EFFECT OF LEVAMISOLE ON THE IMMUNE RESPONSE OF PARENTERAL VACCINE FOR SWINE DYSENTERY

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Levamisole (1,2,3,5,6-tetrahydro-6-phenoylimidazo-(2,1-B) thiazole hydrochloride) is a potent antihelminthic drug. It and the racemic mixture, tetramisole, have been used widely in the therapy of nematode infections in humans and animals. The drug enhances immunity or resistance to certain infectious diseases. Thus, levamisole increases the resistance of mice to Brucella abortus infections after vaccination, although it has no effect on those with primary infections (Renoux and Renoux, 1971, 1973). The drug increased the resistance of mice to Corynebacterium pseudotuberculosis infections both in vaccinated animals and in those with primary infections (Irwin and Knight, 1975). An effect on humoral immunity is suggested by the finding that levamisole increases the number of immunoglobulin M antibody-forming cells (direct plaque-forming cells) after intravenous immunization with sheep erythrocytes (Renoux and Renoux, 1972). An effect on T-cells for mice is indicated by increased graft-versus-host reactivity of cells from levamisole-treated donors (Renoux and Renoux, 1972). Reports on the effect of incubation of lymphocytes with levamisole and mitogens concurrently are conflicting, with some authors reporting an increase (Lichtenfield et al., 1974) in mitogenic response and others reporting no change. However, the drug often appears to exert an effect on cell-mediated immunity (CMI). The purpose of this study was to determine the effect of levamisole on the immune response of swine to Treponema hyodysenteriae vaccine given parenterally.

Conventionally raised pigs (8 weeks old) were used in the study. The pigs were placed in isolation under filtered air at 72 + 2°C and fed a commercial ration of 16% crude protein containing no antibiotic. Eighteen pigs were allotted to 3 groups each. Each major group was further divided into 2 subgroups and treated in the following manner:

Group I

(a) 3 pigs - Particulate antigen (only) S.C.
(b) 3 pigs - Particulate antigen + Levamisole S.C.

Group II

(a) 3 pigs - Soluble antigen (only) S.C.
(b) 3 pigs - Soluble antigen + Levamisole S.C.

Group III

(a) 3 pigs - No antigen (Saline)
(b) 3 pigs - No antigen (Levamisole + Saline)

The pigs were vaccinated with 2 ml of the respective antigen containing 1 mg of protein/ml T. hyodysenteriae in the flank near the regional lymph node with 2 doses spaced 2 weeks apart. Soluble antigen of T. hyodysenteriae was obtained as previously described (Jenkins, 1979). Particulate antigens were whole or sonicated ruptured cells. The protein concentration was adjusted to contain 500 µ/ml. All pigs were challenged by contact with pigs affected with swine dysentery 2 weeks after the last vaccination dose.

The levamisole-treated pigs received 2 ml injections of the drug with the respective vaccine as indicated above. The humoral antibody response (HAR) of vaccinated and control pigs was determined by an immunoadherence test (IAT), while cellular immune response was determined by a leukocyte migration-inhibition agarose test (LMAT) (Jenkins, 1976; Jenkins, 1979).

Levamisole given at the recommended dose level with particulate vaccine did not significantly enhance or suppress ($P > 0.05$) the CMI response. However, a suppressive CMI effect of the drug was seen in pigs given soluble antigen, and in addition, levamisole generally suppressed the HAR throughout the immunization schedule of pigs given soluble or particulate vaccine. There was no significant suppression ($P > 0.05$) of clinical signs of swine dysentery (SD) in animals given particulate vaccine and those receiving the vaccine plus levamisole.

However, pigs receiving soluble vaccine plus levamisole had significantly ($P < 0.05$) fewer clinical signs of SD as well as less shedding episodes of T. hyodysenteriae than those given soluble antigen alone. When compared with the control pigs, vaccinated swine had fewer diarrhea days and shedding episodes of T. hyodysenteriae. However, the onset of diarrhea of vaccinated pigs was not significantly delayed ($P > 0.05$) when compared to the unvaccinated swine.

The migration-inhibition was dependent, not only on the lymphocyte, but also on the migrating polymorphonuclear leukocyte. Neutrophils and eosinophils migrate the farthest from the margin of the well, monocytes migrate feebly and lymphocytes did not migrate at all. Leukocytes from T. hyodysenteriae infected pigs were inhibited in the presence of T. hyodysenteriae antigen whereas cells of normal or uninfected pigs were not inhibited. This observation was similar to studies performed on pigs infected with African Swine Fever Virus, Pseudorabies Virus, and transmissible gastroenteritis (Schimizue, 1976; Gutekunst, 1979a; Woods, 1977).

Conclusions:

The humoral antibody response was suppressed both in animals vaccinated with particulate and soluble antigen when levamisole was simultaneously administered. In this respect, the results support the work of Renoux and Renoux (1978) who were unable to demonstrate antibody production to Brucella after vaccination. However, a CMI response was demonstratable prior to HAR. Thus, the early CMI response may play a role in the initial event after T. hyodysenteriae infection, perhaps as a host defense in delaying clinical signs of the disease, but does not prevent the development of SD.

Selected References: Renoux and Renoux, C. R.: Acad. Sci., 1971, 274D:756-767. Renoux, G. and Renous, M.: Infec. Immunol., 1973, 8:544-548. Renoux, B. and Renoux, M.: Acad. Sci., 1972, 274D: 756-767. Irwin, M. R. and Knight, H. D.: Infect. Immun., 1975, 12:1098-1103. Copeland, D. T. and Harris, J.: Cancer Chemother. Rep., 1974, 58:167-170. Jenkins, E. M.: Am. J. Vet. Res., 1979, 41:338-340. Jenkins, E. M.: Proceedings and Livestock Conserv. Inst., St. Paul, Minn., 1976, 98-101.

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