially those of Maclagan *et al.*(3) except that exogenous L-thyroxine and L-triiodothyronine were injected at levels of 2 mg/kg and 1.68 mg/kg respectively. DDIH dissolved in cotton seed oil was injected in 2 equal portions, the first injected intraperitoneally approximately 5 hours prior to the injection of the thyroid hormone, and the second 24 hours later. Measurement of O_2 uptake was made 48 hours after first injection of DDIH.

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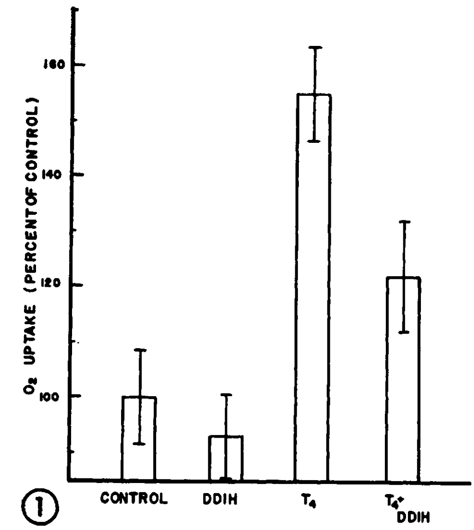
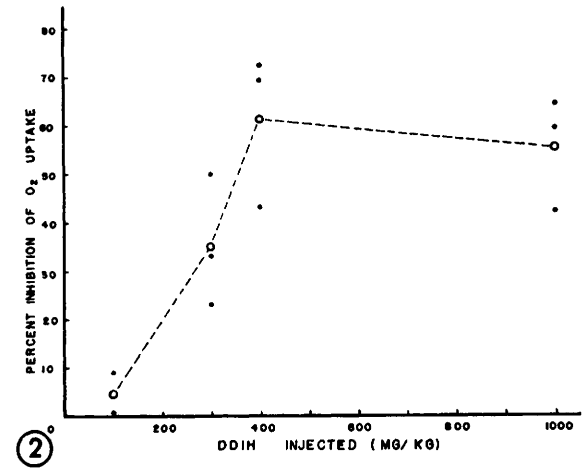
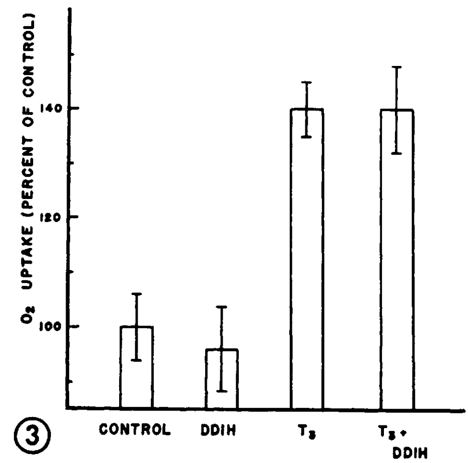
Results. The influence of DDIH on O_2 consumption of mice is shown in Fig. 1. DDIH at a dose level of 400 mg/kg has no significant influence on O_2 consumption of untreated mice. Mice injected with 2 mg/kg of L-thyroxine, however, have significantly inhibited O_2 uptakes in presence of DDIH ($P = < 0.001$).

The influence of various concentrations of DDIH on O_2 uptake of mice is shown in Fig. 2. DDIH appears to induce a measurable effect at a total dose of 300 mg/kg. The maximum inhibitory effect appears to be at 400 mg/kg. Beyond this level the inhibitory action appears to have reached a plateau.







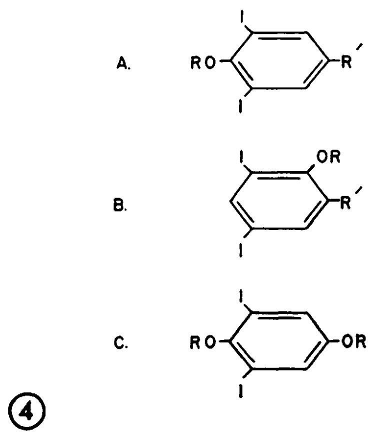


FIG. 1. Influence of a total dose of 400 mg/kg of the diacetyl derivative of 2,6-diiodohydroquinone (DDIH) on O_2 consumption of mice in presence or absence of 2.0 mg of exogenous L-thyroxine (T_4). Vertical line at top of each bar is 2 stand. deviations in length.

