shaved abdominal skin of each of 5 rabbits with no visible reaction within the ensuing 4 days.

A solution of 1200 units of bacitracin per cc of normal saline at pH 7.0 was instilled into the conjunctival sac of rabbits and the lids were held closed for 2 to 5 minutes. Even though the residual solution was not washed out, only faint evidences of irritation were noted in each of the 5 rabbits used. The faint reddening of the conjunctiva disappeared within 4 hours in all animals.

It is to be noted that the foregoing results were obtained with relatively impure commercial bacitracin concentrates as currently produced. Somewhat different results may be obtained with pure materials.

Summary. 1. Following prolonged daily administration of crude bacitracin concentrates in dogs and monkeys, no significant changes in blood morphology were observed. 2. Injection of bacitracin solution (6000 units per cc) into the shaved abdominal skin, and instillation of bacitracin (1200 units per cc) into the conjunctival sac of the rabbit caused little irritation. 3. Repeated intramuscular injection of 1000 units of bacitracin per kg 3 times each day for 23 days into the dog produced local induration. 1500 units per kg twice a day for 45 days in the same area in monkeys produced both induration and small areas of necrosis. 4. In the dog, urine samples remained negative for sugar and albumin while in the monkey, sugar and albumin appeared in the urine as the animals continued on test. 5. Large doses of bacitracin, approximating the LD_{50}, produced damage to the renal tubules, with tubular necrosis in the mouse. In the rat and the dog, the lesions were, insignificant, while in the monkey, necrotic cells were found in two instances only, and then in comparatively insignificant numbers as contrasted with the mouse.

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Comparison of Intestinal Lengths and Peyer's Patches in Wild and Domestic Norway and Wild Alexandrine Rats.*

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The two most common species of rats in the world, the Norways and the Alexandrines or roof rats, have very different resistance to poisoning with alpha naphthyl thiourea (ANTU) and show very different symptoms. Alexandrines have an LD_{50} of 250 mg/kg which is more than 30 times as high as the LD_{50} of the Norways, 6.9 mg/kg.[1] Furthermore, in the latter species ANTU produces a marked pulmonary edema and pleural effusion, while in the former species it causes no detectable change in the lungs or in any other organs.[2] At present these species differences in toxicity and physiological effects remain unexplained. The observation[2] that herbivorous animals such as rabbits, guinea pigs, meadow mice, prairie dogs, ground squirrels, and monkeys have a high resistance to ANTU poisoning and show no lung effects, while carnivorous or omnivorous animals such as dogs and pigs do show a marked pulmonary edema and pleural effusion and a relatively low resistance, may throw some light on this problem,† The Alexandrine rat superficially resembles the Norway rat; often inhabits the same houses and buildings; and in general

* This work was begun under a grant from the Rockefeller International Health Board and completed under a grant from the Public Health Service.

1 Dieke, S. H., and Richter, C. P., PROC. SOC. EXP. BIOL. AND MED., 1946, **62**, 22.

2 Richter, C. P., *J. A. M. A.*, 1945, **129**, 927.

also lives in close association with man and man's food. It may, however, belong to the herbivorous group of animals listed above, or at least when compared to the Norway it may have a more herbivorous diet. Many workers who have observed the Alexandrine rat in the field believe that it does have a predominately herbivorous diet.

To throw some light on these questions we have now undertaken several comparative studies on Alexandrine and Norway rats. Some of these studies are anatomical, concerned with physical characteristics, while others are behavioristic, concerned with dietary selections. The present report deals with a comparison of the gross anatomical characteristics of the intestinal tracts of these two species of rats; the lengths of the small and large intestines and the number of Peyer's patches on the small intestines. Intestinal lengths were selected for examination since it is well known that in general herbivores have longer large intestines than do carnivores or omnivores, and often shorter small intestines.[3,4] The laboratory or domestic Norway differs anatomically and physiologically in a number of ways from its wild Norway counterpart, so it was also included in the present study. Our observations were limited to the wild form of Alexandrine rats because these rats have not been domesticated.

