of death were the same as for the controls (1) pneumonia, (2) paratyphoid, (3) sarcosporidia infection, and (4) nephritis.

Whether or not any of the known facts concerning the effect of oil of gaultheria over a long period on the physiology of the organism can explain this delay in the age incidence of carcinoma is problematical. At least certain effects of this oil may be significant.

Oil of gaultheria, in common with some other salicylates,[4, 5] retards enzymic activity, especially of the digestive enzymes. According to some observers basal metabolism is elevated in patients suffering with carcinoma.[6] Is there a disturbance of basal metabolism in the earliest stages of carcinoma? Is it possible for this disturbance to be present even before cancer is obvious? Does the addition of oil of gaultheria to the diet correct this variation of basal metabolism and so exert an influence on the age incidence of cancer? These problems require more research.

These observations are being repeated on several distinct stocks of mice. At the same time the experiments call for further investigation. Is oil of gaultheria unique in this possible respect of delaying the incidence of cancer, or are other essential oils, especially those used in food flavoring, comparable? This problem is being investigated. The second problem is the effect of administration of the essential oils used in food flavoring (especially oil of gaultheria) on younger animals. It is hoped that perhaps the time at which cancer normally develops may be thus indefinitely postponed.

6495

Functional Sites in Normal and Segmentally Necrotic Renal Tubules.

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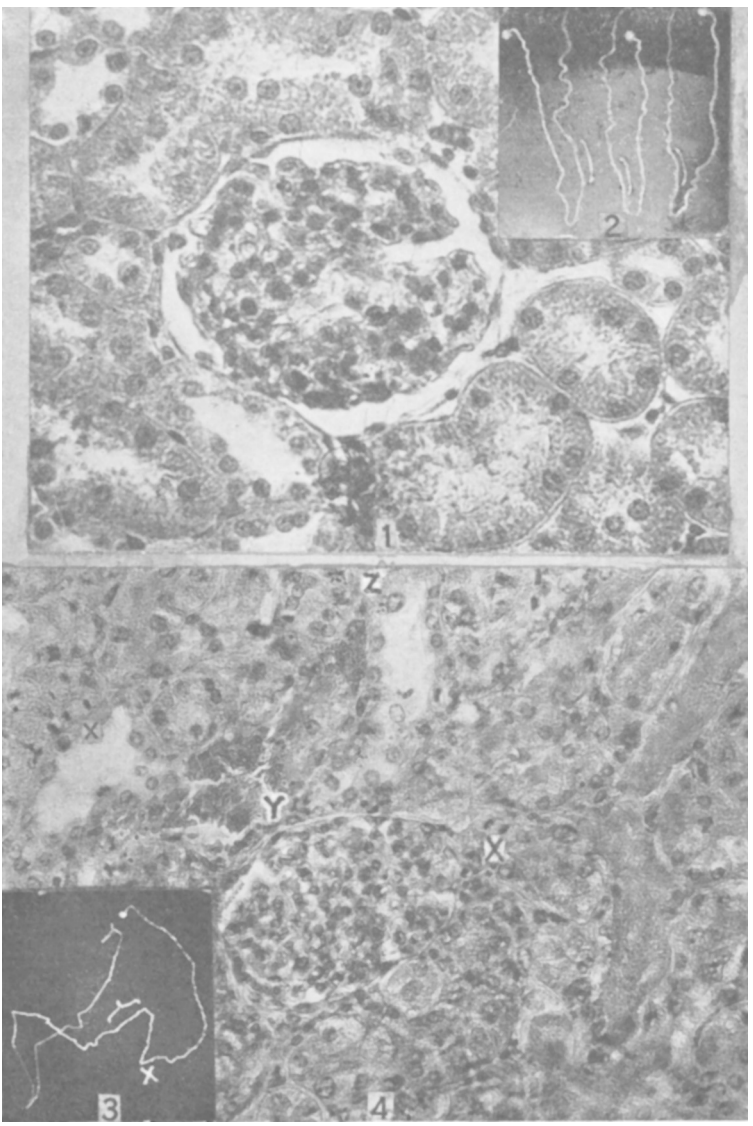
Intraperitoneal or lymph sac (frog) injections of 1% solutions of ferric ammonium citrate and sodium ferrocyanide were made in 50 rats, 10 turtles and 100 frogs. The presence of either salt or both in the kidney of these animals, depending on whether one or the

[4] Bastedo, Materia Medica, Pharmacology and Therapeutics, 3rd Ed., 1932.

[5] Cushny's Pharmacology and Therapeutics, 9th edition, 1928.

