cotton swab. The dates of virus collection and testing are given in Table I.

All of the above tissues proved capable of producing typical confluent papillomatous growths in domestic rabbits. The incubation period in each case was approximately 2 weeks except for tissue No. 1, for which the incubation period was about 3½ weeks.

Summary. Cottontail papilloma tissue stored in 50% glycerine at 4°C remains infective and capable of producing confluent papillomatosis for as long as 20 years. All 6 of the tissues tested after storage from 6 to 20 years were found viable. This seems to establish that Shope virus is extremely stable when stored under refrigeration.

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A Pithed Rat Preparation Suitable for Assaying Pressor Substances.

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Although pithed cats and pithed dogs are very useful as sensitive test preparations for studying or assaying pressor substances, the cost for procurement and maintenance of the animals is a considerable disadvantage. Because rats are more readily available and are much more economical to use when large numbers of test animals are involved, an effort was made to develop a pithed rat preparation which would satisfy the requirements for pressor sensitivity and reproducibility. In the present paper a technic is described for setting up a satisfactory rat preparation which compares favorably with, and in several respects is superior to, the pithed cat or dog.

Young male rats (albino or hooded) weighing 150-300 g were used. The rat was anesthetized by the intraperitoneal injection of sodium amytal, 0.09 mg/g body weight. Atropine sulfate (1.2 mg) was given along with the anesthetic. The trachea was exposed and a piece of plastic tubing or rubber catheter 6 cm long and 2.5 mm in diameter was inserted into the opened trachea. Tubing of this size fitted snugly and did not need to be tied in place.

Either the femoral or common carotid artery was isolated for cannulation. A short cannula of small diameter (0.5 mm) was tied in the artery and connected to a mercury manometer by plastic or rubber tubing. A dilute solution of heparin was used to prevent clotting in the cannula. (It is advisable to use a small bore [3.0-3.5 mm] mercury manometer to minimize the loss of blood from the rat by displacement into the manometer during rises in blood pressure.)

The vagi were then cut and the jugular veins and carotid arteries tied. With the rat on its back and the hind feet pinned to the operating board the animal was ready to be pithed. The pithing rod, 2.2 mm in diameter, 25 cm long, with one end bluntly pointed, was made from an ordinary wire coat hanger. By holding the rat's head taut and in line with the vertebrae, with the thumb in the angle of the mandible and the forefinger around the top of the skull, the point of the pithing rod was inserted obliquely into and through the eye socket at an angle of approximately 45° to the long axis of the rat. After the skull was entered the rod was realigned with the vertebral column and passed through the cranium and thence down the whole length of the spinal canal. The pithing rod was left in place on the assumption that it would afford mechanical compression of blood vessels torn by the rod in the process of pithing.

The tracheal cannula tubing was then promptly connected to the respirator system which included a side tube fitted with an adjustable screw clamp. The respirator used was an air-driven, windshield wiper type with adjustments for varying both rate and

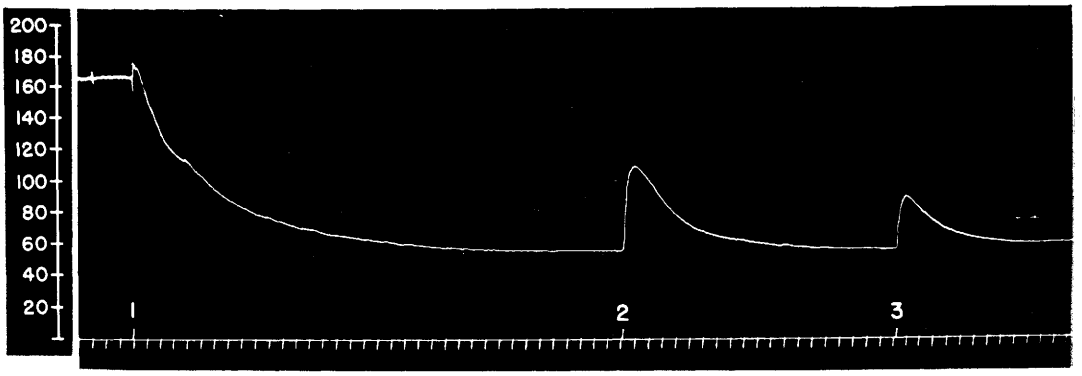

FIG. 1.
Record of mean blood pressure in a pithed rat preparation. Wt. 180 g. 1. Rat pithed. 2. I.V. injection of 6 μg of a "laboratory standard" angiotonin powder in 0.2 ml saline. 3. I.V. injection of 0.1 μg epinephrine hydrochloride in 0.2 ml saline. Ordinate scale—blood pressure in mm Hg. Time marker—1 minute. (32ZD-14.)

volume. (Great care must be taken to avoid hyperventilation or overdistention of the lungs if the development of pulmonary edema is to be prevented.) Respiratory rates of 50-60 per min. were found to be optimum for the rat. Slower rates of 30-40 were tolerated but oxygenation of the blood appeared to be inadequate. With rates slower than 20 the rats lived for only a short time.

