Journal of the Minnesota Academy of Science

Volume 27 | Number 1 Article 29

1959

Cortisone Acetate As a Biological Stressor

Frank Noice
North Dakota State College

I. A. Schipper
North Dakota State College

ZOOLOGY

CORTISONE ACETATE AS A BIOLOGICAL STRESSOR

FRANK NOICE* AND I. A. SCHIPPER
North Dakota State College, Fargo

INTRODUCTION:

The influence of stressors, physical, biological and nervous, upon the susceptibility of a host for a disease of a specific etiological nature initially resulted from the investigations of Hans Selye (1956). Since the conception of the stress principles, as outlined by Selye, many researchers have studied the role of stressors to increase the susceptibility of laboratory animals to certain virus diseases. Among the more dramatic experiments of the stress-virus disease interaction have been the investigations using cortisone as the stressor to enhance the poliomyelitis virus in Syrian hamsters. From the work of Shwartzman (1954), with confirmation by other researchers, it was found that the Syrian hamster is inconsistently susceptible to infection of the poliomylitis virus and then only when injected by the intracerebral route. With a pretreatment of cortisone Syrian hamsters demonstrated a violent and uniformly fatal poliomyelitis infection. Not only was the infection consistent in the cortisone treated animals but also infection could now be effected by peripheral routes, i.e. intraperitoneal, intramuscular and subcutaneous as well as intracerebrally.

This paper presents results from an experiment in which laboratory rabbits that had been pretreated with cortisone developed gastric ulcers upon injection of the bovine mucosal disease (BMD) virus-like agent.

Bovine mucosal disease was first described by Ramsey and Chivers (1953) and since that time has been reported by a number of investigators in various parts of the United States. The incidence of BMD in the upper midwest was first reported by Schipper, *et. al.* (1954) with a morbidity of as high as 90% and a mortality of approximately 10%. The symptoms of BMD as reported by Schipper are occasional high temperature (105.0 to 107.5 F.), profuse diarrhea, depression, anorexia, lacrimation, nasal discharge and salivation. Examination of the oral cavity usually revealed extensive ulceration and erosion on the dorsal and lateral tongue surfaces, hard palate, and in some instances, the gums. Necropsy examination revealed varying degrees

* Dr. Noice is also on the staff of the Biology Dept., Concordia College, Moorhead, Minnesota. Published with the approval of the Director, No. Dak. Exp. Stat., Fargo. Funds for this investigation were in part provided by the No. Central Comm. on Mucosal Disease, NC-34.

of ulceration, erosion and hemorrhage of the mucosa of the entire digestive tract, particularly in the pyloric portion of the abomasum, ileocecal and rectal areas. Ulcerations were noted in the trachea in some instances. Subepicardial and subendocardial hemorrhages were observed commonly. Lungs were usually mildly edematous and frequent pneumonic lesions were observed.

No bacterial, mycotic or parasitic etiological agent has been consistently isolated from animals infected with BMD. Attempts to transmit BMD to laboratory animals, guinea pig, rabbit, hamsters, white mice, white rat and young chickens, by all conventional routes of injection have been inconsistent or failed. Attempts to culture the agent in embryonated hens eggs has been unsuccessful.

A virus or virus-like agent was reported isolated by tissue culture methods from the spleens of animals with typical symptoms and pathology of BMD by Noice and Schipper (1959). This agent upon injection caused calves, previously found negative for BMD neutralization antibodies, to display mild symptoms of the disease. Blood from these animals contained neutralizing antibodies for BMD virus-like agent from 15 to 25 days post-injection. Upon necropsy the challenged animals had pathology typical of BMD, though less pronounced than field cases.

The tissue culture isolated virus-like agent was injected intravenously into laboratory rabbits and while such animals developed virus neutralizing antibodies from 10 to 20 days post injection no symptoms or pathology of BMD were demonstrated.

METHODS AND MATERIALS:

40 laboratory rabbits of approximately the same age and weight were selected and housed in separate cages with individual feed and water containers. Preinjection blood was obtained by cardiac puncture from each of the 40 animals, the serum of which was tested and found negative for BMD neutralization antibodies.

