TABLE II. Renal Clearance of Orotidine.

	Urine flow, ml/min	Serum orotidine, cpm/ml	Urine orotidine, cpm/ml	Orotidine clearance, ml/min	Creatinine clearance, ml/min
Patient I*	7.7	50	340	53	125
" II†	3.8	39.5	784	73	157
	8.3	14.5	276	139	131

Patient III‡	Serum orotidine, μmoles %	Serum orotidine (corrected for 79% recovery), μmoles %	Urine orotidine, μmoles/min	Orotidine clearance, ml/min
Day 1 of therapy	1.5	1.9	1.6	85
Day 2	2.7	3.4	4.2	125
Day 3	3.2	4.0	4.9	120
Day 6	2.6	3.3	3.2	116

* 61-yr-old man with chronic lymphocytic leukemia.
† 57-yr-old man with chronic lymphocytic leukemia.
‡ 60-yr-old man with chronic myelogenous leukemia receiving 6-azauridine therapy.

Summary. 7-C^{14}-labeled orotidine was prepared and administered parenterally to men and rats. The compound was recovered quantitatively in the urine and cleared from the plasma at rates approaching the glomerular filtration rate.

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Potassium Concentration in the Small Intestine of Guinea Pigs. (28770)

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The efflux of potassium from the small intestine of the guinea pig has been demonstrated *in vitro* to be influenced by certain drugs(1,2,3,4). These observations appear to lend themselves to adaptation as a possible bioassay of analgesic drugs, as reported by Benjamin(4). In our own investigation, it became apparent that the relationship between drug activity and potassium efflux varied considerably among isolated strips taken from different segments of the small intestine. Moreover, we were acutely aware of differences between adjacent strips. Such irregularities would appreciably alter or mask the effects of drugs and confuse rather than clarify the influence of drugs on potassium

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"escape." Therefore, it appeared pertinent to investigate the concentration distribution of tissue potassium and potassium escape as they relate to the various segments of the small intestine.

Materials and method. Guinea pigs of both sexes, 300 to 500 g, were sacrificed by a blow on the head and the small intestine exposed. Strips of small intestine, 2.5 cm long, from the pyloric to the ileal segments were removed and lavaged with potassium-free Tyrode solution (37°C). The strips were prepared by inserting a glass rod (O.D. of 4.3 mm) into the lumen and ligating the ends of the strip to the rod. Each preparation was placed individually in a 15 ml bath of potassium-free Tyrode solution for periods ranging from 5 to 80 minutes at 37°C and 2 ml aliquots were removed for potassium determination. All potassium determinations were reported on the basis of the 15 ml volume.

Tissue potassium was obtained by extracting minced intestinal strips with 10 ml of 1.0 N HCl for 24 hours. The results obtained with this extraction process were in good agreement with those obtained by incineration of strips at 500°C for 4 hours and extracting the ashes with 1.0 N HCl. All potassium determinations were measured with a Perkin-Elmer flame photometer in duplicates. Both dry and wet weights of the intestinal strips were determined. The dry weights were determined after exposing the strips to infrared light for 15 minutes. Tissue and escape potassium values were related, for each individual strip, to both dry and wet weights.

Experimental. 1. *Tissue potassium.* In a total of 13 animals from which 800 strips were analyzed, it was found that the tissue potassium concentration of isolated strips differed among the various segments of the small intestine and between adjacent strips (Fig. 1). On the basis of wet weight, it was observed that the lowest concentration (Fig. 1) occurred in the middle third of the small intestinal tract. At the cephalic and caudal portions, the concentrations were greater. A similar relationship was observed when the dry weight of the strips was used as a basis

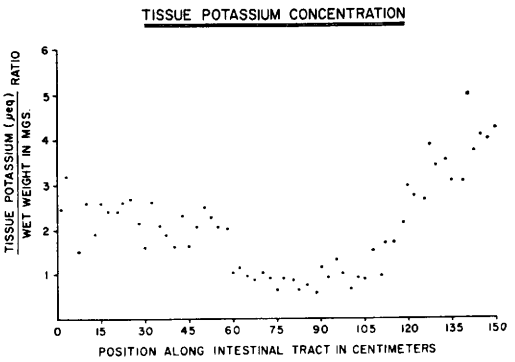

FIG. 1. Relationship of tissue potassium concentration on the bases of wet weight and spatial orientation of the intestinal strip along the length of the small intestinal tract of a guinea pig.

for evaluation. The dry weight relationships were difficult to reproduce consistently since there were certain inborn errors in the use of the infrared drying technique.

