the table, it is seen that, when individuals are subjected to drugs of the same concentration (1×10^{-4}), Doryl produces vigorous intestinal contractions in the shortest period of time. Acetylcholine and physostigmine come next in order of effectiveness and appear to be equally potent. Prostigmine and acetyl-B-methyl-choline are the least effective of all the drugs utilized in this experimental work.

Summary. 1. Prostigmine, acetylcholine, carbaminoyl-choline and acetyl-B-methyl-choline produce in *Simocephalus vetulus* vigorous intestinal contractions.

2. The period which elapses between the addition of the drugs and the onset of the characteristic effect is definitely dependent, with the exception of carbaminoyl-choline, on the concentration of the drug.

3. Carbaminoyl-choline did not exhibit a graded action within the range of concentrations employed in this work.

4. Atropine blocks the action of the drugs employed in this work. However, it acts more slowly and less effectively in antagonizing the action of carbaminoyl-choline.

5. Prostigmine causes intensification and prolongation of the effects of acetylcholine and it reduces considerably the time which elapses between the administration of acetyl-choline and the appearance of the vigorous intestinal contractions.

6. In contrast with carbaminoyl-choline, a marked antagonism was found to exist between acetyl-B-methyl choline and atropine.

7. Carbaminoyl-choline differs from acetyl-choline primarily in its greater stability and more powerful action.

8. The action of prostigmine, acetyl-choline, carbaminoyl-choline and acetyl-B-methyl-choline is remarkably similar in certain respects to the action ascribed to them on the digestive tube for a number of mammals.

16386 P

A Latent Pneumotropic Pasteurella of Laboratory Animals.

E. JAWETZ. (Introduced by N. H. Topping.)

From the Division of Infectious Diseases, National Institute of Health, Bethesda, Md.

Laboratory mice are known to harbor a variety of latent pneumotropic agents including bacteria,[1] pleuropneumonia-like organisms[2,3,4] and viruses.[5-12] Increasing interest in human respiratory infections has led to many attempts to adapt agents causing such diseases to small laboratory animals. Blind passage of lung material by the respiratory route frequently leads to the production of lung lesions in the experimental animals due to the activation of latent agents. Eliminating such a possibility is an important step in ascertaining the relationship of the agent studied to the lesions produced.

In the course of attempts to adapt to Swiss

1 Dingle, J. H. Biology of the Laboratory Mouse, The Blakiston Co., Phila. 1941. Chap. 12, pp. 380-474.

2 Sullivan, E. R. and Dienes, L., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 620.

3 Edward, D. G. F., *J. Path. and Bact.*, 1940, **50**, 409.

4 Edward, D. G. F., *J. Path. and Bact.*, 1947, **59**, 209.

5 Andrewes, C. H. and Glover, R. E., *Brit. J. Exp. Path.*, 1945, **26**, 379.

6 Dochez, A. R., Mills, K. C., and Mulliken, B., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 683.

7 Gonnert, R., *Klin. Wochenschr.* 1941, **20**, 76.

8 Gordon, F. B., Freeman, G., and Clampit, J. M., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 450.

9 Heinzmann, K., *Klin. Wochenschr.*, 1941, **20**, 910.

10 Horsfall, F. L. and Hahn, R. G., *J. Exp. Med.*, 1940, **71**, 391.

11 Nelson, J. B., *J. Exp. Med.* 1937, **65**, 833.

12 Nigg, C., *Science*, 1942, **95**, 49.

mice an agent causing a minor respiratory illness in human volunteers[13] pneumonic lesions were encountered in animals inoculated intranasally with mouse lung material in serial passage. Some animals showed only a transient illness between the 4th and 15th days after inoculation; others died. In about 60% of the mice there was a grey consolidation of the upper lobes, commonly on the left, often with a yellow necrotic nodular center. Histologically the lungs showed a mononuclear exudate filling alveoli and bronchi with large necroses in the center of the involved areas. All other organs appeared normal.

In smears from consolidated lung areas, there were occasional short rods stained red by Macchiavello's method, and poorly by Gram's. From the lesions a short coccoid bipolar Gram-negative rod was cultured regularly on simple media. Cultural and biochemical characteristics suggested a close relationship of this organism to the Pasteurella group. Similar Gram-negative rods have been observed by others[14,15,16] in the lungs of mice.

At first the disease could be reproduced only by intranasal administration of infected lungs, but not by bacteria-free filtrates or pure cultures of the Pasteurella. Yet all attempts failed to demonstrate other agents which might be responsible for the process either alone or in combination with the isolated bacteria.

With serial animal passage, more of the inoculated mice became ill and showed lung lesions. In the 14th passage 85% died. The Pasteurella recovered from these animals was virulent so that intranasal instillation of undiluted 18-hour broth (about 5 x 10^6 bacteria) regularly killed 21-day-old mice with widespread bronchopneumonia in 2-5 days. Adult mice were somewhat more resistant.

