Used after adrenaline, ergotamine restored the tonus level of the muscle which adrenaline had lowered (Fig. 6).

Conclusion. Spontaneous contractions of the stomach of the cat foctus are already present in foctuses of 58 mm. body length. Both peristaltic and antiperistaltic movements can be observed. Acetylcholine and pilocarpine raises the tonus and in some instances increases the rate of contractions. The effects of these drugs are abolished by atropine. Atropine by itself has a double —inhibitory and excitatory—effect. Adrenaline in small doses stimulates and in large doses inhibits the motility. Ergotamine paralyzes the effect of adrenaline. The usual effect of adrenaline after acetylcholine is one of antagonism but sometimes the 2 drugs act synergistically.

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Tonsillitis in Dogs Due to Hemolytic Streptococci.

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Recent observations in our laboratories were reported indicating the constant presence of hemolytic streptococci of the beta type in the tonsils of the cow, sheep and hog.¹ As in man these organisms constitute part of the normal flora of the lymphoid tissue of the oropharynx of cattle, differing in certain biologic properties from the human streptococci. The rôle of these bacteria in the production of disease in animals is still undetermined. One of us² has observed the occurrence of tonsillitis in dogs with manifestations of enlarged, red tonsils, often with exudate and fever. A study was undertaken to determine the relation of the hemolytic streptococci to this tonsillar infection and the incidence of similar streptococci in normal tonsils of dogs. All of the observations were made during the months of February, March and April, 1936.

Swabs of the tonsils during the acute stage of illness in the dogs and the tonsils removed surgically from the affected dogs were

¹ Pilot, I., Buck, C., and Davis, D. J., PROC. SOC. EXP. BIOL. AND MED., 1936, 84, 233.

² Eastman, D. A., North Am. Veterinarian, 1936, 17, 37.

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sent in the mail by one of us (Eastman) and cultures made within 48 hours after taken. The tonsils were incised beneath the mucous membrane transversely and cultures obtained from the narrow exposed crypts. Dilution-pour-plates were made of the swabs and tonsils in infusion blood (5%) agar with 20% ascites fluid, and examinations made after 24 and 48 hours at 37.5° C.

Cultures of 14 pairs of tonsils yielded beta hemolytic streptococci in predominant number in 9 instances, in pure culture in 3. Of the 5 negative, 3 were overgrown with numerous colonies of the colon group. Three of the 4 swabs submitted yielded similar hemolytic streptococci, in one instance in pure culture. These results indicate a high incidence of beta hemolytic streptococci, often in predominant or pure numbers in cultures from acutely inflamed tonsils.

To determine the incidence of beta hemolytic streptococci in normal dogs, swabs of each tonsil were carefully obtained, avoiding contamination from mouth secretions and cultures made by the same technic. Twelve of 13 young dogs, apparently well, about 6 to 12 months of age, gave positive results for hemolytic streptococci of the beta type. In most instances the colonies numbered from 10% to 20% of the total number of colonies. In biologic properties these streptococci resembled the strains isolated from the dogs with tonsillitis.

One of these dogs developed symptoms like distemper and died of pulmonary complications. At autopsy the tonsils were not enlarged and the lungs revealed a disseminated broncho-pneumonia. Cultures from the lung and the tonsils yielded large numbers of hemolytic streptococci. These findings indicated the possible important rôle the streptococci of the tonsils may play as secondary invaders during distemper and other diseases, similar to the hemolytic streptococci of human tonsils in the course of measles, influenza, etc.³

The young dogs mentioned above were employed in experiments to produce sore throat or tonsillitis by swabbing the surfaces of the tonsils with cultures of strains of hemolytic streptococci. Cultures of the tonsils, temperature readings, and leucocyte counts were made prior to inoculation. In the first group of 6 dogs, swabbing with broth culture (18-hour broth) of hemolytic streptococci obtained in pure culture from an acute tonsillitis in dog failed to produce any change. This strain, however, was on artificial media for several weeks, and may have lost its virulence. A

³ Pilot, I., and Davis, D. J., J. Inf. Dis., 1919, 24, 386.

second group of 7 dogs of various breeds was inoculated by swabbing the heavy suspension of organisms obtained from 18-hour ascites-broth culture of the fresh strain isolated from lungs of the dog who died from pneumonia.

