rabbit to the somatic polysaccharides of Gram-negative bacteria. Further systematic work will be required to delineate the salient features of the hosts' immunological reactions to this kind of bacterial antigen. Nevertheless these experiments provide strong indications that the antibody response evoked by these polysaccharide complexes has distinctive characteristics which set it apart from the pattern established for other kinds of antigens.

Summary. The immunoglobulins of rabbits injected with bacterial cells or isolated somatic antigen of *Salmonella enteritidis* and *Escherichia coli* were separated by Sephadex G-200 gel filtration and the distribution of high and low molecular weight antibodies measured by bactericidal and other techniques. High molecular weight bactericidal antibody was the predominant form produced regardless of amount, form, or schedule in which somatic antigen was administered. However, evidence was obtained that significant amounts of 7S antibody could also be produced.

Addendum. The report by Pike and Schulze on production of 7S and 19S antibodies to the somatic antigen of *S. typhosa* in rabbits (Proc. Soc. Exp. Biol. Med., 1964, v115, 829) appeared after our manuscript had been submitted for publication. Although dealing with the same general issue these papers differ considerably; viz., the present work employed additional enterobacterial specificities, compared bacteria and isolated somatic antigens, utilized a different procedure for serum fractionation and depended on different methods for measurement of antibody activities.

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Suppression of Corticosteroid Production in the Dog by Monase. (29387)

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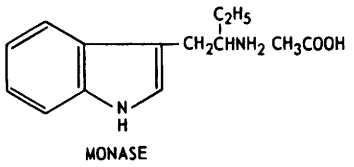
Clinical toxicity encountered following administration of 3-(2-aminobutyl)-indole acetate (Monase*—Fig. 1) has included syncope and hypotension. Hence the effects of this compound on adrenocortical function were studied.

Pharmacologic agents which inhibit the secretion of adrenocortical hormones may act

* The Upjohn Co., Kalamazoo, Mich.



MONASE

3-(2 AMINOBUTYL)-INDOLE ACETATE

FIG. 1. Structural formula of 3-(2-aminobutyl)-indole acetate (Monase).

directly on the adrenal cortex by producing cytotoxic effects(1), inhibiting enzyme systems(2,3) and, indirectly, by acting on the anterior pituitary gland(4) or sensitive loci in the central nervous system(5,6).

In the experiments to be reported here, it was found that Monase inhibited the 17-hydroxycorticosteroid output of dogs anesthetized with pentobarbital.† A continuous infusion of ACTH blocked this steroid-depressant action. Further, the adrenocortical secretion of dogs under ether anesthesia was not affected by Monase administration. Our findings suggest that Monase suppresses ACTH formation or release under certain experimental conditions.

Materials and methods. Adult mongrel male dogs (9-16 kg) were fed a standard commercial ration. Rooms were maintained at 23-25°C. Anesthesia was maintained with sodium pentobarbital or ethyl ether as noted. Techniques for adrenal vein cannulation, hypophysectomy, and 17-hydroxycorticosteroid determinations were described previously (7). Monase, in normal saline solution, was injected intravenously. ACTH‡ in saline solution was given by the same route. Methylene chloride extracts of adrenal vein plasma samples were run on paper chromatograms in the Bush (B-4) system for detection of cortisol and corticosterone by means of UV light absorption.

Results. Effect of Monase on 17-hydroxycorticosteroid production in intact dogs (pentobarbital anesthesia). Initial experiments were designed to determine the acute effects of Monase on 17-hydroxycorticosteroid levels in the adrenal effluent of dogs which had been anesthetized with sodium pentobarbital. Intravenous injection of Monase, at several dose levels, decreased the minute output of 17-hydroxycorticosteroids (Porter-Silber chromogens). A single intravenous injection of Monase at 10 mg/kg produced maximum corticosteroid suppression in the subsequent 15 to 30 minutes (8 dogs).

In each of 12 dogs receiving a single rapid intravenous injection of Monase (5 mg/kg), a fall in 17-hydroxycorticosteroid output was also seen. Observations from 2 representative animals in this series are presented in Fig. 2. Again, a significant depression of 17-hydroxycorticosteroid production occurred within 30 minutes after drug administration followed by a return to normal levels shortly thereafter. A marked reduction in hydrocortisone as well as corticosterone was seen in the chromatograms of methylene chloride extracts of adrenal vein plasma collected at 30 minutes after Monase treatment.