A survey of Swiss mice from the breeding colonies of the National Institute of Health, the Army Medical School,* and 2 commercial breeders indicated that similar organisms could be recovered from 70-95% of the lungs ground with alundum in infusion broth. The same Pasteurella was also recovered from 70% of the lungs of normal guinea pigs and white rats. The organism seems to be acquired early in life, perhaps transmitted from the mother by the respiratory route, because it was recovered 24 hours after birth in the respiratory tract of 50% of newborn mice.

Biochemical and morphological studies supported the belief that this organism is a member of the Pasteurella group. Serological study of 26 strains showed them to belong to one group, with only minor antigenic differences between strains, but quite distinct from such related organisms as *P. pesti, P. pseudotuberculosis, P. multocida, Hemophilus* species, *A. bronchisepticus.*

Virulent strains of the organism resulting from 21 animal passages remained remarkably pneumotropic. For 21-day-old mice the LD_{50} was 5 x 10^5 organisms and the ID_{50} (producing pulmonary consolidation) about 10^4 bacteria, administered intranasally under ether anesthesia. Ten times larger doses failed to produce lesions or death if administered intravenously, intraperitoneally, or subcutaneously to young mice, rabbits, guinea pigs, cotton rats, white rats, hamsters, and chickens. After intranasal inoculation of sublethal doses into young mice the Pasteurella could be recovered for 4 days from lungs, liver, spleen, kidney, and heart blood. During this period the animals were hunched, ruffed, dyspneic, cyanotic, anorexic and "chattering." Later the symptoms of illness disappeared and bacteria were found only in the lung lesions, often persisting for 2 months or longer.

With intracerebral inoculation of mice the LD_{50} was 10^4 organisms, and death occurred within 24-48 hours from a brain abscess without systemic dissemination of bacteria.

The following findings seem to establish the relationship of this Pasteurella to the described disease of mice:

[13] Topping, N. H. and Atlas, L. T., *Science*, 1947, **106**, 636.

[14] Andrewes, C. H., Laidlaw, P. P., and Smith, W., *Lancet*, 1934, **227**, 859.

[15] Hoyle, L., *J. Path. and Bact.*, 1935, **41**, 163.

[16] Kairies, A. and Schwartzer, K., *Zentr. Bakt. Abt. 1. Orig.*, 1936, **137**, 351.

* Through the courtesy of Dr. J. E. Smadel.

1. Pure cultures of the virulent organism regularly produce the disease.

2. Mice immunized with living avirulent or killed bacterial vaccines withstand massive challenge infection.

3. Infected mice can be cured by treatment with streptomycin 0.1 g/kg/day for 4 days. The Pasteurella is inhibited by 2-4 units streptomycin/cc of medium. If mixed with infectious lung suspensions streptomycin regularly prevents the lesions and disease due to this Pasteurella.†

4. Specific antisera protect against the disease after inoculation with infectious lung material or cultures.

A full account of this Pasteurella and its host-parasite relationships will be published later.

Summary. A latent pneumotropic Pasteurella was isolated from the lungs of healthy laboratory animals. In serial passage of lung material this organism was responsible for striking lung lesions, disease and death of Swiss mice. Streptomycin cured infected animals and could be used to prevent transfer of the latent Pasteurella in serial passage of lung material.

† The Gram-negative organism removed by streptomycin from passage lung material by McKee and Hale (*Science*, 1947, **105**, 41) may have been identical with the Pasteurella described here.

16387

Effect of Continued Desoxycorticosterone Administration in Hypertensive Subjects.*

GEORGE A. PERERA.

From the Department of Medicine, Columbia University College of Physicians and Surgeons, and the Presbyterian Hospital, New York City, N. Y.

In hypertensive individuals, as compared to those with normal blood pressure, an accelerated pressor response has been observed following the subcutaneous administration of desoxycorticosterone acetate (DCA).[1] Studies are now reported concerning the effects of this steroid on the blood pressure, electrolyte and fluid balance when injected into patients with hypertensive vascular disease for longer periods.

Methods. Two men and 3 women with uncomplicated hypertensive vascular disease were observed on the wards of the Presbyterian Hospital. The criteria in selection of patients and the methods employed were identical to those previously described,[2] all subjects being maintained on a constant dietary, fluid and sodium chloride intake. Following a 3-week baseline period, DCA† was injected subcutaneously in doses of 10 mg daily for 30 days in 4 patients; a fifth received 20 mg daily for 50 days.

Results. The expected increase in weight and hemodilution which follow DCA injection were noted, together with slight reduction in urinary volume and evidence of sodium and chloride retention.[1-3] These alterations were, however, limited to the first 7-10 days of treatment, and the weight curve, hematocrit, serum protein concentration, urinary volume, 24-hour urine sodium and chloride values returned to baseline levels by the end of the second week. Serum volume, measured with the blue dye T.1824 at weekly intervals

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1 Perera, G. A. and Blood, D. W., *Ann. Int. Med.*, 1947, **27**, 401.

2 Perera, G. A. and Blood, D. W., *J. Clin. Invest.*, 1947, **26**, 1109.

† Desoxycorticosterone acetate (Doca) was supplied through the generosity of Dr. K. W. Thompson of Roche-Organon, Inc., Nutley, N. J.

3 Clinton, M., Jr., and Thorn, G. W., *Bull. Johns Hopkins Hosp.*, 1943, **72**, 255.