side-effects of the two drugs were noted. Animals receiving Dromoran showed a lower incidence of emesis and diarrhea than with morphine.

Summary. The results indicate that Dromoran, as well as morphine, has anti-diuretic activity in the range of doses studied. Comparison of the relative anti-diuretic potencies of the two drugs must of necessity take into consideration their analgesic potencies. Clinical studies indicate that Dromoran is approximately 4 times as potent an analgesic as morphine in the human(15). Since no data are available on Dromoran's analgesic potency in the dog, the AD_{50} doses of Dromoran and morphine obtained in the dog were arbitrarily related to the analgesic potency of these drugs in man.

If the following ratio is computed:

$$\frac{\text{Equivalent analgesic dose (man)}}{AD_{50}\text{ (dog)}} = \text{Anti-diuretic index (A.D.I.)}$$

it is apparent that for equivalent analgesic effects, the larger the dose required to produce 50% inhibition of water diuresis in the dog, the less the anti-diuretic potency. The quotient of this ratio can be arbitrarily termed an anti-diuretic index (A.D.I.)

$$\text{For morphine } \frac{1}{0.9} = 1.1 \text{ (A.D.I.)}$$

$$\text{For Dromoran } \frac{0.25}{0.40} = 0.6 \text{ (A.D.I.)}$$

At equivalent analgesic doses, it is obvious that Dromoran has a lower anti-diuretic index than morphine.

A review of the literature indicated no dose-response relationships in reference to chloruretic responses to morphine. De Bodo obtained chloruresis in the dog with doses larger than those which we employed. Ferrer and Sokoloff noted chloruresis in 2 human patients using a dose of morphine lower than that used by Kraushaar who reported a depression of chloride excretion by morphine in 4 of 6 patients.

The data reported in this paper do not elucidate the mechanisms involved in the anti-diuretic responses. The inhibition of chloride excretion following the second hydration is consistent with inhibition of the posterior lobe during water diuresis. Neither morphine nor Dromoran effected this inhibition of anti-diuretic hormone secretion. The absence of chloruresis in the presence of anti-diuresis suggests that in the doses used, these drugs produce an anti-diuretic effect through a mechanism other than the release of anti-diuretic hormone from the posterior pituitary.

Conclusions. 1. Dromoran is less anti-diuretic than morphine when anti-diuretic activity is related to analgesic potency. 2. In the range of doses employed in these studies, neither morphine nor Dromoran effected a chloruresis. 3. The lack of chloruresis in the presence of anti-diuretic action suggests that these drugs do not act by liberation of the anti-diuretic hormone.

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Dual Antibody Response to Coxsackie and Poliomyelitis Viruses in Patients with Paralytic Poliomyelitis.* (18057)

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Simultaneous excretion of both Coxsackie (C) and poliomyelitis viruses from the intestinal tract of man during both periods of illness and apparent health(1-3), as well as the simultaneous recovery of these two viruses from flies trapped in poliomyelitis areas(4),

* Aided by a grant from the National Foundation for Infantile Paralysis.

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has made it important to establish whether the host is infected by both agents or whether one virus is merely in passive transit through the alimentary tract. This answer is needed before one can consider whether the symptoms of the patient represent a single or a combined infection. Patients excreting both viruses have been shown (1) to develop antibodies to the strain of C virus isolated from their stools, as well as to a homotypic (Ohio) strain. In this report we wish to present evidence that paralytic patients excreting both viruses respond serologically with antibodies to both viruses.

In the course of an investigation of the severe 1949 poliomyelitis epidemic in Easton, Pennsylvania, samples were collected from 48 consecutive patients entering the hospital for poliomyelitis.† From these we isolated *both* poliomyelitis virus and C virus from 15 patients. Two paralytic patients were selected for more detailed study.