Another series of 4 normal dogs was infused intravenously with ACTH at the rate of 25-30 milliunits per minute.

Under these conditions an acute intravenous injection of Monase at doses of 5 mg/kg and 10 mg/kg did not depress 17-hydroxycorticosteroid output (Table I). Thus a continuous exogenous source of ACTH prevented the reduction in corticosteroid secretion seen after acute Monase treatment.

Effect of Monase on corticosteroid production in hypophysectomized dogs (pentobarbital anesthesia). Results obtained from the preceding experiments in which intact animals received continuous ACTH infusion indicated a possible relationship between the effects of Monase administration and endogenous ACTH production.

TABLE I. Lack of Corticosteroid Inhibitory Effect of Monase During Continuous ACTH Infusion in Intact Dogs.

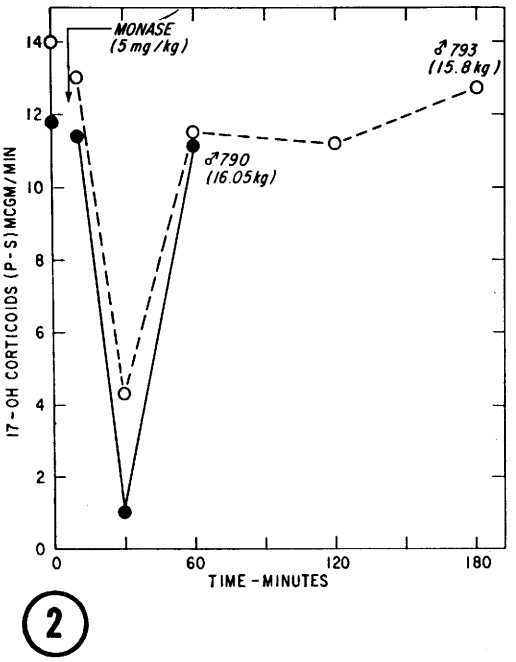
	17-OH Corticoids (μg/min)			
	Dog #1	Dog #2	Dog #3	Dog #4
Pretreatment	8.0	7.1	12.0	7.1
+15 min*	7.1	6.6	10.8	6.4
+30 "	8.4	6.7	9.6	7.0
+60 "	8.8	7.8	11.7	7.5

* Time after intravenous Monase injection. Monase: 10 mg/kg (Dogs 1 and 2); 5 mg/kg (Dogs 3 and 4).

† Sodium pentobarbital (Nembutal, Abbott).

‡ ACTHAR, Lyophilized (Armour).

In a further series of 6 dogs, adrenal vein blood samples were collected before and after Monase treatment while the animals were under sodium pentobarbital anesthesia. These animals were then hypophysectomized. One hour later the dogs were treated successively with ACTH, then with Monase followed by ACTH one-half hour later. Results from a representative experiment are shown in Fig. 3. Again, corticosteroid secretion by the adrenal cortex of this intact dog was depressed after Monase treatment (5 mg/kg). However, after hypophysectomy, the increase in 17-hydroxycorticoid secretion normally seen after an intravenous injection of ACTH (10 milliunits) was not inhibited by administration of Monase (5 mg/kg) 30 minutes earlier. Similar effects were consistently obtained in experiments on 5 additional dogs.



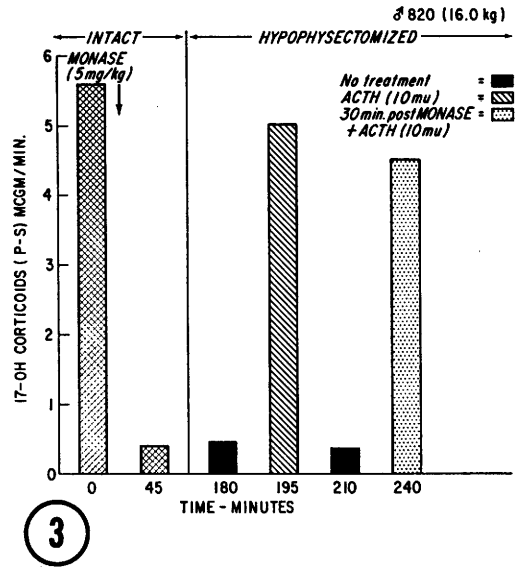


FIG. 2. Acute effects of Monase injection on output of 17-hydroxycorticosteroids in dogs under sodium pentobarbital anesthesia.

