

a reversible effect upon ability of antisera to neutralize the virus. In the present experiment the source of the virus had no effect upon efficiency of the neutralization: antisera against A virus neutralized the A virus from both BALB/c mice and A mice, regardless of whether the virus preparations used in antisera production had been derived from A mice or BALB/c mice.

In control groups a significantly earlier age of tumor development was found in the group of mice given A/3 virus, than in groups given A (in BALB/c or in A tissue) or C3H virus. This difference with regard to the A/3 and the A viruses will be discussed elsewhere.

Summary. No antigenic differences were found when the mouse mammary tumor viruses from 3 different strains or sublines (one in 2 different host strains) were compared, using the technic of *in vitro* virus neutraliza-

tion with rabbit antisera followed by injection into susceptible virus-free test mice. Normal rabbit serum and antiserum against virus-free tissue did not neutralize the virus. Antiserum against any of the viruses neutralized that virus and all others tested. Neutralization of the virus was not affected by the tissue source of the virus.

1. Andervont, H. B., Bryan, W. R., *J. Nat. Cancer Inst.*, 1944, v5, 143.
2. Green, R. G., Moosey, M. M., Bittner, J. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1946, v61, 115.
3. Bittner, J. J., Imagawa, D. T., *Cancer Res.*, 1955, v15, 464.
4. Blair, P. B., *Science*, 1958, v127, 518.
5. Bittner, J. J., *Acta Unio Internat. c. Cancrum*, 1959, v15, 729.
6. Bittner, J. J., Hirsch, H. M., Ross, J. D., Gabrielson, R., *Proc. Am. Assn. Cancer Res.*, 1959, v3, 7.

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Experimental Preparation Showing Effect of Reserpine on Tissue Resistance.* (25455)

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Reserpine has been shown to be a potent agent in abetting ulcer diathesis both clinically and in the laboratory(1,2,3). The mechanism of acute ulcer production by reserpine is not clearly understood, although it has been shown that intravenous injection of reserpine causes a marked increase in HCl secretion in human patients(2) and also augments Heidenhain pouch secretion in the dog(3). Whether reserpine has any effect on tissue resistance, however, has not been clearly assessed. Susceptibility of cat's esophagus to the erosive action of human gastric juice has been well documented in this laboratory(4). Using a modification of this technic, the peripheral effect of reserpine has been observed and is here reported.

Method. Adult mongrel cats were used. The animals were divided into 2 groups. In both groups, the animals were anesthetized with pentobarbital, 30 mg/kg, and positive pressure respiration was maintained automatically through a cervical tracheostomy. In Group I the cervical esophagus and gastric cardia were cannulated for outflow tracts. A left thoracotomy through 7th interspace was achieved and the esophagus mobilized. A No. 26 T-tube with $\frac{3}{4}$ cm "limbs" was inserted through longitudinal incision in mid esophagus, each limb being secured in place by an umbilical tape. By alternate occlusion of the limbs of the T-tube, the upper or lower segments of the esophagus could be perfused separately. In Group II animals the entire esophagus was utilized for perfusion, with the perfusate being introduced through a cannula in the cervical esophagus and drained at 20 cm outflow pressure at the lower end of the

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esophagus(5). The perfusate used throughout this experiment was human gastric juice collected on ice in the postoperative period from 11 p.m. to 7 a.m. from patients who had not undergone gastric surgery. The specimens were analyzed first for pH, free acid and pepsin and were then acidulated to a pH of 1.6 with 0.1 N HCl, providing an optimal range for peptic activity. The technic of perfusion in Group I cats was as follows: An overnight specimen was divided into 2 equal portions of at least 250 cc each. The control segment of the esophagus was perfused for 2 hours at a rate of 30 drops per minute with a constant outflow pressure of 20 cm. At the end of this time, the perfused portion of the esophagus was thoroughly irrigated with saline. Reserpine, 0.5 mg, was given *via* the femoral vein, which had been exposed previously, and after a 2 hour period, the alternate segment of the esophagus was perfused for a period similar to the control by changing the position of the occluding clamp. The control and test portions were alternated to preclude the possibility of increased susceptibility of the cephalad or caudad segment of the esophagus. In the Group II animals, the overnight specimens were also split into portions of at least 250 cc each. The control cat was perfused for a 2 hour period with this gastric juice, and the test cat was perfused for a similar 2 hour period, after a 2 hour period to permit reaction of 0.5 mg of reserpine given intravenously through the femoral vein. At the conclusion of the perfusions, the animals were sacrificed and the esophagi were removed. The control and test sides were graded 0 to 5+ with reference to the esophageal injury noted(5); 0,

TABLE I. Comparison of Digestion of Cat's Esophagus between Control and Reserpine Treated Animals.

Grade of digestion	Group I (12 cats)		Group II (7 pairs)	
	Control	Reserpine treated	Control	Reserpine treated
0	5	0	5	1
1+	5	2	0	1
2+	1	3	1	1
3+	1	5	1	2
4+	0	0	0	0
5+	0	2	0	2

1+ signifies mucosal reddening without injury; 5+ denotes perforation.