Patient I, a 3-year-old girl, became ill on August 30 with sore throat and pharyngitis. She developed paralysis of the abdominal muscles and was admitted to the hospital on September 1. The cerebrospinal fluid contained 52 cells per cmm. She made an uneventful recovery. Both C and poliomyelitis viruses were isolated from a pool of stools collected on September 5, 6 and 7. C virus could not be recovered from throat swabs taken on September 1, 2 and 3, nor from a late stool sample of October 12. Serum was obtained for antibody tests on September 1 and again on September 30.

Patient II, a 5-year-old girl, became ill on August 30 with nuchal rigidity and weakness of the left leg. She soon developed paralysis of the left leg and weakness of the right leg and abdominal muscles. She was hospitalized on September 2. A spinal fluid examination was not done. On April 12, 1950, her left leg was still paralyzed. Both viruses were isolated from a pool of fecal specimens collected on September 3, 7 and 10. C virus was again isolated from a sample of stool collected October 4. It is worth noting that the infective titer of the stools in newborn mice fell from $10^{-3.0}$ in the acute phase specimens to $10^{-1.0}$ in the late sample. Throat swabs collected on September 2, 3 and 5 gave negative tests for C virus. Serum was obtained on September 2 and again on October 2.

The virus-containing stools of each patient were found to contain poliomyelitis virus in a titer of 10^{-2} in monkeys. This titer enabled us to use this original human source of material as the virus in the neutralization test. The C virus titer of the two virus pools in newborn mice was $10^{-1.0}$ and $10^{-3.0}$, respectively. For the C virus, the original human stool virus as well as mouse passage virus was used in neutralization tests. Sera were used in serial threefold dilutions.

The tests were set up by mixing an 18,000 r.p.m. supernate of the stool (10^{-1} concentration) with an equal volume of serum at the dilutions indicated in Table I. After an incubation period of 2 hours at room temperature, each serum-virus mixture was inoculated into 3 monkeys to test for poliomyelitis virus antibodies and into at least 8 newborn mice to test for C virus antibodies. With mouse-passage C virus, 100 ID_{50} doses were added to the serum dilutions. The highest serum dilution of Patient I which neutralized C virus on the third day of the disease was 1:10, by the thirty-second day this titer had been increased to 1:90. Calculated on the basis of that serum dilution which protects 50% of the animals, the respective titers were about 1:50 and about 1:300. The tests carried out with 100 ID_{50} mouse passaged C virus showed for the convalescent serum titers of 1:50 for complete neutralization and 1:150 for 50% protection, the acute phase serum being negative.

That Patient I also responded to infection

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† We are indebted to Dr. N. W. Larkum and Miss Natalie Levin for their generous aid in collecting the clinical samples for this study.

TABLE I. Simultaneous Development of Antibodies to Poliomyelitis Virus and C Virus.

Patient	Day of disease serum collected	ID_{50} in 10% suspension of patient's stool	Final serum dilutions			Highest serum dilution neutralizing virus completely	Dil. of serum protecting 50% of animals	Neutralization of 100 ID_{50} doses of passaged C virus: Highest serum dilution neutralizing virus completely	Neutralization of 100 ID_{50} doses of passaged C virus: Dil. of serum protecting 50% of animals
			1:10	1:30	1:90	1:270			
I		1		C virus : in mice					
	3		0/8	4/15(3)			a50	0	0
	32		0/15	0/8	0/14	3/12(3)	a300	50	150
		10		Polio virus : in monkeys					
	3		0/3	2/3		1/0	20		
	32		0/3	0/3	0/3	0/3	>270		
II		100		C virus : in mice					
	4		3/18(2)	7/14(7)		0	30	0	0
	32		0/6	0/6	0/14	4/7(3)	230	50	110
		10		Polio virus : in monkeys					
	4		1/3	3/3		0	15		
	32		0/3	0/3	1/3	1/3	270		

Denominator indicates the number of animals used per serum dilution. The numerator indicates the number of animals with disease. The number in parentheses indicates the number of mice with observable paralysis. All monkeys with disease showed some degree of paralysis (mild to severe) and all sick animals had typical poliomyelitis lesions in the spinal cord. No CNS lesions were found in monkeys which failed to develop paralysis.

with poliomyelitis virus is shown by the rise in titer between the acute and convalescent phase sera. A dilution of 1:10 of the acute phase serum neutralized completely the patient's poliomyelitis virus; the convalescent phase serum was able to do this at a dilution as great as 1:270. Using a 50% protection endpoint there was an increase of titer from 1:20 to one greater than 1:270.

