A Device for Controlling Humidity in Biosynthesis of Drugs[1]

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In the course of experiments on the biosynthesis of labeled drugs we encountered some difficulty in growing young *Digitalis lanata* plants in a sealed atmosphere. Excess moisture in the atmosphere of the terrarium was considered as one of the major factors detrimental to their growth. Consequently, a device for controlling the excessive humidity was devised. The necessity of preventing loss of any $C^{14}O_2$ from the terrarium required the construction of an air-tight unit such as that illustrated in Fig. 1.

It consists of a motor-driven blower[3] housed in an air-tight 9″ × 12″ battery jar covered with a circular piece of glass plate and sealed with a 50/50 mixture of beeswax and rosin. Moisture-laden air is drawn from the terrarium, through the motor-blower, into a condenser, and thence back into the terrarium, the excess moisture being condensed and the condensate being collected and drained off from the bottom of the unit.

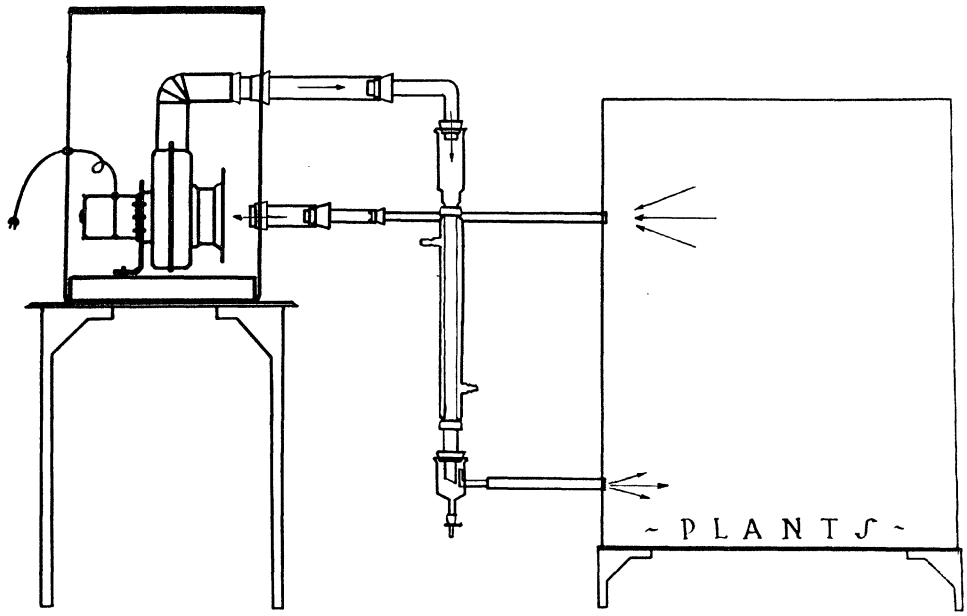

FIG. 1. Drawing illustrating blower-condenser unit with blower-motor housed in battery jar (left) and terrarium (right). The water condenser is connected between the exit of the blower unit and the entrance to the terrarium.

Employing this blower-condenser unit, we have been able to grow radioactive *Digitalis lanata* in sufficient quantities and with radioactivity of desired intensity.

The Production of Unilateral Epileptiform Convulsions From Otherwise Quiescent Foci by the Administration of Benzedrine

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Ruch (*5*) has recently reported the sedative effect of cerebral excitant drugs on hyperactivity in macaques with prefrontal lesions. The effect of this class of drug in changing the behavior resulting from cortical insult suggested to us that latent characteristics of a surgically-altered nervous system might be elicited by changing its chemical environment. The consequences of an investigation of this possibility justify a preliminary report of the occurrence of unilateral Jacksonian seizures following administration of benzedrine (amphetamine sulfate) to an immature male macaque with symmetrical bilateral prefrontal removals.

This animal was acquired in October 1946 and was trained to mastery of the following problems: (a) visual-spatial delayed response to a criterion of 90% correct at 30 sec, (b) auditory discrimination between a bell and a buzzer to a criterion of 90% correct, and (c) auditory delayed response to a criterion of 90% correct at 12 sec. The preoperative period of observation of approximately 6 months revealed no unusual physiological or behavioral characteristics. On May 7, 1947, a bilateral removal of

[1] Supported by the Life Insurance Medical Research Fund.

[2] Research assistant, Life Insurance Medical Research Fund.