Methods. The wild Norway rats were trapped in Baltimore and surrounding farms by the City Rodent Control Department and the Rodent Ecology Division of the School of Hygiene of the Johns Hopkins University. Almost all of the wild Alexandrine rats came from ships in the Baltimore harbor where they had been killed by fumigation.‡ Some of the domestic Norways came from our laboratory colony, descendants of a colony of Wistar rats established 20 years ago. Others came from the Carworth Farms, and still others from Dr. E. V. McCollum's colony. The wild and domestic Norways were killed with ether. Within one hour afterwards the intestinal tract was removed, freed from all connections, washed, and evacuated. It was suspended over a strip of cross-section paper and then both were laid flat on a table. The location of the pyloric and cecal ends of the small intestine and the cecal and rectal ends of the large intestines were marked on the paper and measured. The location and size of the Peyer's patches were also indicated by dots on the chart paper. The size of the dots was made to conform roughly to the size of the Peyer's patches. For the Alexandrine rat the technique was much the same except that the rats were killed with cyanide gas and were not always autopsied within the first few hours after death; in a few instances they were not autopsied until 18 hours post-mortem. When not autopsied immediately they were kept in a refrigerator. To give a clear definition to the Peyer's patches, particularly in very young rats, the intestines were in some instances filled with a 1% solution of hematoxylin which stained all of the walls of the intestines except the intestinal patches; in other instances the rats were given olive oil by stomach tube several hours before they were killed.

Observations were made on 54 wild Norways; 58 domestic Norways; and 50 wild Alexandrines. Each group contained approximately the same number of males and females.

Results. Intestinal Lengths. Fig. 1 summarizes the results of the observations made on intestinal lengths of the two strains of Norway rats. The ordinates give intestinal length in centimeters; the abscissae body weight in grams. The rats were fairly evenly distributed over the total body weight range. The heaviest wild Norway that we could get for this study weighed 499 g; the heaviest

† Cats, which definitely belong to the carnivorous group of animals, show all of the lung effects that are found in rats, pigs, and dogs, but they do not have as low an LD_{50}, at least when they receive the ANTU by stomach tube. Their ready ability to vomit may explain the higher LD_{50}. We have not determined the parenteral LD_{50}.

3 Buddenbrock, W. von, *Grundriss der vergleichenden physiologie,* Berlin, 1928, p. 650.

4 Dukes, H. H., *The Physiology of Domestic Animals,* 4th edition, Comstock Publishing Co., 1937.

‡ Dr. M. F. Haralson, in charge of the Quarantine Station of the City of Baltimore, kindly supplied us with these rats.

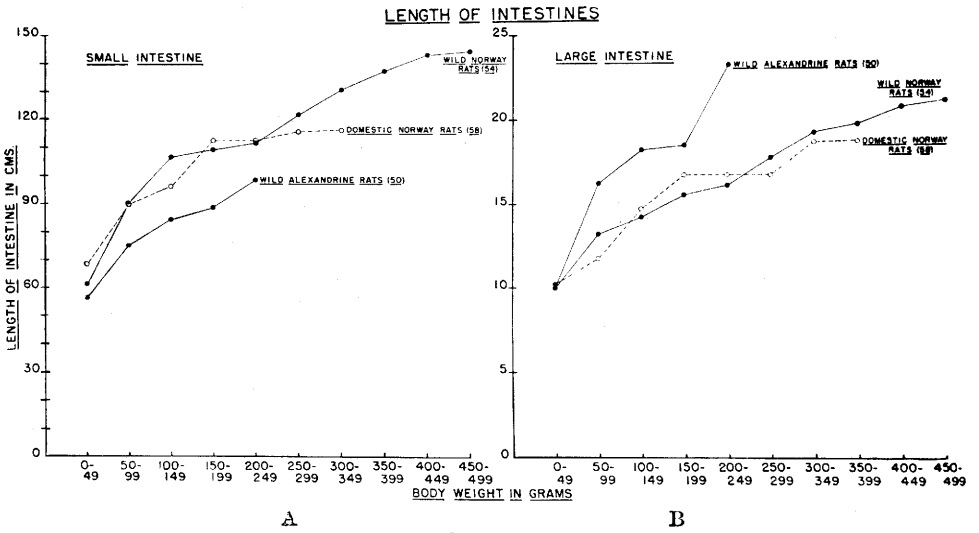

FIG. 1.

Graph showing the relation between the length of the gastro-intestinal tract and body weight. 1A. Small intestines. 1B. Large intestines.