20 rabbits were injected intramuscularly with 25 mg. of cortisone acetate* daily for 5 days resulting in a total dosage of 125 mg. Ten of the animals (lot 1) were then injected intravenously with 5 ml. of the tissue culture virus of a constant titer. 10 rabbits (lot 2) did not receive injections of the virus-like agent and served as controls on the effect of the cortisone. 10 rabbits (lot 3) were injected intravenously with 5 ml. of the virus-like agent without having had pretreatment with cortisone to serve as controls on the effect of the agent alone. The remaining 10 rabbits (lot 4) were not injected with either cortisone or the agent to serve as complete controls on the experiment.

All the animals were bled by cardiac puncture 15 and 30 days following the date of the virus-like agent injections. 30 days following the agent injection all the animals were sacrificed for necropsy.

RESULTS:

The experimental results are tabulated in Table 1. The gastric ulcers demonstrated in 6 of the animals of lot 1 were well defined and apparent to the naked eye. The diameter of such ulcers varied from

*Cortone acetate ®, Merck Sharp and Dohme.

2 to 8 mm., and from histological sections it was seen that the ulceration extended into the submucosa. 3 of the 5 animals from lot 1 that did not show the ulceration of the gastric mucosa displayed a definite hemorrhage in that tissue. The hemorrhaged areas varied from petechial to diffuse. Such hemorrhages were also apparent on the gastric mucosa of animals of lot 1 that did have the ulcers. Only one animal from lot 1 showed no pathology of the gastric mucosa. No other pathology to an organ or tissue other than the gastric mucosa was observed either grossly or histologically in the animals of lot 1. Symptoms of infection of animals in lot 1 prior to necropsy were inconsistent but when present consisted of nasal discharge and diarrhea. The only pathology observed in animals of lot 2 was a general inflammation of the gastric mucosa of 2 of the 10 animals, neither of which had any hemorrhage, ulceration or erosion of the gastric mucosa. The animals of lots 3 and 4 were negative for pathology.

Postinjection serum from all animals of lots 1 and 3 obtained either at the 15 or 30 day bleeding intervals demonstrated BMD virus-like agent neutralization antibodies. No such antibodies were demonstrated from serum from animals of lots 2 and 4.

TABLE 1. EXPERIENCE AND RESULTS

	Tissue culture virus injection	Cortisone pre-treatment	Gastric ulceration and/or gastric hemorrhage	BMD neutralizing antibodies
Lot 1 10 animals	10	10	10/9	10
Lot 2 10 animals	0	10	0/0	0
Lot 3 10 animals	10	0	0/0	10
Lot 4 10 animals	0	0	0/0	0

SUMMARY:

A virus-like agent was isolated from cattle having symptoms and pathology typical of bovine mucosal disease. Laboratory rabbits having been pretreated with cortisone acetate, developed ulcers and/or hemorrhage of the gastric mucosa upon injection of this virus-like agent. Control rabbits that received the virus-like agent or cortisone alone did not demonstrate such pathology.

LITERATURE CITED

NOICE, F. AND SCHIPPER, I. A. 1959. Isolation of mucosal disease virus by tissue cultures in mixture 199, Morgan, Morton and Parker. *Proc. Soc. Exp. Biol.* and *Med.* 100:84-86.

RAMSEY, F. K. AND CHIVERS, W. H. 1953. Mucosal disease of cattle. *North Am. Vet.* 34:629-633.

SCHIPPER, I. A., EVELETH, D. F., SHUMARD, R. F., AND RICHARDS, S. H. 1955. Mucosal disease of cattle. *Vet. Med.* 50:431-434.

SELYE, H. 1956. *The Stress of Life.* New York. McGraw-Hill Book Company, Inc.

SHWARTZMAN, G. 1954. New aspects of pathogenesis of experimental poliomyelitis. *Jour. of the Mt. Sinai Hosp.* 21:3-18.