[6] Palmer, Walter W., Metabolism, Chapter 2, Vol. 3, *Nelson's Loose-Leaf Living Medicine,* November, 1926.

other or a mixture was injected, was revealed by the Prussian blue reaction. In the kidney of the rat the cellular excretion of ferric iron is sharply localized in a segment of the *proximal* convolution, 2-3 mm. long, beginning 6-8 mm. from the glomerulus (Figs. 2 and 3, portion marked by a bracket). The excretion of ferrocyanide is not similarly localized. To the extent that it may be excreted by



FIGS. 1, 2, 3, 4.

the cells of the proximal convolution, all of them appear equally active. When the 2 salts are injected as a mixture, the locus of excretion of both is the same as that stated for the excretion of the ferric salt alone. A probable explanation for this peculiarity is to appear in another publication. The accuracy of the determination of the presence and extent of this locus is the result of macerating and mounting the renal unit (Fig. 3) of the variously treated animals parallel to each other on a glass slide and studying them unstained under the microscope.

The characteristic appearance of P. blue in finely particulate form in the cells of that portion of the proximal convolution active in the excretion of iron is shown by the darker, stippled-appearing cells of the tangential section (Fig. 4, "Y"). In the kidney of the turtle and frog, the cellular excretion of both ferric iron and ferrocyanide is shared equally by the cells of the entire proximal convolution and the appearance of P. blue in such cells is very similar to that seen in the one segment of the proximal convolution of the rat.

The intracellular content of P. blue in the described sites for the excretion of iron in the kidneys of the 3 animals is increased approximately 50% by the use of urethane as an anesthetic in mildly hypnotic doses.

The cells of the ascending limb of the renal tubule of the rat and its equivalent in the turtle and frog (the proximal ⅓ of the distal convolution), those of the distal convolution proper and its duct portion in the kidney of the 3 animals are differentially resorptive as follows: water is resorbed by the cells of the ascending limb and its equivalent in the turtle and frog and solids by those of the distal convolution and its duct portion. The former is shown by the progressive luminal concentration of the iron salts (also dyes); the latter by the presence in the cells of particles of P. blue of such large size as are found elsewhere only in the lumen of this portion of the tubule (Fig. 4, black particles in section of distal convolution at left of "Z" and duct portion at its right. *Cf.*, these particles with those in section designated by "Y".)

A noteworthy support for the foregoing was found in the unexpected appearance of tubules partially necrotic in the same site of the proximal convolution for each tubule, in the kidneys of an apparently normal rat (Fig. 3, glomerulus to "X". Fig. 4, right quadrant to be compared with Fig. 1, normal renal cortex and Fig. 2, normal proximal convolutions). Since the damaged portion of the proximal convolution did not extend as far as the normal site of the excretion of iron, the appearance and presence of P. blue in various

parts of the tubule distal to the damaged portion was as already described for the normal tubule. The sharp and uniform localization of a necrotic portion within the proximal convolution indicates an antecedent functional differentiation in this portion which predisposed it to injury in this instance. Repair of the damaged epithelium was shown to have been active (Fig. 4, "X").

6496

Further Studies on Extracts Made from Holly.

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The author has shown that extracts made from holly have a digitalis-like effect upon the frog's heart.[1] The present work is a continuation and a more detailed study of the same problem, and an attempt to isolate the active principle in pure form. Some species of holly contain caffeine. A number of other substances have been isolated. Pancoast[2] found the berries of American holly *(Ilex opaca)* to contain pectin, albumin, 2 crystalline principles and organic salts of potassium, calcium and magnesium. The leaves of the European holly *(Ilex aquifolium Linne)* have been more carefully examined than those of any American species. They are said to contain a bitter principle, ilicin, a yellow coloring substance, ilexanthin, and a peculiar acid, ilicic acid. According to Allen's laboratory[3] Mate' which consists of the leaves of *Ilex paraguayensis* contains 0.13% caffeine.

Three species of the Ilex (Family Aquifoliaceae) were investigated, *I. opaca* (American Holly), *Ilex aquifolium* (European Holly) and *Ilex paraguayensis*. Both the fruit and the leaves of the European and the American holly were extracted but the leaves only of the South American species were available.

Preparation of Extracts. The first extracts were prepared by macerating the drug with alcohol. When used, the greater part of the alcohol was evaporated off and replaced by saline solution. Attempts were made to obtain the substance in the pure state and if

[1] Waud, R. A., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 976.

[2] Pancoast, D. P., *Am. J. Pharm.*, 1856, **28**, 314.

[3] Allens Commercial Organic Analysis, 4th ed., **6**, 642.