radiosensitive (200 r) but the other cells were not destroyed below 1200 r.

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Comparative Uptake of BR^{82} by the Hypophysis and Other Tissues.* (19506)

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Bernhardt and Ucko(1), and Zondek and Bier(2) reported that bromide was a normal constituent of the blood, that it could be detected in a variety of tissues, and that the content of the hypophysis was strikingly high. In both man and the dog hypophyseal tissue gave values of 5 to 30 mg of bromide per 100 g of wet tissue as compared to 0.5 to 1.5 mg % for the blood and most other tissues. More recently Dixon(3) and Ucko(4), using newer analytical methods, failed to confirm the existence of any preferential concentration of bromide in the hypophysis of either the ox, pig, or man. Perlman, Morton, and Chaikoff(5) employing Br^{82} could not demonstrate a high concentration of radiobromide in pooled samples of pituitary tissue from a group of 8 rats.

A selective collection of bromide by the pituitary gland would be of considerable interest because of the implication that bromine might participate in the synthesis or discharge of pituitary hormones. Moreover, a therapeutic application of radiobromine for localized radiation of the gland would be possible if the collection of the isotope greatly exceeded that attained by other tissues. In the present study a determination was made of the uptake of Br^{82} by the hypophysis and by other organs of the rat and rabbit. Any uncertainty as to the specificity or reliability of a chemical method is avoided by the use of the radioactive isotope.

Methods. Br^{82} obtained from Oak Ridge National Laboratories in the form of irradiated KBr was assayed by comparison with a Radium D plus E standard obtained from the National Bureau of Standards. Correction for the difference between the energy of beta particles of the standard and Br^{82} was accomplished by extrapolation to zero-absorption from counts obtained with a series of aluminum filters. Rate of decay was measured in order to verify the absence of appreciable quantities of K^{42} which, although present in fresh samples of KBr immediately after irradiation in the pile, rapidly disappears from the mixture because of its relatively short half-life.

Eleven rats and 12 rabbits were given Br^{82} in a dose of 0.5 to 1.0 millicurie per kilo by slow intravenous injection. The amount of KBr received averaged 28 mg/kilo and ranged from 18 to 45 mg/kilo. After 24 hours the animals were anesthetized with ether and exsanguinated by incision of the dorsal aorta. Tissue samples were weighed in the wet state. With small organs such as the pituitary, thyroid, adrenals, and ovaries, the whole gland was digested with 10% KOH and evaporated to dryness in a one-inch steel counting cup. Beta counts were obtained with a mica window Geiger counter and corrections made for self-absorption. When, as with larger organs, a sample weighing more than 0.1 g could be obtained, the activity was measured by gamma counting. This was accomplished by means

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TABLE I. Tissue Content of Br^{82} at 24 Hr. The meaning of concentration ratio is explained in the text.

Tissue	Concentration ratio and stand. error of mean 11 rats	12 rabbits	Tissue-plasma ratio 11 rats	12 rabbits
Serum or plasma	3.64 ± .05	3.18 ± .12	1.00	1.00
Whole blood	2.78 ± .03*	2.30 ± .01	.74*	.83
R.B.C.'s	1.62 ± .03*	1.82	.44*	.65
Stomach contents	—	3.67 ± .43*	—	1.01*
Stomach	2.84 ± .30	2.10 ± .24	.79	.70
Kidney	1.66 ± .30	1.51 ± .10	.46	.48
Spleen	1.55 ± .19	1.22 ± .08	.43	.39
Liver	.80 ± .08	.82 ± .08	.22	.26
Gonad: Testis	1.87 ± .03	—	.52	—
Ovary	—	1.17 ± .18	—	.37
Adrenal	.84 ± .08	.65 ± .03	.21	.21
Small intestine	1.25 ± .40*	.90 ± .02*	.36*	.25*
Large "	.48 ± .10*	—	.14*	—
Brain	.47 ± .02*	.68 ± .01	.13*	.22
Muscle	.44 ± .05	.38 ± .04	.12	.13
Thyroid gland	1.91 ± .18	.80 ± .03	.49	.26
Pituitary gland†	1.34 ± .15	.84 ± .08	.36	.28

* Performed on half of total number of animals.
† No attempt was made to separate the anterior and posterior lobes.

of an ionization chamber fitted with a well into which a test tube could be introduced, and which was connected to a Vibrating Reed Electrometer and Brown Recorder. The tissues were counted without digestion. It was established that variations in the shape or size of a sample (between 0.1 and 2 g) had no significant effect on the magnitude of a count. Standards obtained from the original solution used for preparation of the administered doses were counted along with each series of tissue samples. Physical decay of the Br^{82} was thereby corrected automatically. The content of Br^{82} was calculated as a ratio of the activity per g of tissue of an organ divided by the activity of the dose administered per g of animal.

