ACTH

THE ARMOUR LABORATORIES

1425 WEST 42ND STREET, CHICAGO 9, ILLINOIS · TELEPHONE YARDS 7-4100

December 14, 1951

[redacted]

Dear [redacted]:

I enjoyed very much having the opportunity to talk to you on the phone concerning your proposed experiments on the effects of ACTH on poliomyelitis virus in hamsters. It is unfortunate that I neglected to mention that a considerable amount of work has been done with ACTH on virus growth and proliferation in various species. You might be interested in reading the articles by Kalter, Proc. Soc. Exp. Biol. & Med. 74 (1950) 605-607, and Loosli, Journ. Lab. Clin. Med. 37 (March, 1951) 464. A great deal more work remains to be done to establish the role of the adrenal cortical hormones in resistance to virus infection.

We shall send you 1.4 grams of ACTH preparation 146R-S3, which has a potency of approximately 3.65 times our La-1-A Standard. The 1.4 grams which you will receive is, therefore, equivalent to approximately 5.2 grams of the Standard material. We estimate that 2.74 milligrams of this material will be approximately equivalent to your 10 milligram daily requirement. I would suggest that you dilute the ACTH with a small amount of saline, adjust to a pH of approximately 3.5, and suspend the solution in gelatin so that the final concentration of gelatin will be approximately 40%. 20%

I certainly feel that it would be interesting for you to study the effects of pituitary growth hormone in relation to this question of virus proliferation. After your preliminary experiments with ACTH, we can probably arrange to provide you with a satisfactory growth hormone preparation.

If there are any further questions, or if you need additional materials, please do not hesitate to call on us,

Sincerely yours,

[redacted]

1.4

7.0cc

IB/cwk

Acid prep. gel.

February 19, 1952

[redacted]

Dear [redacted]

I am writing to you in reference to the ACTH which you so kindly sent to [redacted]

Our experiments have now been completed, but the results are rather difficult to interpret since we cannot be certain that the ACTH had any physiological activity in the hamsters. The course of poliomyelitis infection in the hamster was unaltered either by 10 units of ACTH given daily in three divided doses for eight days or by ACTH in combination with 5 mg. of cortisone administered on the day of virus inoculation. As you know, it had been postulated that previous failures of ACTH to produce a cortisone-like effect on experimental poliomyelitis was thought to be due to either the low dosage of ACTH or the fact that the ACTH, in addition to stimulating the secretion of cortisone, caused the adrenal to produce an inhibitory substance which counteracted the cortisone effect. Since we could demonstrate neither of these effects, we have had to question either the physiologic response of the hamster or the activity of the ACTH.

In testing the latter thesis we found that a control group of 20 weanling hamsters which received the full course of 80 units of ACTH continued to gain weight at the same rate as a normal untreated group. This was in striking contrast to the abrupt cessation of growth brought about by the administration of a single dose of 5 mg. of cortisone to hamsters of the same age. These observations were also unexpected in view of published reports that ACTH inhibits growth in young mice and rats and premature children.

We attempted to assay the activity of the ACTH by measuring the drop in circulating eosinophiles after ACTH administration. However, the hamster apparently is so sensitive to stress of any kind that the mere handling of these animals caused a complete disappearance of eosinophiles over a period of eight hours. Furthermore, the administration of saline caused an eosinopenia which lasted at least two days.

As you can see, in evaluating our results it becomes most important for us to know if this preparation of ACTH is active, because if it is, there is the suggestion that ACTH does not influence adrenal-cortical activity in hamsters as it does in other animals. Since all of your preparations are assayed, it does not seem likely that the ACTH was inactive. However, would it be possible for you to suggest some other method by which we could assay the activity of this ACTH in the hamster? We also would be most appreciative if you could make any further suggestions.

Thanking you, I am

Sincerely yours,

AHF/maj

[redacted]

THE ARMOUR LABORATORIES

1425 WEST 42ND STREET, CHICAGO 9, ILLINOIS · TELEPHONE YARDS 7-4100

February 21, 1952

[redacted]

Dear [redacted]

Thank you very much for your letter of February 19. I am very sorry to hear that your experiment on the effects of ACTH and Cortisone on the course of poliomyelitis infection in the hamster did not produce more definitive data.

