siblings. 2) Thyroids of untreated dwarf mice did not show accumulation of radioactive iodine (I^{131}), whereas injection of thyrotropin (0.16 U.S.P.) significantly stimulated the glands to iodine uptake. 3) From these data, and previous observations, it is concluded that the dwarf mouse is a secondary myxedematous animal because of deficient production or complete lack of thyrotropic pituitary hormone.

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Distemper and Measles Viruses. I. Lack of Immunogenic Crossing in Dogs and Chickens.* (24892)

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The demonstration of distemper antibodies in human serum and gamma globulin suggested at first an infection of humans with distemper virus at an early age, with possible clinical involvement of a respiratory nature (1,2). Although the presence of these antibodies in humans was confirmed(3) and their time of appearance in children studied(4), the question as to whether distemper virus *per se* was responsible for human illness has remained unanswered. More recently, a possible relationship between measles and distemper viruses was presented as another likely explanation for the appearance of distemper antibodies in humans(5,6,7). An investigation was therefore initiated in this laboratory to study the suggested similarity between the 2 viruses by a variety of laboratory methods. This communication reports on the search for measles and distemper antibodies in sera from puppies and chickens immunized with distemper virus, and in those of chickens which received multiple injections of measles virus.

Materials and methods. Virus strains. The canine distemper (CD) strain used for both immunization of puppies and chickens and for neutralization tests was the Lederle chick-embryo-adapted CD virus(8). Virus stock consisted of a 30% infected chorio-allantoic membrane (CAM) suspension which was maintained in frozen state. The 50% chick-embryo-infective titer (CED_{50}) was $10^{3.2}$-$10^{3.7}$ per ml. Puppies were challenged with a suspension of Snyder Hill strain CDV(9) prepared and stored as described earlier(10). A pool of Edmonston strain† measles virus (MV), having 50% tissue-culture, infective titer (TCD_{50}) of $10^{6.3}$/ml, was used for immunization of chickens. It represented a second monkey kidney passage of chick-embryo-tissue-culture adapted virus(11). Serum neutralization was carried out with a pool of the same MV strain derived from human-amnion tissue culture. This pool had a TCD_{50} titer of $10^{3.5}$-$10^{4.5}$/0.1 ml and was prepared in HeLa cells following 5 consecutive passages of the virus in this laboratory in an established human amnion cell line and one passage in HeLa. *Tissue culture.* HeLa cultures used for the propagation and titration of MV, and in the MV neutralization test, were grown in Eagle's solution(12) containing 20% calf serum. Just before inoculation, these cultures were renewed with the same solution containing 5% calf serum. *Control immune sera. CD.* A susceptible puppy was injected subcu-

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taneously with 2 ml of the 30% infected CAM suspension described above. It was bled out 5 weeks later and its serum was stored in the freezer. Repeated titrations of the serum gave neutralizing titers from 1:1000 to 1:7000 against 20 to 200 CED_{50} of CDV. *MV.* This serum was obtained from a cynomolgus monkey which, in the course of another experiment, had been simultaneously injected 1) intracerebrally with 1 ml of human-amnion-tissue-culture propagated Edmonston strain MV and 2) intramuscularly with 200 mg cortisone acetate. Repeated titrations of this serum gave neutralization indices of 316 to 3,160. *Neutralization tests. CD.* Five-fold dilutions of serum and approximately 100 CED_{50} virus suspension were mixed and incubated for 4 hours at 4°C. Each mixture was then inoculated in 0.2 ml amounts on the CAM of six 7-day-old chick embryos by Gorham's technic (13). After 7 days incubation at 35-36°C, the large top of each egg was removed and the CAM examined for lesions indicative of CD infection. Serum neutralization titers (SN_{50}) were calculated by Reed and Muench's formula(14). Titration of virus stock was carried out with each set of tests. *MV.* Undiluted normal and test sera were each mixed with equal volumes of undiluted MV, and incubated for 30 min. at room temperature. Residual virus in each mixture was titrated as follows: 10-fold dilutions were made in pH 7.2 phosphate buffer and 0.1 ml of each dilution inoculated into each of 2 HeLa culture tubes. The tubes were incubated at 37°C and examined for 14 days for the appearance of multinucleated giant cells characteristic of measles. Renewal medium was changed every 4 days. Neutralization indices were derived from the difference between virus titers in presence of normal control and test sera. All sera were routinely inactivated at 56°C for 30 minutes before use in neutralization tests. Normal and immune serum were included with each set of CD antibody titrations, and an immune serum control with all measles tests. *Complement-fixation (CF) test with MV.* CF antigen consisted of a HeLa culture virus pool which was concentrated 3 to 4 times by dialysis in the cold against undiluted, buffered glycerine. It was used in the test at a dilution of 1:4. The test was carried out by mixing 0.1 ml of 2-fold serum dilutions with 0.1 ml antigen (2 units) and 0.2 ml complement (2 units). After incubation in a 37°C water bath for one hour, 0.2 ml sheep cells sensitized with 2 units of hemolysin were added and a reading was made after further incubation for 20 minutes at 37°C. Under these conditions, the immune monkey control serum gave titers between 1:128 and 1:256.

