grafts reveals normal cortex tissue. Adequate evaluation of the condition of the medulla has not yet been made but the indications are that it has degenerated. Since it is highly improbable that such grafts would reestablish nerve connections, it appears that nervous innervation is not necessary for a normal secretory activity of the cortex. Also, since the medulla has been shown to be non-functional when denervated we assume that it could have played no part in maintaining the normality of these animals.

7042 C

Relation of Resistance and Allergy in Tuberculosis as Shown by Vaccinating Rabbits with B. C. G.

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Resistance. Resistance to a subsequent inoculation of a virulent bovine strain of the tubercle bacillus was developed by vaccinating with B. C. G. Four rabbits were inoculated at 4 weekly intervals with 1 mg. of B. C. G. in 1 cc. of salt solution in each of the following methods: (1) living organisms, subcutaneously; (2) living organisms, intravenously; (3) heat killed (60° C. for 30 minutes) organisms, subcutaneously; and (4) heat killed organisms, intravenously.

The basis of the 4 methods of administering the vaccine was suggested by previous experiments with streptococcic vaccination in which it was found that the intravenous method of giving the vaccine was superior to the subcutaneous method in developing resistance and in not producing allergy. This was true with both living and heat-killed organisms.

Three weeks after the last injection of the B. C. G. vaccine, 9 nonvaccinated rabbits, 4 rabbits vaccinated intravenously with the timothy grass bacillus, and the 16 rabbits vaccinated with B. C. G. were inoculated intravenously with 0.01 mg. of virulent bovine tubercle bacilli. The length of life following the injection of the virulent strain and the degree of involvement, if tuberculous lesions were present, were compared in the nonvaccinated and vaccinated injected animals.

The 9 nonvaccinated rabbits died with extensive pulmonary and generalized tuberculosis, 27, 30, 31, 36, 44, 54, 71, 76, and 97 days

respectively after receiving the lethal dose of the virulent bovine strain. The average length of life in these 9 animals after injection was 52 days.

The 4 animals which were vaccinated with the timothy grass bacillus were used for controls for specificity of any resistance which might develop from the vaccination. Following the inoculation with the bovine bacillus these 4 animals rapidly developed pulmonary and generalized tuberculosis and died 26, 33, 35, and 45 days respectively after the virulent injection. The average length of life after injection was 35 days. No protection was evident from vaccination with this organism. It was even suggested that the vaccination with the timothy grass bacillus might in some way have hastened the course of the infection.

One of the 4 rabbits vaccinated subcutaneously with living B. C. G. died the night following the injection. At necropsy no tuberculosis was found. The animal had a positive Mantoux test. It is possible that death was due to an allergic shock. The remaining 3 animals of this group were in good condition 142 days after the injection at which time they were killed. One had multiple firm tubercles in the lungs and kidneys. The amount of involvement was much less, however, than in the non-vaccinated animals. The remaining 2 animals, when killed, had no lesions. Not including the animal which died on the day of inoculation, it is seen that the average length of life of the rabbits in this group was more than 142 days.

Of the 4 animals vaccinated intravenously with living B. C. G., 2 died with extensive pulmonary tuberculosis 52 and 102 days respectively after being injected with the virulent bovine strain. The third was killed in the 141st day. Many firm tubercles were found in the lungs. The fourth animal was killed at 156 days after injection. There were several firm tubercles in the lungs and kidneys. The degree of involvement was decidedly less than in the nonvaccinated animals. The average length of life in this group was more than 113 days.

One of the 4 animals vaccinated subcutaneously with heat-killed B. C. G. died 85 days from the time of injection with the virulent bovine strain and one at 96 days. Both had extensive pulmonary tuberculosis. Two are living at 108 days but show clinical evidence of tuberculosis. The involvement in the animals which died was as great as in the nonvaccinated animals.