[3] Delco Appliances, General Motors Corporation. (115 volts, 60 cycles, 40 watts, 0.45 amps.)

prefrontal cortex was made on this animal, the lesion including all tissue anterior to a plane 5 mm in front of the arcuate sulcus on the dorsal surface and about 2 cm in front of the optic chiasm on the orbital surface. Recovery was uneventful. In the three days immediately following operation, the remarkable increase in locomotor progression characteristic of prefrontal macaque preparations developed gradually to its peak. Tests given 10–14 days postoperatively showed perfect retention of the auditory discrimination habit, but only chance scores on the visual and auditory delay problems. Considerable formal training in the subsequent months did not improve his performance. The monkey was kept under observation and almost daily trained and tested for 14 months following the operation. Throughout this period the activity level remained high, but no behavior suggestive of Jacksonian fits or epileptoid seizures was observed.

On July 19, 1948, at 10: 00 A.M., he was given 6 mg of benzedrine by subcutaneous injection (his weight at this time was 8 lbs). Activity continued as before dosage, but food given was not swallowed, remaining in the food pouch. Twenty minutes later he was given 4 mg additional (the total amount given being about half the minimum lethal dosage, *1*). During the next 40 min greatly increased activity, muscular incoordination, attacks on the cage walls, and general violence, but no convulsions, were noted. This condition was followed by prostration. He was then given 30 mg of Nembutal intraperitoneally. In the afternoon he was sitting up and moving about quietly. Partial paralysis of the left limbs, affecting the arm more than the leg, was observed. The right limbs appeared weak and uncoordinated. At 6: 30 P.M. he was again prostrate and started having Jacksonian-type seizures, beginning with the corner of the mouth and spreading to the hand, arm, trunk, and leg of the left side. At no time in any convulsion did the clonic movements spread to the right side of the body. Later the convulsions started from the ear and were followed by adversive head movements and progressive involvement of the left limbs and trunk. At 7: 15 P.M. the convulsions were starting with the adversive head movements. Each seizure lasted about 40 sec with about a 5-min interval between seizures. This interval gradually decreased until at about 8: 00 P.M. the convulsions were coming every 2 min. In all, about 30–40 convulsions were observed. At 8: 20 P.M. he was given 60 mg of Nembutal intraperitoneally, and the convulsions stopped within 5 min. Twenty minutes later convulsions again started, and he was given another 60 mg of Nembutal in two doses in the next hour and 105 mg more at 11: 30 P.M. At 3: 30 A.M. the animal was awake, prostrate, and quiet, and remained this way until evening. During the morning following he was given saline solution subcutaneously, and in the afternoon he drank a cup of orange juice and ate two pieces of fruit. That night he was sitting up, capable of movement but quiet and unresponsive. The paralysis and weakness were somewhat alleviated, but the left side was still less efficient than the right. The next morning he had regurgitated all the food previously eaten and appeared very weak and stuporous, lying down much of the time. Late that afternoon he was sacrificed and perfused with 10% formalin. The brain was removed 48 hrs later. There was no hemorrhage or other gross abnormality which could account for the severe symptoms following the administration of benzedrine. There was scar tissue of about 2–3 mm in extent in the anterior part of the remaining frontal cortex on both sides.

It has been suggested by Hebb and Penfield (*2*) that maximum physiological and behavioral dysfunction may result from pathologically functioning tissue rather than from lack of tissue *per se*. Further, Penfield and Erickson (*4*) have localized adversive seizures, similar to the type described here, in the cortex of the frontal lobe immediately in front of the sensorimotor area. Kopeloff, *et al.* (*3*) have shown that a focus of irritation in the cortex produced by local application of a disc containing certain inactive materials may fail to cause seizures until sensitizing agents such as alumina cream are introduced parenterally. Our findings indicate that (a) irritative lesions, though insufficient to produce epileptic discharge, may be present after cerebral excisions; (b) benzedrine may increase sensitivity to these irritative effects; and (c) observed abnormalities of behavior, such as hyperactivity and failure in the delayed response test, following brain lesions may be due to the irritative action of pathological tissue which is subliminal for fits.

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The Pharmacological Properties of Some 2-Substituted-4-hydroxymethyl-1,3-dioxolanes[1]

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Certain simple monoethers of glycerol were recently shown to cause a transient paralysis of the voluntary skeletal muscles without embarrassment of respiration (*2*). In smaller doses these substances had a controlling influence on various types of tremors and other involuntary movements, as well as a relaxing effect on spasm, spasticity, and rigidity (*1*, *3–6*). The purpose of this

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