Results. Immunization of puppies with CD virus. Of a litter of nine 10-week-old mongrel puppies, 6 were each injected subcutaneously with 2.0 ml of 30% CD-infected CAM suspension. Five weeks later, 3 of the vaccinated and the 3 unvaccinated animals were each inoculated intravenously with 1.5 ml of a 10% dog brain suspension containing about 1500 50%-lethal doses (LD_{50}) of Snyder Hill strain CD virus. All immunized puppies, including those which were challenged, remained normal throughout the observation period. In contrast, non-vaccinated puppies which were given virulent CD virus developed signs of the disease; one recovered, one had a prolonged illness and was sacrificed when moribund 44 days after inoculation and the third died of distemper on the 25th day. All puppies were bled at the time of vaccination and 4 to 5 weeks later. Bleedings were also obtained from challenged animals as follows: 8-10 weeks post challenge from those previously vaccinated as well as from the surviving control; on the 21st day from the control that died and on the 35th day from the sacrificed animal. Results of neutralization tests for CD and measles antibodies with all collected serum specimens are summarized in Table I. It is seen that all puppies, save the one that died of distemper, developed appreciable levels of CD antibodies. Titers were of the same order following vaccination alone or after vaccination and challenge. In contrast, no measles antibodies were detected in any animals either after vaccination or following challenge.

Hyperimmunization of chickens with CD or MV. Two groups of six 7-months-old Peterson strain Cornish Red Cross roosters, weighing approximately 8 lbs each, were inoculated, one with CD and the other with MV according to the following schedule: Day 0—

TABLE I. Results of Testing of 9 CD Immune Puppies for CD and Measles Neutralizing Antibodies and for Measles CF Antibodies.

Immunization status	Challenge outcome	CD-serum neutralizing dose 50 (SND_{50})			Measles antibodies					
					Pre-vaccin.		Pre-chall.		8-10 wk post-chall.	
		Pre-vaccin.	Pre-chall.*	8-10 wk post-chall.	CF	NI	CF	NI	CF	NI
Vaccinated	Not challenged	<1:5	1:1400		<1:4	0	<1:4	0		
"	"	"	1:1200		"	0	"	0		
"	"	"	1:1400		"	0	"	0		
"	Remained normal	"	"	1:1400	"	0	"	0	<1:4	0
"	"	"	1:940	1:280	"	0	"	0	"	0
"	"	"	1:1600	1:8600	"	0	"	0	"	0
Not vaccinated	Sickened—sacrificed 44th day	"	<1:5	1:330 †	"	0	"	0	"	0
"	Sickened—recovered	"	"	1:400	"	0	"	0	"	0
"	Sickened—died 25th day	"	"	1:10 ‡	"	0	"	0	"	0
CD immune dog serum control		1:1,000 to 1:7,000			CF = <1:4		NI = 0			
Measles immune monkey serum control		Not tested			CF = 1:128-1:256		NI = 315 to 3,150			

* These bleedings were obtained 4 to 5 wk following vaccine admin. † Serum drawn on 35th day after challenge. ‡ Serum drawn 4 days before death.

