however, variations in latent period might be due to differences in the period before initial carcinogenesis, or in the number of malignant cells originally produced.* But the correlation between latent period and growth rate suggests that here, too, growth rate is an important factor. The short latent period in the induction of tumors by virus would necessarily be explained by the fact that large numbers of malignant cells are produced simultaneously. These observations are consistent with those of Mottram[9] that latent periods and growth rates of tar warts and epitheliomata extrapolate in the same way.

Summary. There is a high degree of correlation between the malignancy of chemically induced tumors, as measured by growth rate and mitotic index, and shortness of the latent period before appearance of palpable tumors. This relation holds true in the various responses of different strains of mice to the same agent, and in responses to different agents and modes of administration.

It is suggested that the growth rate of a tumor in the microscopic stage is important and may be the main factor determining the latent period in carcinogenesis.

10910 P

Observations on the Specific Cause and the Nature of "Quail Disease" or Ulcerative Enteritis in Quail.*

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Ulcerative enteritis of quail (so-called quail disease) constitutes the most important disease problem in propagation of quail in captivity. Many game breeders have had their entire stock decimated or practically wiped out by an epizootic of this disease. Once introduced on a game bird farm, the infection is extremely difficult to eradicate. Heavy losses from this disease have occurred in wild trapped quail

* Similarly, it is well known[8] that the latent period after transplantation of tumors depends on the number of tumor cells inoculated.

8 Schrek, R., *Am. J. Cancer*, 1936, **28**, 364.

9 Mottram, J. C., *J. Path. and Bact.*, 1935, **40**, 407.

* This work has been aided by a grant from Mr. A. B. Freeman and Mr. Robert Newman, of New Orleans.

held in concentration stations for restocking purposes. This indicates that the disease may profoundly affect the population density of wild quail in their natural habitat.

The purpose of this communication is (a) to record the previously unrecognized† specific cause of quail disease, (b) to describe the technical method by which others can readily confirm this, (c) to direct attention to the chronic carrier as a factor in maintaining and spreading the infection and (d) to record observations indicating transmission of the infection to young quail chicks through eggs laid by carriers.

The disease is characterized by numerous lentil-shaped intestinal ulcers located mostly in the lower third of the ilium and less numerous in the caeca. They vary in size from pin-point to half the circumference of the intestine or even larger. The small pin-point lesions are buried deep in the mucous membrane, between, and involving, the villi. Larger lesions present an open, crater-like ulcer, with very much thickened base.

In microscopic sections through the very small lesion one finds it to consist of a mass of necrotic tissue, containing large numbers of Gram-negative bacilli which can be seen to be invading the surrounding living tissue. In sections through larger lesions with open ulcers one finds this same Gram-negative bacillus and also many other secondary organisms, especially near the surface. If a small unbroken lesion (necrotic plug) is teased out, crushed on a slide and stained, one always finds large numbers of the characteristic organism. Occasionally spores can be found on slide preparations made direct from the lesions.

I have isolated this organism in pure culture 7 times—5 from intestinal lesions, one from a similar very small metastatic lesion in the liver and one from the yolk-sac of a baby quail. It is strictly anaerobic and grows slowly. The best growth I have obtained has been in glucose agar (0.25% agar) to which was added a small amount of an aqueous extract of macerated quail intestine (lower third of ilium). Oxygen must be driven off by boiling the medium before it is inoculated. In properly inoculated tubes of such medium the organism grows, in very small colonies, to within about 1 cm of the surface.

The best technic I have used for demonstrating the specific or-

† L. C. Morley and P. W. Wetmore, in a brief report published in the *Proceedings, North American Wildlife Conference*, Feb. 3-7, 1936, described a Gram-positive corynebacterium which they considered to be the cause of quail disease. We have often found the organism which they described, in open ulcerated lesions, but it is a secondary invader and is not the specific cause of the disease.

ganism is as follows: (a) Kill a sick bird, (b) clip out a piece of intestine containing a very small lesion that has not ulcerated into the lumen, (c) wash this tissue by shaking it vigorously in salt solution, (d) spread it out on a slide or glass plate, (e) with 2 teasing needles dig out the small greyish plug, (f) place it on a slide and crush and spread with the end of another slide, (g) fix with heat, and (h) stain by the Gram technic.