FIG. 2. Effect of increasing concentrations of inj. DDIH on inhibition of elevated O_2 consumption of mice receiving 2 mg of exogenous L-thyroxine. Each solid circle represents an individual reading with a separate group of 8 mice. Open circles represent avg of a given series of individual readings.

FIG. 3. Influence of a total dose of 1000 mg/kg of DDIH on O_2 consumption of mice in presence and absence of 1.68 mg of L-triiodothyronine. Vertical line at top of each bar is 2 stand. deviations in length.

FIG. IV. Generalized structures of compounds with antithyroid activities. R and R' may be hydrogen or aliphatic groups.

The influence of DDIH on mice O_2 uptake elevated by injections of L-triiodothyronine instead of L-thyroxine is shown in Fig. 3. It is apparent that DDIH has no inhibitory action in mice injected with L-triiodothyronine.

Discussion. The observation that DDIH inhibits the elevation of O_2 uptake in mice injected with L-thyroxine but not in those injected with L-triiodothyronine suggests that DDIH functions as an antithyroid compound in the same manner as n-butyl-3,5-diiodo-4 hydroxybenzoate (BHDB). Wilkinson *et al.* (4) have theorized that BHDB acts as an antithyroid substance by virtue of its ability to prevent deiodination of thyroxine to triiodothyronine, the active form of the thyroid hormone(5).

These data do not establish whether DDIH is inhibitory *per se* or whether it must first be hydrolysed to the free hydroquinone to induce an inhibitory response. Preliminary studies with I^{131} labeled DDIH indicate however that the major portion of injected DDIH is excreted via the urine in an unchanged form. If the compound is inhibitory *per se* this would indicate that an inhibitor of the deiodinase responsible for thyroxine degradation need not possess a free hydroxyl group. This possibility has already been suggested by earlier authors(1).

Sheahan *et al.*(6) have generalized as to the structures of compounds which exhibit BHDB characteristics. They suggest that one of structures A or B of Fig. 4 is required for BHDB-like action. Our data would indicate that structure C must now be added to this group of antithyroid substances.

Summary. The diacetyl derivative of 2,6-diiodohydroquinone has been shown to behave as an antithyroid substance. The available evidence would suggest that the compound inhibits the deiodinase responsible for conversion of thyroxine to triiodothyronine.

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Effect of Pregnenolone, Progesterone, and Derived Metabolites on Mammary Gland Growth in Rats.* (26821)

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A number of steroid compounds have been shown to have varying mammary gland growth promoting (mammogenic) capacities when injected into ovariectomized mice(1). Differences in extent of lobule-alveolar growth were evaluated by visual examination of whole mounts of glands, and criterion of response was based on percentage of mice showing a minimum amount of lobule-alveolar growth after 10 daily subcutaneous injections of material to be assayed. More recently, improvements have been made in the method of measurement of mammary gland growth of mouse (2) and rat(3), using desoxyribosenucleic acid (DNA) as an index of normal and experimental mammary gland growth. With these methods and employing a 19-day injection period (normal gestation) it is now possible objectively to quantitate amount of mammary gland growth resulting from injection of a given amount of steroid.

Recent studies(4) have established a steroidogenetic pathway involving the following transformations: pregnenolone → progesterone → 17α-hydroxyprogesterone → androstenedione → testosterone. Progesterone in synergism with estradiol has been shown to stimulate mammary gland growth in rats equal to that stimulated during pregnancy as measured by total DNA(3). It seemed of interest to determine whether pregnenolone would be converted to progesterone efficiently in ovariectomized rat as measured by mammary gland growth and further to determine whether steroids involved in the biosynthetic transformation of progesterone to androgens showed mammary gland stimulating properties which might result from these further biogenetic changes.

Materials and methods. Sprague-Dawley-Rolfsmeyer rats with an initial weight of 220-250 g were ovariectomized. Animals killed 35

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† U.S.P.H.S. postdoctoral Fellows of Nat. Inst. Health.