Results and discussion. The activity of Br^{82} found in various organs after a 24-hour interval is presented in Table I. The ratio of activity of tissue to that of plasma in the final 2 columns allows comparison with similar ratios previously obtained by chemical methods. Bromide, administered in pharmacological doses, moves into the interstitial fluid in equilibrium with plasma in the same way as chloride, except in brain and spinal fluid where Br/Cl ratios are lower than in other organs(6,7). In the event that the tissue/plasma ratio of Br^{82} should exceed unity, conclusive evidence would be at hand that the cells of the organ are able to concentrate bromide ion. If the cells do not take up this ion the activity of tissue would vary with the content of interstitial fluid and the small component of retained blood. In order to detect a small increment of intracellular Br^{82} the extracellular fluid volume of the sample would have to be measured. The method here employed is applicable only for the detection of gross increases in cellular concentration.

As would be expected, the highest concentration in all groups of animals was in plasma. Red cells contained approximately half as much as plasma. The relatively high values for stomach contents and stomach tissue may be explained on the basis of partial substitution of bromide for chloride in gastric juice. I^{131} has been shown to behave similarly(8). The hypophysis did not contain a consistently higher concentration of Br^{82} than other glandular organs nor was the thyroid remarkably high in activity.

The above findings are in accord with the chemical determinations of Dixon(3) who did not find an unusually high content of bromide in the pituitary and who moreover demonstrated that the Br/Cl ratio of this organ was similar to that of a variety of other tissues in both man and several other experimental animals. His tissue-serum ratio of bromide in the pituitary of the pig was 0.22. This compares reasonably well with the ratio of 0.28 for rabbits and 0.36 for rats in the present series, and contrasts sharply with the ratio of 17 obtained by Bernard and Ucko(1).

The results are also in agreement with those of Perlman *et al.*(5), who found no selective uptake of Br^{82} by the hypophysis of the rat. At variance is the failure to demonstrate preferential uptake by thyroid tissue. Perlman and coworkers found a higher concentration of Br^{82} in the thyroid gland than in plasma, and also succeeded in augmenting the content of the gland by 30% with thyrotropin. The lack of such selective concentration of Br^{82} in the animals of the present series might be dependent on either a fortuitously low level of thyroid activity in the animals, or the existence of a state of relative iodine saturation. It would appear from the work of Bauman, Sprinson, and Marine(9) that a significant substitution of bromine for iodine requires the presence of a pre-existing iodine depletion. In a recent report by Verkhovskaya(10) the Br^{82} uptake of the pituitary, while in most instances not different from that of other organs, was in 2 out of 19 rats, 15 to 30 times greater than in the remainder of the animals. Although it is possible that a variation in the functional status of the gland might be responsible for such divergent values, a technical error would seem to be a more likely explanation. Dixon found no more bromide in the pituitary of the ox, in which gonadotropin synthesis should be very pronounced, than in the cow or bull.

Summary. In confirmation of previous work(3,5), no evidence was adduced for the selective concentration of bromide in the form of Br^{82} by the pituitary gland of the rat and rabbit. The activity of gastric contents and gastric tissues was relatively high, but no preferential uptake by thyroid tissue(5) was demonstrated.

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Some Results of Substituting Other Nerves for the Phrenic. (19507)

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The reports of Brown and Satinsky(1,2) on successful substitution of the phrenic nerve by the vagus caudal to its inferior laryngeal branch suggested the possibility of using other nerves for the same purpose. The results of a variety of such cross anastomoses are reported in this paper. In general, powerful contractions of the diaphragm are obtained on direct stimulation of these nerves, but lack of proper central control makes them inadequate to serve as the only route for respiratory impulses. In this respect the results of the present study differ from those obtained by Brown and Satinsky after vago-phrenic anastomosis, and likewise from the results reported by Colledge and Ballance(3) following cross anastomosis of the descendens hypoglossi and the phrenic nerve.

Materials and methods. Under nembutal anesthesia the trapezius portion of the acces-