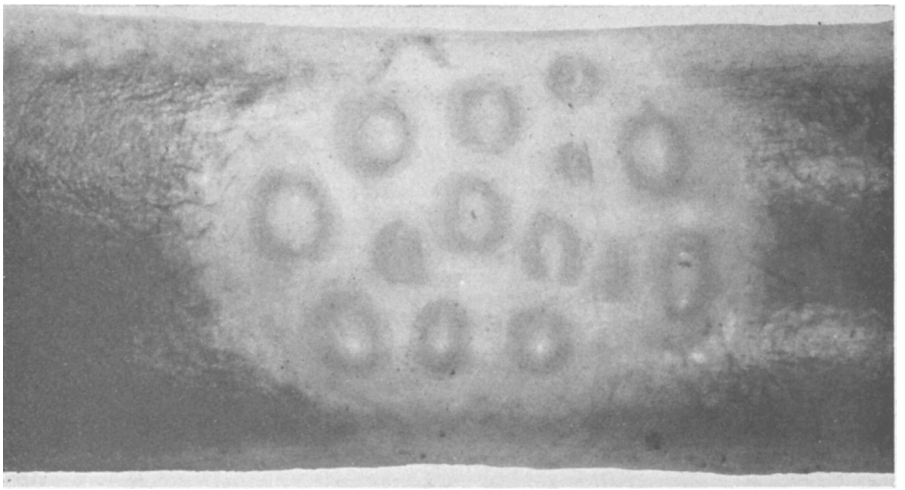

FIG. 2.

Photograph of typical Peyer's patch. Intestine filled with hematoxylin.

domestic Norway 349 g; and the heaviest Alexandrine 248 g.

Fig. 1a shows that the Norway rats, both wild and domestic strains, had definitely longer small intestines than did the wild Alexandrines. In the 200-249 g range the small intestines of the Norways had an average length of 113 cm while those of the wild Alexandrines averaged only 98 cm. The small intestines of the domestic Norway were of essentially the same length as those of its wild congener in all weight ranges investigated up to 300 g.

Figure 1b shows that the reverse relationship holds for the length of the large intestines. The wild Alexandrines had definitely longer large intestines than did either the wild or domestic Norways. For the 200-249 g weight group the length of the large intestine averaged 23.0 cm for the wild Alexandrines, and only 16.0 and 16.5 cm respectively for the wild and domestic Norways. Here again the

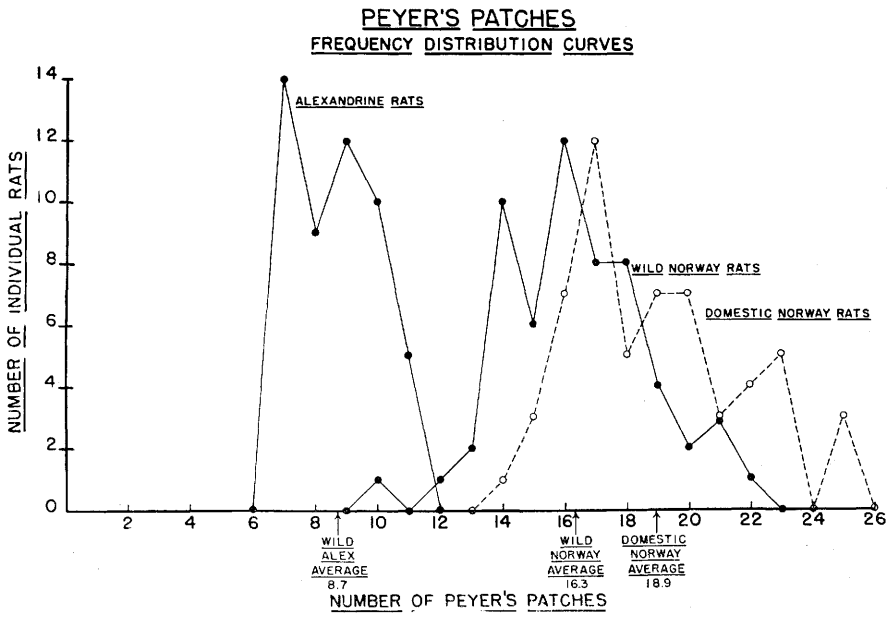

FIG. 3.
Chart showing frequency distribution curves of Peyer's patches.