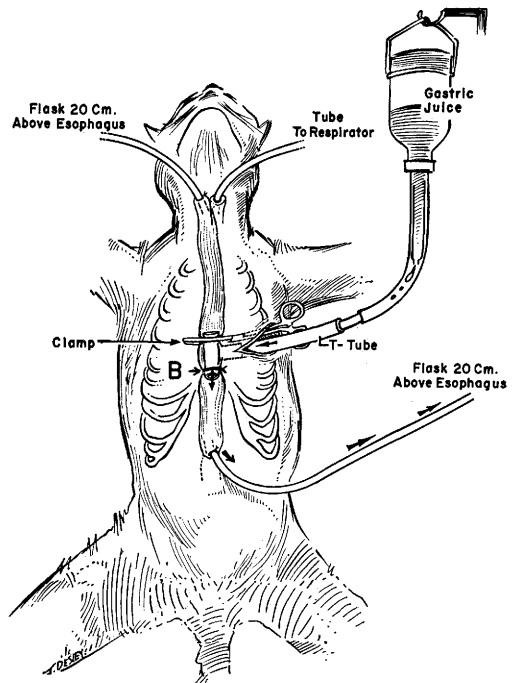


FIG. 1. Tissue resistance preparation using the same cat's esophagus as the control and test specimen.

representing no injury, 1+, representing slight mucosal reddening, and 5+, denoting perforation of the esophagus.

Results. There were no perforations in the control animals of either Group I or Group II, whereas in the reserpine treated experiments there were 4 perforations (Table I). In Group I, 7 of the 12 segments of esophagi treated with reserpine demonstrated an injury of 3+ or greater as opposed to only 1 of 12 in the control specimens, and indeed, 10 of 12 specimens, or 83.3%, showed a significant increase of digestion of 2+ or more after reserpine administration. In the Group II animals, 4 of 7 cats treated with reserpine demonstrated an esophageal injury of 3+ or more as opposed to only 1 out of 7 of the control animals. In fact, 5 of the 7 or 71.4% of reserpine tested preparations demonstrated 2+ or higher difference in digestion over the control group.

Discussion. The results attending intravenous administration of reserpine indicate a significant decrease in tissue resistance of cat's esophagus perfused with human gastric juice.

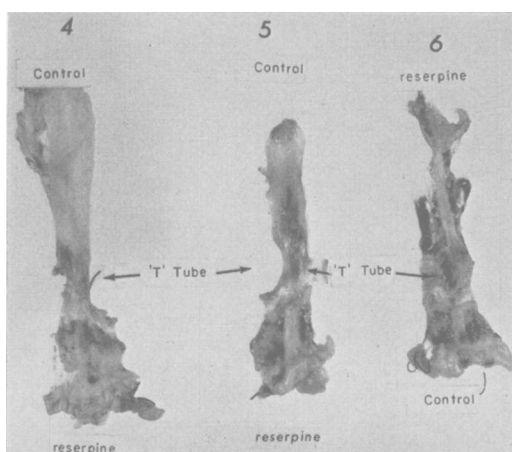


FIG. 2. Perfused preparations representing Group I or divided cat esophagus. Specimen 4: control side grade 0 digestion; reserpine treated side grade 1+. Specimen 5: control side grade 1+ digestion; reserpine treated side grade 3+. Specimen 6: control side grade 2+ digestion; reserpine treated side grade 5+.

This is revealed in increased digestion observed in the divided esophageal perfusion as well as in experiments using a separate cat's esophagus.

The mechanism this decreased tissue resistance produced by reserpine remains obscure. Increased ACTH release through hypothala-

mic stimulation(6) with resultant corticosteroid secretion may play a role in this increased tissue susceptibility. Serotonin release(7) and local factors such as vascular spasm or decreased blood flow because of hypotension may be important. These various possibilities are being investigated by use of this preparation.

Summary and conclusion. The I.V. administration of reserpine lowers significantly the susceptibility of the intact cat's esophagus to injury by digestive action of human gastric juice.

1. Hussar, Alan E., Bruno, Emil, *Gastroenterology*, 1956, v31, 500.
2. Schneider, Edward M., Clark, Mervin I., *Am. J. Digest. Dis.*, 1957, v1, 22.
3. Barnett, W. E., Plummer, A. J., Earl, A. E., Rogie, B., *J. Pharm. and Exp. Therap.*, 1955, v113, 3.
4. Baronofsky, Ivan, Wangenstein, Owen H., *Bull. Am. Coll. Surg.*, 1945, Feb., 1-4.
5. Perry, John F., Jr., Yonchiro, Earl G., Ya, Po M., Root, Harlan D., Wangenstein, O. H., *Proc. Soc. Exp. Biol. and Med.*, 1956, v92, 237.
6. Harwood, Theresa, Masin, John, *J. Endocrinol.*, 1957, v60, 239.
7. Brodie, Barnard; Pletcher, Alfred; Shore, Parkhurst A., *Science*, 1955, v122, 968.

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Familial Primary Amenorrhea Due to Testicular Feminization: A Human Gene Affecting Sex Differentiation.*† (25456)

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The chromosomal constitution of individuals suffering from gonadal dysgenesis (Turner's syndrome) has been demonstrated to consist of only 45 chromosomes, the autosomes of which were normal in number and morphology, but the sex chromosome condition being XO(1,2). Such patients do not undergo ordinary developmental changes of puberty, but remain essentially sexually infantile females. The Barr Test for nuclear chromatin, which when positive indicates existence

of at least 2 X chromosomes, is negative. Chromosomal delineation of the somatic cells of these patients demonstrated that in man, the Y chromosome contains genes necessary for development of male characteristics, a situation unlike that of *Drosophila*, but similar to that in the mouse(3). Another patient with clinical diagnosis of female pseudohermaphroditism was studied(2) and reported to display cytologically normal female (XX) chromosomes. Hungerford, *et al.* reported a case of true hermaphroditism(4) to have displayed an XX chromosomal condition. The present report deals with another female patient, exhibiting primary amenorrhea asso-

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