Comparable increases in titer developed in the serum of Patient II. C virus excreted with her stools was completely neutralized at a dilution of 1:90 by serum obtained 32 days after the onset of the disease, whereas serum collected 4 days after the onset of the disease was negative. There was a correlative increase in titer when it was calculated on a 50% protection endpoint: the acute phase serum had a titer of 1:30 whereas the convalescent phase serum had a titer of 1:230. With mouse-passage virus, the convalescent serum yielded titers of 1:50 for complete neutralization and 1:100 for 50% protection. The acute phase serum again gave a negative test.

As in the case of Patient I, the serum of Patient II also developed neutralizing antibodies against her own strain of poliomyelitis virus. At a dilution of 1:10, serum of Patient II taken on the fourth day after the onset of the illness did not completely neutralize poliomyelitis virus; however, a 1:30 dilution of the serum taken on the thirty-second day of the disease did neutralize the virus completely. On the basis of a 50% protection endpoint, the respective titers for the acute and convalescent phase sera were 1:15 and 1:270.

When the paired sera of each patient were titrated against 100 ID_{50} of the Easton-2 strain of C virus, the same results were obtained as in the tests against the mouse-passage strains obtained from Patient I and from Patient II. Inasmuch as the Easton-2 strain is antigenically indistinguishable from Dalldorf's Type I strain, it would appear that the strains isolated from both patients belong to this latter type(3,4).

On the basis of the neutralization tests reported here and the finding of both viruses

in the stools of 13 other patients in this epidemic, we believe that the failure to detect poliomyelitis virus in the stools of a paralytic patient excreting C virus should be regarded as a technical difficulty, and should not necessarily be regarded as an indication that C virus caused the lesion resulting in paralysis. For the present, and until it is proved otherwise, the patient's paralytic manifestations should be considered to result from CNS infection with poliomyelitis virus. However, the finding of dual infections in poliomyelitis appears to occur too frequently to be regarded merely as coincidence. Is it possible that infection with poliomyelitis virus would have been a mild affair in these patients had not C virus infection been superimposed on the poliomyelitis infection? Consideration is being given to the possibility that C virus infection may be one of the predisposing factors which may turn a nonparalytic into a paralytic case.

Summary. Both poliomyelitis virus and Coxsackie virus (C virus) were isolated from the acute phase stools of several paralytic patients during an epidemic of poliomyelitis which occurred in Easton, Pa., in 1949. In 2 such cases, neutralizing antibody tests were carried out with acute and convalescent serum reacting with a suspension of virus obtained directly from acute phase stools. It was found that both patients responded to their illness by simultaneously developing antibodies both to poliomyelitis virus and to C virus.

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Effect of 17-Hydroxy-11-Dehydrocorticosterone (Compound E) and of ACTH on Arthus Reaction and Antibody Formation in the Rabbit. (18058)

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Hench and his coworkers(1) reported the beneficial effects of adrenal cortical hormone, compound E, and the adrenocorticotropic hormone in patients with rheumatoid arthritis. Subsequently, encouraging therapeutic results were obtained with these hormones in the treatment of the acute phase of rheumatic fever(2,4), periarteritis nodosa(3) and disseminated lupus erythematosus(4). These 4 diseases have in common numerous clinical manifestations and similar basic pathological alterations consisting of focal necrosis of collagen and damage to the cardiovascular system(5). Rich and Gregory(6,7) have demonstrated that hypersensitivity of the Arthus type can produce periarteritis nodosa as well as cardiovascular lesions in the rabbit resembling those of rheumatic fever. Since these observations suggest that anaphylactic hypersensitivity may play a role in the pathogenesis of this group of diseases, a study of the effect of compound E and ACTH on the development of the Arthus state in the rabbit

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