FIG. 3. Monase suppression of 17-hydroxycorticoids in an intact dog with subsequent lack of effect in same animal after hypophysectomy and ACTH treatment.

Effect of Monase on 17-hydroxycorticosteroid production in intact dogs (ether anesthesia). Ether anesthesia was used in 3 dogs from which adrenal vein blood samples were obtained before and after intravenous injection of Monase (5 mg/kg). Monase did not depress normal output of 17-hydroxycorticosteroids in adrenal venous blood samples collected at 15 minutes and 30 minutes after treatment (17-hydroxycorticosteroids, μg/min: pretreatment—dog (a) 4.7, (b) 5.4, (c) 6.5; 15 minutes post (a) 5.6, (b) 5.0, (c) 9.2; 30 minutes post (a) 5.2, (b) 7.7, (c) 8.4).

Discussion. These results demonstrate that an acute intravenous injection of Monase decreases 17-hydroxycorticosteroid levels in the adrenal vein blood of intact dogs under pentobarbital anesthesia. However, this corticosteroid depressant effect of Monase did not occur during continuous ACTH infusion in intact dogs nor when hypophysectomized dogs were injected with ACTH. These findings indicate that in the presence of Monase the steroidogenic system responsible for cortisol synthesis is sensitive to ACTH. Thus the inhibition of 17-hydroxycorticoid secretion in the intact dog under pentobarbital anesthesia appears to reflect a deficit of circulating ACTH which is overcome by the excitatory effects of ether.

Further, Monase inhibition of corticosteroid secretion was not observed in animals anesthetized with ether. In studies on rats, Royce and Sayers(8) have reported that pentobarbital anesthesia lacks the initial ex-

citatory action of ether on ACTH secretion. The increase in circulating ACTH which occurs during the early phases of ether anesthesia in intact dogs may well be adequate to account for the failure of Monase to inhibit corticosteroid secretion in contrast to the marked corticosteroid suppression observed during barbiturate anesthesia. Whether Monase alters secretion of ACTH by pharmacological effects on peripheral sensory receptors or by acting on some area of the central nervous system remains to be determined.

Summary. Clinical toxicity encountered with 3-(2-aminobutyl)-indole acetate (Monase) has included syncope and hypotension. Hence the effects of this compound on adrenocortical function were studied. A sharp decrease in adrenocortical steroid output of dogs under pentobarbital anesthesia was seen shortly after intravenous injection of this compound. Doses of 5 mg/kg and 10 mg/kg were used. Adrenal venous blood levels of 17-hydroxycorticosteroids returned to normal at 1-2 hours after drug administration. ACTH infusion as well as ether anesthesia prevented this corticosteroid depressant action. After hypophysectomy, Monase did not alter the increased corticosteroid secretion induced by exogenous ACTH. The data suggest that the pharmacologic action of Monase in reducing 17-hydroxycorticosteroid secretion in intact dogs is a result of suppression either of formation or release of ACTH in dogs under pentobarbital anesthesia.

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Identification of Rabbit, Monkey, and Dog Antibodies with PCA Activity for Guinea Pigs.* (29388)

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Allergic reactions in man are known to be caused by reagins, an antibody type distinct from human γ_2 antibodies(1). Recent studies of the antibodies responsible for anaphylactic reactions in experimental animals revealed that guinea pigs(2), rats(3), dogs (4), and mice(5) possess in addition a special antibody type, distinct from γ_2 globulins, responsible for anaphylactic reactions in each of these animal species. The anaphylactic antibodies of these various animal species and of man have faster electrophoretic mobilities than their γ_2 globulins and bind to tissues of their respective species to sensitize them for anaphylaxis. Only anaphylactic antibodies of the guinea pig and the mouse have been well characterized, being the only ones produced in sufficient quantities to allow specific isolation and study. They have been found to belong to a distinct antibody type, which has been called γ_1 globulin, to dis-

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