Of the 4 rabbits vaccinated intravenously with heat-killed B. C. G., one died with a nontuberculous bronchopneumonia 111 days

after receiving the lethal bovine injection. A few small firm tubercles were found, however, in the lungs and kidneys. The other 3 animals, though in good condition, were killed 141 days after infection. Two had a few firm tubercles in the lungs and kidneys. The degree of involvement was much less than in the nonvaccinated animals. One of the 4 had no gross or microscopic evidence of tuberculosis. The average length of life in this group was more than 141 days.

Allergy. Allergy or hypersensitiveness, indicated by a positive skin reaction following an intradermal injection of 1 mg. of old tuberculin, was studied in animals vaccinated by the above methods. Tests for hypersensitiveness were made on 30 rabbits, 9 of which were included in the experiments on resistance. Of the 30 animals, 5 were vaccinated subcutaneously with living organisms, 10 intravenously with living organisms, 7 subcutaneously with heat-killed organisms, and 8 intravenously with heat-killed organisms.

All of the 5 animals vaccinated subcutaneously with living organisms had a positive skin test 2 to 3 weeks after the last injection of the vaccine. Five of the 10 vaccinated intravenously with living organisms had positive tests for allergy. One of the 7 vaccinated subcutaneously with heat-killed organisms gave a positive test. Allergy was not present in any of the 8 animals which were injected intravenously with heat-killed organisms. The skin tests were repeated in most cases at intervals up to 16 weeks after the last injection of vaccine. A positive test did not appear later in any, if it had not been present at the first testing (2 to 3 weeks after the last injection of the vaccine).

It may be concluded from the greater length of life in the vaccinated than in the nonvaccinated animals, following injection, and from noting the less amount of involvement or absence of infection in the vaccinated animals and the absence of any resistance in the group vaccinated with the timothy grass bacillus, that vaccination with B. C. G., living or heat-killed, gives a marked degree of specific resistance to rabbits against subsequent infection with a virulent bovine strain. This resistance besides the greater length of life was manifested as retarded and fewer lesions and in a few cases in complete absence of lesions. While resistance was present in all of the above 4 groups, it seemed to be greatest in the groups vaccinated subcutaneously with living B. C. G. and intravenously with heat-killed B. C. G. All of the first were allergic, and allergy was not present in any of the second.

The experiments on resistance and allergy seem to show that,

while allergy may be an associated phenomenon of resistance, a high degree of resistance against a tuberculous infection may be developed without a measurable amount of allergy.

7043 P

Minute Volume Determinations in Mitral Stenosis During Auricular Fibrillation and when Restored to Normal Rhythm.

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Lewis,[1] using dogs and cats, was able to demonstrate that the minute output of the heart was decreased about 20% when the auricles were caused to fibrillate by faradic stimulation. He made the observation also that the more rapid the ventricular rate, the greater the decrease in minute volume.

Eyster and Swarthout,[2] in similar experiments on dogs, were able to produce a decrease in minute volume of from 15-79% when the auricles were caused to fibrillate. The ventricular rate in their experiments was increased after fibrillation was induced so that the actual decrease in minute volume cannot be entirely attributed to the fibrillation of the auricles.

Smith, Walker and Alt[3] found that the minute volume increased approximately 30% when normal rhythm was restored by quinidine in cases of auricular fibrillation which had been previously compensated by digitalis. Realizing that in mitral stenosis auricular contraction plays an appreciable rôle in the filling of the left ventricle, we used only mitral stenosis cases in our series. The experiments were carried out as follows: Four cases of mitral stenosis with auricular fibrillation, some of which were decompensated, were treated with digitalis until well compensated and until the ventricular rate was between 60 and 70 per minute. These cases were kept on digitalis and this rate was maintained for some period of time before the actual measurements of minute volume were begun. These were done by the acetylene method as advocated by

[1] Lewis, *J. Exp. Med.*, 1912, **16**, 395.

[2] Eyster and Swarthout, *Arch. Int. Med.*, 1920, **25**, 317.

[3] Smith, Walker and Alt, *Arch. Int. Med.*, 1930, **45**, 706.