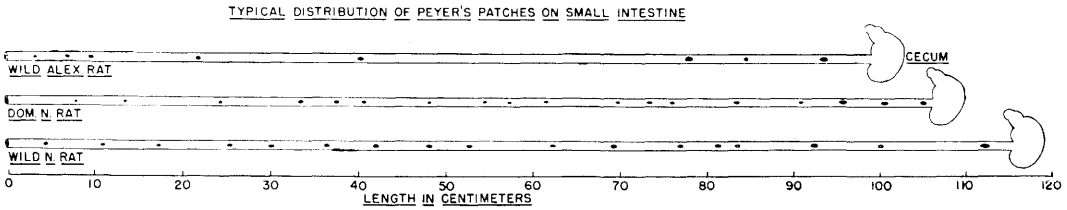

FIG. 4.
Drawing of 3 intestinal tracts from wild Alexandrines, domestic Norways, and wild Norways respectively, showing distribution of Peyer's patches.

wild and domestic Norways had essentially the same intestinal lengths in all weight groups.

Peyer's Patches. Fig. 2 shows a photograph of a Peyer's patch which is fairly typical for the two Norway strains and for the wild Alexandrines. The intestine of this rat was filled with the hematoxylin solution. This patch contained 13 follicles.

Fig. 3 gives the frequency distribution curves for the number of Peyer's patches found in the 3 types of rats. It shows that the Norway rats had many more patches than did the Alexandrine rats. For the Alexandrines the average number and its standard error were 8.7 $\pm$ 0.19, for the wild Norway 16.3 $\pm$ 0.31, and for the domestic Norway 18.9 $\pm$ 0.37. The curves for the wild Alexandrines and Norways showed almost no overlap at any point. Fig. 4 shows a typical distribution of Peyer's patches on the small intestines of a wild Alexandrine, domestic Norway and wild Norway respectively. The sizes of the patches are drawn roughly to scale. In the wild Alexandrine most of the patches were usually found near the two ends of the intestine, while in the 2 Norway types the patches were distributed at fairly regular intervals throughout the entire length of the intestines. For all the 3 types of rats the patches tended to become much larger in the lower third of the intestines. We were not able to establish any relationship between number of Peyer's patches and age or sex. At an age of approximately 15 days when the patches first became visible the number pres-

ent was comparable to that found in adult rats.

Discussion. The results show that compared to the omnivorous or carnivorous Norway rats, the Alexandrine rat has a definitely shorter small intestine and a longer large intestine. Thus, according to these findings, the Alexandrine rat either belongs to the herbivorous group of animals, or at least when compared to the Norway it must have a much more herbivorous diet. It should thus be able to utilize larger amounts of cellulose material.

These findings in themselves do not prove that the Alexandrine rat is an herbivore. They will have to be substantiated by the results of dietary selection studies. They do indicate, however, that the high resistance of the Alexandrine rat to ANTU poisoning and its lack of any lung effects may depend on some factors which the herbivorous animals have in common. The observation that the Alexandrine rats have only about half as many Peyer's patches as do the Norways has an interest quite apart from any light that it might throw on the question whether or not the Alexandrine rats belong to the herbivore. The Peyer's patches on the intestines have been counted in a number of different animals, horses, cows, sheep, pigs, dogs, cats and rabbits. They range in number from 2-4 for cats to 180-320 for horses.[5] Kelsall[6] recently counted the number of patches in different strains of mice and found that the means varied from 6.3 in the C57 black strain to 10.7 in the C3H strain, while intermediate groups including strains C, Swiss, and dba, had 8-9 Peyer's patches. Clearly, in number of patches the mice show a much closer relationship to the Alexandrine rats (which had an average of 8.7 patches) than they do to the Norways with an average of 16-18 patches.

Mice as well as the Alexandrine rats appear to prefer an herbivorous diet. They live largely on grain, flour, and cereal. This suggests that a correlation may exist between the dietary habits and the number of Peyer's patches, or indirectly the total amount of lymphoid tissue in the body. An association of a lower amount of lymphoid tissue with an herbivorous diet however would not agree with the well-known fact that in general, herbivorous animals have more lymphoid tissue than do carnivorous animals.[7] This discrepancy may result from the assumption that the number of Peyer's patches bears a direct relation to the total amount of lymphoid tissue in the body. Although in general appearance, behavior and habits, mice appear to be more closely related to Alexandrine rats than they do to Norways, they have a lower resistance to ANTU poisoning than do Alexandrines, and also show pulmonary edema and pleural effusion.