Two of the 7 dogs developed a severe reaction in the throat 48 hours later. In one, the temperature rose to 104°F. on the fourth day and examination revealed enlarged red tonsils with follicular exudate and marked congestion of the vessels of the throat. The dog appeared sick and nonresponsive. Cultures yielded predominant numbers of the streptococci. The redness and congestion declined on the fifth day and the tissues and temperature became restored to normal on the ninth day. The second dog fell sick on the second day and on the fourth was very toxic, with fever of 104.4°F., marked redness and swelling of the tonsils. Death occurred on the fifth day and at autopsy the tonsils were enlarged, covered with diffuse layer of fibrinopurulent exudate. The lymphoid tissue of the pharynx was markedly engorged and the cervical lymph glands enlarged and soft. The lungs revealed an early bronchopneumonia. Cultures of the tonsils, pharynx and lungs revealed predominant numbers of the hemolytic streptococci. The other 5 dogs at times showed some redness but no exudate, elevation of temperature or marked illness. Three had nasal discharge which yielded hemolytic streptococci.

Five dogs were inoculated with a fresh strain of an encapsulated hemolytic streptococci (S. epidemicus) of human origin from a case of acute tonsillitis. The results were uniformly negative and at no time were the encapsulated mucoid streptococci recovered from the throat of the dogs.

This same group of 5 dogs was inoculated in a similar way with a strain isolated from the lung of a second dog who died of distemper. Two became ill and revealed enlarged red tonsils, one with exudate, yielding large numbers of streptococci. Their temperature rose to 103.2°F. and 103.4°F. Recovery was apparent on the eighth day.

Twenty-two canine strains, 9 from excised tonsils, 12 from the throat of normal dogs, and one from lung of bronchopneumonia were studied and found to conform to the animal type of hemolytic streptococci. None were mucoid like *S. epidemicus*. The hemolytic zones were of the beta type measuring 2 to 4 mm. across. In tests for fibrinolysis all were negative for oxalated human blood. Eleven of the 22 hydrolysed sodium hippurate, 13 fermented trehalose, 9 did not; only one fermented sorbitol, 21 were nega-

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tive. Acid production was high, varying from pH 4.5 to 4.8. Five of 11 strains killed mice injected intraperitoneally in doses of 0.5 cc. of broth culture.

Conclusions. (1) Hemolytic streptococci are constantly present in the tonsils of apparently normal dogs (92.3%). They occur in predominant numbers in acute tonsillitis of dogs and are secondary invaders in the bronchopneumonia of distemper. (2) Experimentally acute tonsillitis is produced by swabbing freshly isolated canine strains on the surface of the tonsils of dogs. A human strain (S. epidemicus) failed to produce a reaction. (3) The streptococci from dogs conform to the animal type and differ from the human type.

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Combined Staphylococcal Endo- and Exo-Antigen.

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The pathogenic activity of microörganisms may be due to toxic substances of either cellular or extracellular nature or both. These substances are usually designated endotoxin and exotoxin, although it is likely that no sharp division line exists.

An ideal antigen for active immunization in the case of invasive microörganisms, which produce both endo- and exotoxin, should contain both endo- and exotoxic principles. Likewise, an ideal antibody-solution when administered therapeutically should be able to neutralize both the endo- and exotoxin of the homologous organism.

Staphylococcus pyogenes produces a soluble exotoxin¹ which is readily converted into formol-toxoid, and is used for active immunization of laboratory animals and human beings. The staphylococcus contains endotoxin,² and vaccines have been used for a long time in the prophylaxis and treatment of localized staphylococcal infections. Bacteriophage-solution is also used therapeutically, both on account of its lytic activity towards the organisms and be-

¹Burnet, F. M., J. Path. and Bact., 1929, **32**, 714; 1931, **34**, 471; Leonard, G. F., and Holm, A., J. Immunol., 1935, **29**, 209.

² von Lingelsheim, Aetiologie u. Therapie d. Staphylokokken Infektion, Berlin-Wien, 1900; Borrisow, P., Beitr. z. path. Anat. u. z. Allgem. Path., 1894, 16, 432.

³ Larkum, N. W., Am. J. Pub. Health, 1933, 23, 1155; Proc. Soc. Exp. Biol. AND Med., 1933, 30, 1395.