ADSORPTION OF THE EARLY PRODUCTS OF BOVINE TUBERCLE BACILLI IN RABBITS BY ANTHRACITE DUST

BY

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The late Dr. J. Haldane, in an oft-quoted passage of an address to the South Wales Institute of Engineers in 1923, expressed his opinion that coal dust was inimical to tuberculosis. "It is difficult," he said, "to resist the conclusion that in some way the inhalation of dust in coal-mines tends to prevent phthisis."

In 1931 certain experiments were reported which showed that anthracite dust was capable of adsorbing a relatively large amount of tuberculin *in vitro* (Cummins, Weatherall, and Waters, 1931), a fact substantiated by further experiments (Cummins and Williams, 1938). Though we drew the conclusion that anthracite dust, of which a large amount is inhaled in West Wales coal-mining and in "trimming," must have the effect of adsorbing a great deal of the products of tubercle bacilli in the tissues, we were at that time unable to devise a method of testing this in the bodies of laboratory animals.

Later, however, when engaged upon experiments to show the lesions produced by anthracite and other dusts when inoculated into the lungs of rabbits along with dead human tubercle bacilli (Cummins, 1940)—an effect apparently separate from the adsorption of auto-tuberculin—I perceived that a somewhat similar experiment might serve to show whether the products of living tubercle bacilli were adsorbed or not. It was realized that the amounts of dust and tubercle bacilli might be difficult to adjust, but it was decided to try. The following experiments were therefore put in hand.

Experiment I (December 14, 1939)

Rabbits Nos. 372 and 376 were intratracheally inoculated with 0.3 c.cm. of a living emulsion of extremely virulent bovine tubercle bacilli; Rabbit No. 372 received 0.3 c.cm. of an emulsion containing approximately 0.1 mg., and Rabbit No. 376 the same amount of an emulsion containing 0.01 mg., of bacilli per 1 c.cm.

Rabbits Nos. 374, 371, and 373 were intratracheally inoculated with 0.2 gramme of anthracite dust and 0.3 c.cm. of emulsion of living bovine tubercle bacilli; No. 374 receiving this amount of an emulsion containing 0.1 mg. of the bacilli per 1 c.cm., and Nos. 371 and 373 the same quantity of an emulsion containing 0.01 mg. per 1 c.cm. The amount inoculated was in every case made up to 1 c.cm. The infection was given by means of a hypodermic syringe and needle into the trachea, exposed through a narrow incision for this purpose.

RESULT

Rabbits Nos. 372 and 376 died on January 23 and 14, 1940, respectively, of generalized tuberculosis, there being a "collar" of tuberculosis around the trachea. Rabbits Nos. 371 and 373 were killed on February 7, as both appeared to be very breathless. They were found to have extensive pulmonary tuberculosis as well as typical "collars" around their tracheas. Rabbit No. 374 died of acute diarrhoea and coccidiosis a few days after the inoculation, no visible tuberculous lesions being present, although anthracite dust and tubercle bacilli were seen by the microscope within the lungs. This rabbit is excluded from the experiment as it died from a pre-existing illness too soon to show tuberculous lesions.

Of the four rabbits surviving long enough to show results it is significant that those inoculated with bovine

tubercle bacilli alone died of generalized tuberculosis considerably before those to which anthracite and bovine bacilli had been given. The latter were killed about ten days after the death of the second "bovine alone" rabbit, and were found to have much less infection than the former two, a fact which might have allowed of their survival for some weeks longer. The production of "collars" of tuberculous tissue in all four of these rabbits caused interference with breathing and made it clear that another method of introducing the bacilli should be sought.

Experiment II (March 13, 1940)

Authority was obtained from the Medical Research Council for the purchase and maintenance of rabbits for this experiment. The method of introducing the inoculum was as follows in every case: The end of a small rubber catheter was made to fit over a rather wide and slightly bent hypodermic needle, attached to a syringe. This was introduced through the mouth into the larynx, the plunger of the syringe being drawn up so as to demonstrate that the end was in a free air tube and not in the oesophagus.

Rabbits No. 386, 387, and 390 were infected with 0.2 c.cm. of an emulsion of living bovine bacilli of a strength of 0.001 mg. per 1 c.cm., the amount being made up to 1 c.cm. by the addition of sterile saline solution.

Rabbits Nos. 388, 389, and 391 were similarly infected with 0.2 gramme of anthracite dust (under 25 μ , Lessing), together with 0.2 c.cm. of an emulsion of living bovine tubercle bacilli containing 0.001 mg. per 1 c.cm., the inoculum being made up to 1 c.cm. with sterile saline.

RESULT

Rabbits Nos. 390, 387, and 386, infected with living bovine bacilli alone, died of acute generalized tuberculosis on May 10, May 21, and June 18 respectively (see Chart),

Chart of Experiment II. Rabbits Nos. 386, 387, 390 (bovine); Rabbits Nos. 388, 389, 391 (bovine with anthracite dust).

No. 386 having, in addition to the usual lung and kidney lesions, a miliary tuberculosis of the bowel, suggesting that some of the inoculum had found its way into the intestine. Rabbits Nos. 390 and 387 had no bowel lesions; only massive tuberculosis of lungs and kidneys. It was probably owing to this division of the dose between lungs and bowel that No. 386 lived so much longer than the others.