Kelsall[6] reported a direct correlation "between the amount of intestinal lymphoid tissue, as measured by the number of Peyer's patches, and the incidence of spontaneous mammary tumors." She reported that in the strain of mice which had only an average of 6.3 patches the incidence of tumors was very low, while in the breeding females of those with an average of 10.7 patches it was 95%. On this basis the Norway rats with their much higher number of Peyer's patches should exhibit a higher incidence of tumors than do the Alexandrines. Our results show that domestic Norway rats have more Peyer's patches than do the wild Norways. We have no explanation for this finding. Previous experiments have revealed other differences between the wild and domestic rats.[8-12] In this connection one of the most interesting differences is that the domestic rats have much smaller adrenal glands.[12] This recession of

5 Patzelt, V., *Handb. der Mikro. Anat. des Mensch.*, Julius Springer, Berlin, 1936, **5**, 218.

6 Kelsall, M. A., PROC. SOC. EXP. BIOL. AND MED., 1946, **61**, 423.

7 Ehrich, W. E., *Ann. New York Acad. Sc.*, 1946, **46**, 823.

8 Dieke, S. H., and Richter, C. P., *J. Pharm. and Exp. Therap.*, 1945, **83**, 195.

9 Fish, H. S., and Richter, C. P., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 352.

10 Griffiths, W. J., Jr., *Science*, 1944, **99**, 62.

11 Griffiths, W. J., Jr., *Am. J. Physiol.*, 1947, **149**, 135.

12 Rogers, P. V., and Richter, C. P., in press.

the adrenals might have resulted in an increase in lymphoid tissue, since it is well known that after removal of the adrenals the thymus and other lymphoid tissue hypertrophies.

Summary. 1. Alexandrines or roof rats (*Rattus rattus*) have shorter small intestines and longer large intestines than do Norway rats (*Rattus norvegicus*). 2. The intestines of Norway rats have about twice as many Peyer's patches on the average as do those of Alexandrine rats, averaging 16-19 as compared to 9. 3. The intestines of domestic Norway rats have more Peyer's patches than do those of wild Norways. 4. Peyer's patches first become visible when the rats reach an age of 15 days. The number does not appear to change with age.

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Effect of Interval Between Hypophysectomy and Injection of Gonadotrophin on Ovulation in the Rat.*

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Hertz and Meyer[1] have shown that if young adult female rats are hypophysectomized during the first 2 hours of proestrus ovulation is prevented during the subsequent 46-hour period. It was concluded that a hypophyseal hormone (LH) is required for ovulation in the rat and that the quantity required is secreted subsequent to early proestrus.

The work reported here was undertaken to determine how long after hypophysectomy mature follicles retain their ability to ovulate in response to a single intravenous injection of human chorionic gonadotrophin, and is preliminary to a series of experiments designed to study the hormonal requirements for normal development of follicles and ova just prior to ovulation.

Method and Materials. The 72 rats employed in this experiment were 3- to 5-month-old virgin females of the Sprague-Dawley strain.

All hypophysectomies were carried out during the first 3 hours of proestrus using virtually the same technique described by Hertz and Meyer.[1]

The intravenous injections of the purified human chorionic gonadotrophin, prepared essentially by the method of Gurin, *et al.*,[2] were given in one of the tail veins with the exception of a few injections which were made into the heart. Fifty and 100 γ doses of the dry powder in an alkaline saline solution at a concentration of 100 γ/cc were given but since the results for the 2 doses were comparable, they have been combined in Table I. The timing of the injections in relation to hypophysectomy is also shown in this table.

Autopsies were carried out 30 to 50 hours after the injections allowing ample time for all the ova which had ovulated to reach the oviduct. The sella was examined with magnifying spectacles to determine if the hypophysectomy had been complete. The ovaries and oviducts were removed and fixed in FAA or Zenker's solution.

Serial sections of one ovary and oviduct from each rat were made and stained with hematoxylin and eosin. The sections were then examined for the presence of ova in the ovi-

* Supported in part by the Research Committee of the Graduate School from funds supplied by the Wisconsin Alumni Research Foundation.

1 Hertz, Roy, and Meyer, R. K., PROC. SOC. EXP. BIOL. AND MED., 1946, **63**, 71.

2 Gurin, S., Bachman, C., and Wilson, D. W., *J. Biol. Chem.*, 1939, **128**, 525.