2. *Potassium escape.* In all 11 animal experiments it was found that the escape of potassium from isolated strips placed in potassium-free Tyrode solution was related to duration of exposure in the external bath. Rate of release was greatest during the first 10-minute period. Subsequently the rate decelerated, but the total amount of potassium escaping more or less reached a plateau at about 80 minutes. Accepting the 80-minute period as stable, all subsequent studies of potassium escape were carried out at this period of exposure.

Twelve additional animal experiments were performed and the results after evaluating about 1,000 intestinal strips indicated that the potassium efflux was greatest at both the cephalic and caudal segments and least at the middle segment of the small intestinal tract. Moreover, there were considerable differences in amount of escape potassium between adjacent strips. In 7 of the above animal experiments both tissue concentration and escape potassium analyses were performed. It was found that 78.5 $\pm$ 3% of the tissue potassium extractable from the isolated strips escaped into the external bath after 80 minutes of exposure.

Comments. It has become obvious to us that the concentration of potassium in the tissue of the small intestine of the guinea pig

varies considerably throughout the length of the tract. Moreover, measuring potassium escape from isolated strips as an index of drug activity can be very misleading, particularly since it has been found that the amount escaping is a function of the amount already available in the tissue. It would appear more realistic to evaluate the drug effect on the isolated intestinal strips in terms of the ratio of available tissue potassium and escape potassium.

Summary. 1. Tissue potassium concentration in the small intestine of the guinea pig differs appreciably along the length of the tract. 2. The escape of potassium from isolate strips is a function of the available tissue potassium.

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Interaction of Newcastle Disease Virus with Megakaryocytes in Cell Cultures of Guinea Pig Bone Marrow.* (28771)

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Influenza and Newcastle Disease Virus (NDV), members of the myxoviruses, agglutinate red blood cells(1), leukocytes(2) and blood platelets(3). NDV is also hemolytic(1). We have suggested(3) that the platelets and red blood cells have similar surface receptors for myxoviruses. Electron micrographs indicated that following adsorption myxoviruses were incorporated into platelets(4). Both influenza and NDV affect the coagulation and clot retraction activities of blood platelets(5), but only NDV alters the shape of the platelets, presumably because of its lytic properties(6). Since platelets are fragments of megakaryocytes, the interaction of NDV with megakaryocytes seemed worthy of investigation.

Materials and methods. Bone marrow suspensions. Bone marrow was obtained from femurs of guinea pigs weighing 300-350 g. After dissection of the femurs from the surrounding tissue they were cut lengthwise, and the marrow aseptically removed into 17 ml of Tyrode solution containing antibiotics (250 units/ml penicillin and 125 μg/ml streptomycin) in a siliconized tube. The tube was gently shaken for 2 minutes, incubated for 15 minutes at 37°C, the Tyrode supernate changed and the marrow tissue was agitated by means of a syringe to a homogenous suspension. The suspension was washed in Tyrode by centrifugation at 4°C for 5 minutes at 800 rpm. Half of the supernate was discarded, the remainder gently shaken, 8.5 ml of Tyrode added and the cells washed again for 5 minutes at 800 rpm. The cells were then suspended in 2 ml of the remaining supernate; it contained 0.3-0.4% of megakaryocytes. It was adjusted to 2×10^7 total cells/ml.

Cultures. Bone marrow cells were diluted 1:20 in nutrient medium and cultures prepared on cover glasses attached to aluminum slides(7). The nutrient medium consisted of 2/3 Tyrode's solution with antibiotics and 1/3 chicken plasma (with heparin as anticoagulant).

Virus. NDV and control allantoic fluids were prepared as previously described(5). 0.25 ml of virus suspension (hemagglutinat-

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