For making intravenous injections a small portion of skin was cut away from the area overlying the femoral vein. Into one end of a 6-inch piece of very small plastic tubing (1 mm O.D.)* was fitted the shaft of a 24-gauge hypodermic needle which had been cut off below the syringe hub. The needle was inserted into the femoral vein and left in place, the application of a ligature being unnecessary. Syringes of 0.25 or 1.0 ml capacity and graduated in 0.01 ml were fitted with 26- or 24-gauge hypodermic needles the beveled points of which had been ground off flat. Usually 0.1 to 0.2 ml of test sample was given, syringe and needle removed from the plastic tube and replaced by a second syringe and needle with 0.1 ml physiological saline wash. Care had to be taken to avoid the inclusion of very small air bubbles when changing syringes. This could be accomplished by injecting 0.02 ml of saline and quickly replacing syringe and needle with the test sample syringe and needle. During this exchange a slight outward flow of saline would expel the small air bubble usually present as the result of the transfer.

The animal was left undisturbed for ½ hour before injections were begun during which time the depth of respiration was observed and altered if necessary according to the color of the arterial blood and the extent of movement of the thorax. With a little practice it was found that the optimum exchange of air could be gauged with reasonable accuracy from the excursions of the chest wall.

Thirty to 40 minutes after the rat was pithed the mean blood pressure usually leveled off between 40 and 60 mm Hg. Pressor responses of 30-40 mm Hg were obtained in most of the preparations with only 0.05-0.1 μg of epinephrine. Occasionally comparable rises in blood pressure were obtained with as little as 0.0125 μg. In general, the sensitivity to angiotonin was from 2 to 5 times as great as that exhibited by the pithed cat. A sample record of typical pressure curves is shown in Fig. 1.

With proper maintenance of the depth and rate of artificial respiration, satisfactory pressor responses were obtained for periods averaging 5 to 7 hours. Over 120 pithed rats have been prepared by the method described and approximately 90% of these have been satisfactory test animals. In the ma-

* "V-1" plastic tubing, A. C. Balfour Associates, Englewood, N.J.

jority of instances technical errors or the use of rats which showed signs of illness were thought to be responsible for preparations which exhibited poor pressor responses or died prematurely.

Summary. A simple method is described for setting up a sensitive pithed rat preparation suitable for assaying small quantities of pressor substances.

Grateful acknowledgment is made to Mr. C. Wilson whose technical experience in preparing pithed cats has been a valuable aid in the present study.

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Effect of Pentaquine in Patients with Hypertension.*

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The recent observation that pentaquine [6-methoxy-8-(5-isopropylaminoamylamino)-quinoline], a new antimalarial agent, produces postural hypotension in normal man[1,4] raised the question of its usefulness in treating hypertensive patients. The purpose of the present report is to summarize briefly the results of a clinical trial of this compound in a random group of 17 patients with long standing essential hypertension including 3 in the malignant phase of the disease.

Procedure and Results. Pentaquine was administered orally in amounts varying from 120 to 240 mg of the base per day, given in equally divided doses every 4 hours. Arterial pressure was measured in the arm by the standard auscultatory method using a mercury manometer. Measurements were made with the patient resting comfortably in the supine position, and also, during and after 5 minutes (or less if syncope intervened) of motionless standing. Mean arterial pressure was calculated as one-half the sum of the systolic and diastolic blood pressure. The pulse rate was palpated at the wrist or auscultated at the cardiac apex. Patients were hospitalized for at least 3 days prior to treatment, and were maintained on essentially the same regimen before, during and after the period of drug therapy.

In the majority of cases (Table I), after 2 to 7 days of treatment at dosages of 120 to 240 mg per day, a reduction of systolic and diastolic blood pressure occurred, varying from 10 to 40% of the mean arterial blood pressure. At the same time there was usually a further fall in blood pressure in the erect position associated with narrowing of pulse pressure. The pulse rate remained unchanged, or actually decreased in the supine position, and in the majority of patients failed to rise abnormally in the upright position even during marked hypotension.

The development of postural hypotension was not observed in all cases. Four patients exhibited a definite fall in resting blood pressure without the development of a further hypotension when erect. Others maintained a lower resting blood pressure for several weeks after the disappearance of the postural effect. However, one patient exhibited a reduction of blood pressure only in the upright position. In a few patients the depression of arterial pressure first appeared several days after the medication had been discontinued because of toxic reactions.

* This investigation was supported in part by the Squibb Institute for Medical Research, New Brunswick, N.J. The pentaquine used was supplied by James A. Shannon, M.D., of the Squibb Institute.

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