

## LETTERS TO THE EDITOR

### The Effect of *Haemophilus pertussis* Vaccine on Lymphoid Tissue in the Rat

SIR,—The hypothesis has been put forward by Miller (1961) that during embryonal and early neonatal life the thymus gland in the mouse produces the progenitors of immunologically competent cells which mature and migrate to other sites. More recently (1962), he has reported that the thymus in adult mice may be essential for complete recovery of the immune mechanism after sub-lethal irradiation. In fact, "the thymus may provide the environment wherein cells can differentiate and acquire the capacity for immunological competence by direct cell-to-cell interaction or by the elaboration of some specific humoral-like maturation factor by non-lymphoid thymic cells."

It is well known that rats (like mice) are highly resistant to histamine but they can be made sensitive by treatment with drugs such as thyroxine (Parratt and West, 1960), by removal of the adrenal glands (Spencer and West, 1962), or by a single dose of *Haemophilus pertussis* vaccine (see Sanyal and West, 1959). When given together with another antigen, *H. pertussis* vaccine also raises the blood antibody titre of that antigen so that fatal anaphylactic shock results when the challenge is made with the specific antigen. The vaccine presumably stimulates the reticulo-endothelial system of the rat (particularly the spleen and thymus) to allow a more effective production of antibody. A study has therefore been made of the effect of the vaccine on the thymus gland of the rat.

It was essential, before carrying out the study, to establish control values for the weight of the two lobes of the thymus gland at different ages. These are shown in Figs. 1 and 2, each value being the mean of 5 rats at each body weight. Although the thymus increases in size from birth until the rat weighs about 150 g. and is sexually mature, the rate of its growth in relation to the body weight reaches a maximum just about weaning time (21 days, body weight about 40 g.). This result in the rat is similar to that already reported in the mouse (Kay, Playfair, Wolfendale and Hopper, 1962).

Groups of 5 Wistar albino rats (about 150 g.) were given either *H. pertussis* vaccine (20,000 million bacteria) and killed at various times up to 17 days, or the same dose of vaccine with antigen (horse serum, 1 ml.) and challenged

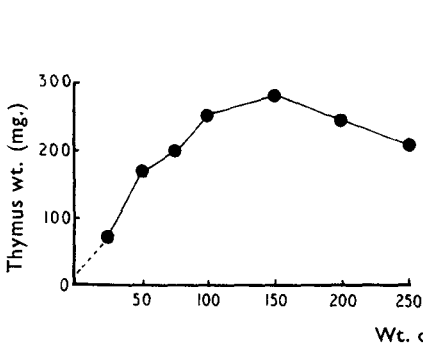


FIG. 1. The relationship between thymus weight and body weight in rats. Note the peak at about 150 g. body weight.

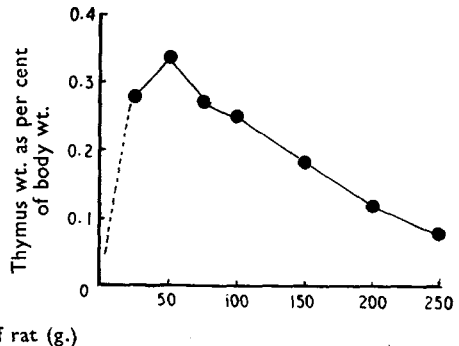


FIG. 2. The relationship between thymus weight expressed as a percentage of body weight and the weight of the animal. Note the peak at about weaning time (body weight about 40 g.).

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intravenously with horse serum (1 ml.) 10–14 days later. Other groups of rats were thymectomized 7 days before treatment with the vaccine or with the vaccine and antigen. Anaphylactic shock was severe whether the thymus was present or not and all these rats died within 4 hr. of the challenge; on dissection, the thymus glands were found to be of normal size in the unoperated animals. The thymus glands were also of normal size in unoperated rats receiving only the vaccine. But in both instances, enlargement of lymph nodes lying just above the thymus was noted. This “extra thymus” consists of a varying number (4 to 8) of nodes and is easy to dissect if haemorrhage is kept to a minimum; in control rats, it never weighs more than 40 mg. (the value reached when the rat weighs 150 g.). After *H. pertussis* vaccine, it rapidly increased in size to reach a maximum at 14 days when its weight almost equalled that of the two thymus lobes (see Fig. 3). This six-fold increase in weight of the “extra thymus” occurred equally well in the thymectomised rats receiving either the vaccine or the vaccine and antigen. A small number of rats were then splenectomised or splenectomised and thymectomised; after *H. pertussis* vaccine, these two showed grossly enlarged “extra thymus” tissue.

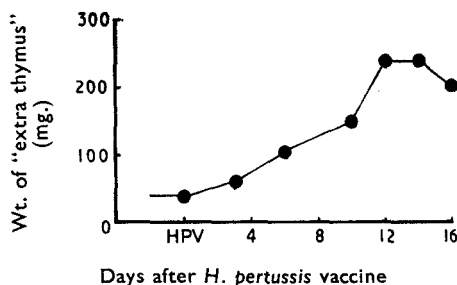


FIG. 3. The effect of a single dose of *H. pertussis* vaccine (HPV) on the weight of the “extra thymus” in rats of 150 g. body weight. Note the peak after about 14 days.

In the adult rat, therefore, the thymus and the spleen may not be important in initiating immunogenesis, and other lymphoidal tissue may be activated by procedures such as the single injection of *H. pertussis* vaccine.

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