Rabbits Nos. 388, 389, and 391 survived longer than the three animals receiving living bovine tubercle bacilli alone. Rabbit No. 388 died on June 22 from acute tuberculosis

affecting the lungs and kidneys, which had not, however, involved the intestine. Rabbit No. 389, after gaining weight to a remarkable extent, finally wasted rapidly and died on July 23. It proved to have tuberculosis of lungs, kidneys, and intestines, but the tuberculosis of the lungs, although widespread, was markedly restrained in type. Rabbit No. 391 continued to gain weight until September 13, when, as it had never shown any symptoms of illness during six months, it was killed and examined. No trace of tuberculosis was found in the organs or tissues; but, microscopically, columns of polynuclear leucocytes crowded together, apparently within lymphatics, were observed in certain areas of lung substance, although the lungs were otherwise quite healthy. Anthracite dust was also seen, though not abundantly, in the lung sections examined; and anthracite dust was present in the tracheo-bronchial lymphatic glands. Dust was to be seen as well in the lungs of Rabbits No. 388 and 389, as also in the walls of the intestine of No. 389. In all three it was in small quantity, and never in the large masses seen when anthracite and numerous dead human tubercle bacilli are introduced into the lungs.

Discussion

The average period of survival of the three rabbits infected with living bovine bacilli was seventy-five days; that of the two rabbits infected with the same dose of bovine bacilli along with 0.2 gramme of anthracite dust, and subsequently dying, was 116 days. This is what might be expected if the anthracite had adsorbed a considerable amount of the toxic substances produced by the tubercle bacilli in the course of their growth. Once the growing tubercle bacilli had been transported to new sites away from the anthracite dust they would, of course, increase rapidly and cause the death of the animal.

The complete freedom from tuberculosis of the third rabbit, No. 391, is difficult to explain. It might, of course, have died of it at a later date, but the absence of signs of tuberculosis in the tissues makes this unlikely. It was not anticipated that any of the animals infected could survive, but rabbit No. 391 appears to have developed enough immunity during the "protected" phase to stamp out its tuberculosis completely.

Conclusions

The addition of a small quantity of anthracite dust to quanta of living bovine tubercle bacilli has led, in five animals, to their survival for considerably longer periods than the five control rabbits receiving bovine bacilli alone, and, in one, to complete recovery up to six months.

This appears to be due to the adsorption by anthracite dust of a proportion of the toxic products of living tubercle bacilli in the tissues.

My thanks, for much help in these experiments, are due to Dr. Enid Williams, Mr. J. Moore, and Mr. J. Taylor. I am indebted to Dr. R. Lessing for the sample of anthracite dust used; to the Medical Research Council for authority to purchase some of the animals employed; and to Prof. J. B. Duguid for permission to work at this subject in his laboratory.

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In a letter to the *South African Medical Journal*, July 27, 1940, Dr. H. Huserl states that during the four-years war of 1914-18, when he was an Army surgeon in the Turkish Army in Asia Minor, he had a patient who had burns "of all degrees" over three-quarters of the body surface. In the absence of any other remedy he applied powdered charcoal and the patient recovered.

CONVULSIVE CARDIAZOL THERAPY IN CARDIOVASCULAR DISORDERS

BY

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In a previous paper (Good, 1940) I demonstrated that convulsive cardiazol therapy may result in the temporary appearance after the convulsion of cardiac abnormalities due to an exhaustion and anoxaemia of the heart muscle, the heart itself undergoing a temporary and varying degree of acute dilatation, with quick recovery from all of these abnormal phenomena. These occurrences can be easily demonstrated electrocardiographically and radiographically, and would seem in themselves to be contraindications to the use of convulsive therapy in patients with diseased or injured hearts. Further, the numerous abjurations of writers on this topic to eschew patients with cardiovascular disease might make one doubly sceptical if one did not reflect that there are no cases on record of catastrophes resulting from convulsive therapy in patients whose hearts are diseased.

The subject is important at the present time—as one can envisage the employment of some quick and effective form of therapy in the mental cases anticipated as the result of air raids—all the more so since it has been found by Sutherland (personal communication in June, 1940) that in some soldiers with certain types of conversion hysteria cardiazol has proved a brief and efficacious method of treatment. In my own short experience of the treatment of similar cases and in psychoneurotic states in which the predominant signs and symptoms of the patient's illness are focused upon the cardiovascular system, more especially on the heart ("the effort syndrome," "disordered action of the heart") the results have been similarly encouraging. There is the additional fact that the incidence of cardiovascular disorders is higher among civilians than among combatants, and thus the decision whether or not to use cardiazol in these cases would be one of moment.

My purpose is to demonstrate that the possibly beneficial results of convulsive therapy in cases of mental illness need not be withheld because of the existence of cardiovascular disease, past or present. To this end six cases are quoted. Only the relevant details are given.

Illustrative Cases

Case 1.—A housewife aged 49 was admitted to hospital on December 15, 1938. She was frail, undernourished, and of sallow complexion. There was no evidence of cyanosis, oedema, dyspnoea, jaundice, or arteriosclerosis. The pulse was regular in rate and rhythm, and the blood pressure was 170/100 mm. Hg. There was cardiac dullness enlarged to four and a quarter inches to the left of the mid-sternal line in the fifth interspace. The sounds were somewhat soft in tone. A harsh systolic bruit at the mitral area was conducted upwards and outwards to the posterior axillary line. A soft systolic murmur at the aortic area. There were no signs or history of cardiac decompensation. Cardiazol therapy was started on December 26 with an initial subconvulsive dose of 2 c.cm. Including her last dose on January 30, 1939, the patient received fifteen injections, none exceeding 2.5 c.cm., and she had only one convulsion—from the third dose of 2 c.cm. on December 30—with no immediate subconvulsive result. On the evening of January 7 her breathing became noisy and laboured, and her pulse poor in quality and rapid. Chest examination showed signs which were taken to be indicative of acute pulmonary oedema and which responded after some time to three doses of 1/100 grain of atropine sulphate at four-hourly intervals. The following morning she was conscious. Vomiting was copious in amount, was bilious, and was repeated ten times; jaundice started. On January 16 her