In carefully controlled experiments I have transmitted the disease to clean birds by feeding (1) droppings from sick birds, (2) macerated diseased intestine, (3) macerated remains of the yolk-sac (in which the bacilli had been found) of a 19-day-old quail, and (4) pure cultures of the organism; also, by placing clean birds in contaminated cages with, or just after the removal of diseased birds. Death in such infected birds usually occurs within a few days, especially if they are young birds (half grown or younger).

Of a large number of adult birds infected in my laboratory about January 1, 1939, about 75% died during the first 2 months, about 15% during the third month and about 4% during the fourth month. A few live still longer. During the entire period such birds are carriers and potential sources of infection to other birds.

Several of the known carriers laid eggs during the time and were found to have the characteristic lesions and organism when they died. In 3 instances birds laid within 48 hours before death, one of them within 2 hours. There is good opportunity for the egg to become infected during its development in the bird or to become contaminated from the feces when it is laid.

I have found the disease and confirmed the diagnosis by the presence of ulcers and the specific organism in one 10-day-old bird and in one 9 days old. In a 5-day-old bird I found acute inflammation in the section of the ilium where lesions of quail disease are found, and also found an abundance of Gram-negative bacilli that resembled the specific organism of this disease. This intestine was macerated and fed to a clean 10-weeks-old bird. It died on the fifth day and autopsy showed typical acute quail disease and the specific organism. This 5-day-old bird had been kept in a new clean pen since it was hatched and must have acquired its infection from the egg.

In 2 instances, one a 14-day-old quail and the other a 19-day-old bird, dead of quail disease, I have found the characteristic Gram-negative organism in a small encysted tumor of the remains of the yolk-sac. The bacilli were arranged in small masses or clumps within the tumor mass and gave the appearance of very small colonies that had grown there. The organism was isolated in pure culture from one of the yolk-sacs (the 14-day-old bird) and the disease was

produced experimentally in a clean bird by feeding a part of the material direct from the other. Although I have not been able to find the specific organism in an egg before hatching, the observations recorded above indicate that very young birds acquire quail disease through eggs infected with the specific organism and layed by carriers of the infection.

10911

Procaine Base Dissolved by Means of CO_2 and Its Mode of Action.*

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It is well known that the local anesthetic power of procaine hydrochloride or related local anesthetics is augmented by the addition of sodium bicarbonate or other alkaline salts. This effect is readily explained through the stronger action of the uncombined procaine base which is liberated from the salt by sodium bicarbonate, etc. However, only an unknown part of the procaine base is thus liberated since chemical equilibrium exists between procaine HCl and sodium bicarbonate and the resultant products.

The use of procaine base as such in a water soluble form became possible through the observation that procaine loosely combines with CO_2, thus being rendered water soluble, probably as a carbonate. On account of the rapid diffusion of CO_2 in the tissues, this solution can be expected to act as if the procaine base was dissolved as such.

Such a solution of procaine can be made as follows: 2 to 5 g of procaine base are suspended in 100 cc of water which is warmed to, or very slightly above, the melting point of the base (59°C). A steady stream of CO_2 is conducted through the mixture which is shaken vigorously. Further heating is avoided so long as the procaine is still a liquid, since above 60°C the solubility of CO_2 in water is too slight. Should procaine crystals appear, the suspension is reheated to the melting point. CO_2 is rapidly absorbed and the procaine goes into solution.

* This investigation has been partly made with the assistance of a grant from the Committee on Therapeutic Research, Council of Pharmacy and Chemistry, American Medical Association.