After bleeding, each chicken was injected intramuscularly with 2.5 ml of virus-adjuvant mixture (5 parts virus suspension; 1 part Arlacel, (mannide monooleate), 4 parts Bayol F (mineral oil)) into each of 4 sites, and 1 ml of adjuvant-free suspension intravenously. Day 7—Each chicken received 1 ml virus suspension intravenously. Day 21—Day 0 schedule was repeated. Day 31—All chickens were bled. CD virus consisted of either 10 or 20% CAM suspension, whereas MV was administered as undiluted tissue culture fluid. Results of neutralization tests for CD and measles antibodies on sera taken on Days 0 and 31 are given in Table II. It is obvious that response was strictly specific to the antigen injected; all 6 chickens of the first group developed CD antibodies, and only one of the second group failed to respond with measles antibodies.

Discussion. The suggestion by others that CD and MV may possibly share related antigenic constituents stimulated great interest on the part of the present authors. A strain of CD virus had been adapted to chick embryos in this laboratory(8) resulting in a modified agent, totally avirulent but greatly immunogenic for its natural hosts. Should measles and CD virus be truly immunologically related, attempts to immunize man against measles with modified CD virus could have a chance of success.

Under the conditions of the experiments reported above, no relationship could be demonstrated between the two viral agents. Chick-

TABLE II. Serum Neutralizing Antibodies of 12 CD or MV Hyperimmunized Chickens.

Hyperimmunized with	Measles: NI*		CD: SND_{50} titers†	
	Pre-vaccin.	31 days after 1st inj.	Pre-vaccin.	31 days after 1st inj.
Canine distemper	0	0	<1:5	1:940
	0	0	"	1:125
	0	0	"	1:420
	0	0	"	1:240
	0	0	"	1:55
	0	0	"	"
Measles	0	0	<1:5	<1:5
	0	315	"	"
	0	"	"	"
	0	"	"	"
	0	>315	"	"
	0	"	"	"
CD immune dog serum control	0		1:1,000 to 1:7,000	
Measles immune monkey serum control	315 to 3,150		Not tested	

* NI = Neutralization index.
† SND_{50} = Serum dilution causing neutralization of virus in 50% of inoculated chick embryos.

ens were selected for a parallel study of both viruses because they are not known to be susceptible to natural infection by either. In contrast, dogs injected experimentally with MV would be constantly under the threat of a natural CD infection, sometimes even under the most careful isolation conditions. Extension of this study to monkeys and ferrets is in progress, as is the testing of sera from humans who received injections of either an experimental measles vaccine or the chick-embryo-adapted strain of avirulent CD virus.

Summary. Puppies, vaccinated against canine distemper (CD) or immunized and challenged with CDV, developed high levels of homologous antibodies but failed to develop CF or serum neutralizing antibodies for measles virus (MV). Similarly, chickens hyperimmunized with CD virus did not develop measles neutralizing antibodies, although CD antibodies in appreciable levels appeared in 6 of 6 birds. Hyperimmunization of another group of chickens with MV was followed by no neutralizing CD antibodies in any of 6, whereas 5 of 6 birds gave a substantial measles response.

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Effects of Amines and Monoamine Oxidase Inhibitors on Hypothalamic Succinic Dehydrogenase Activity.* (24893)

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Although the mammalian hypothalamus appears to modulate certain activities of the anterior lobe of the hypophysis, the mechanisms remain obscure. Contributions by amines to stimulation of parts of the hypothalamus and perhaps hypothalamo-hypophyseal transmitter systems appear likely, due to: (A) the especially high concentration of certain of these amines as well as monoamine oxidase in the hypothalamus(1,2); (B) pharmacologic evidence of a close connection between central sympathetic stimulation and turnover of diencephalic and mesencephalic sympathin (3); and (C) elevation of posterior hypothalamic electrical activity, respiration and aerobic glycolysis following epinephrine administration(4,5) and elevation of supraoptic and paraventricular acetylcholinesterase and acid phosphatase after administration of serotonin(6). The work reported here employs succinic dehydrogenase system as an anaerobic test system for evaluating effects of physiologically significant amines, related compounds and monoamine oxidase inhibitors. Succinic dehydrogenase activity increases during functional stimulation in several glandular and protein-synthesizing tissues. The present work aims to determine whether this enzyme activity in the hypothalamus responds to amines and drugs possibly active in

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