Although we have had no experience with the hamster in our own laboratories as regards the effects of ACTH, I would expect that this animal would not be a particularly good choice for eosinophil studies. Most animals which are "jittery" will usually have a spontaneous discharge of the adrenal cortical hormones which will effect profound depletion in eosinophils following almost any manipulative procedures.

I should think that your best opportunity short of measuring the corticoid secretion would be to autopsy your animals and to obtain measurements of the adrenal weight. I am almost certain that you will be able to demonstrate a profound change in the adrenal size of the ACTH-treated animals.

Since virus infections are quite specific for various tissues, I am inclined to believe that once an infection is started the only agents which might modify this infection are those which have a rather profound effect on the metabolic pattern of the invaded tissue. Probably our only hope of achieving any positive effects with the endocrines would be from the cut and tried method since I am quite sure that our knowledge of the biochemical patterns which are influencing tissue growth and virus development are not sufficiently well known for us to make any predictions at this time.

I am sorry that I have not been able to give you more definite information on the reasons for your failure to elicit a response. I hope that if we can be of any additional assistance to you in any way you will not hesitate to call on us at any time.

[redacted]

IB/cwk

P.S. Please give my best regards to [redacted]

Effect of ACTH on Poliomyelitis in Hamsters and on Enhancing Effect of Cortisone

Purpose: Since ACTH has been reported to have no effect on poliomyelitis in hamsters, it is the purpose of this experiment to determine whether it stimulates the secretion of a hormone which can neutralize the enhancing effect of cortisone.

Hamsters — Approximately 18-20 Gm. as in previous tests

Group 1 — 20 hamsters — virus only - 0.05cc of 1:100 dilution
" 2 — " " — Cortisone (5mg) once a day + virus
" 3 — " " — ACTH + Cortisone + virus
" 4 — " " — ACTH + virus
" 5 — " " — ACTH only - control

ACTH — 1.4 Gm. of powdered ACTH - preparation 146 R-S3 obtained through courtesy of Dr. Irby Bunding of The Armour Laboratories.
Potency = 3.65 x Armour La-1-A Standard so that 2.74 mg = 10 units (or 10 mg. of former)

Dosage — 10 ~~mg~~ units/day in 40% gelatin per hamster
2.74 mg/day " " " "
164.4 mg/day for 60 hamsters

5 units in 0.2cc gelatin solution to be given at 9 AM and 4 PM for 8 days as follows.
Injection - 1
" - 2
" - 3
" day — cortisone for Group 3
" +1
" +2
" +3
" +4

JAN 11 1952

EFFECT OF ACTH ON POLIOMYELITIS IN HAMSTERS AND ON ENHANCING EFFECT OF CORTISONE

PURPOSE: Since ACTH has been reported to have no effect on poliomyelitis in hamsters, it is the purpose of this experiment to determine whether it stimulates the reaction of a hormone which can neutralize the enhancing effect of Cortisone

HAMSTERS: 14-20 grams as in previous tests - and from sources as indicated in protocol.

GROUP	A - 20 HAMSTERS	♂	CORTISONE (5 mg) ONCE + LANSING 1:100
"	B - " "	♂	ACTH + CORTISONE + LANSING 1:100
"	C " "	♂	ACTH + LANSING 1:100
"	D " "	♂	ACTH ONLY - CONTROL
"	E " "	♂	LANSING ONLY - 0.05 ml of 1:100
"	F " "	♀	LANSING ONLY - 0.05 ml OF 1:100
"	G " "	♀	CORTISONE (5 mg) ONCE + LANSING 1:100

ACTH: 1.4 Gm. of powdered ACTH - preparation 146 R-S_3 obtained thru Courtesy of Dr. Irby Bunding of The Armour Laboratories.

Potency = 3.65 X Armour Lab - ~~1~~ A Standard, so that 2.74 mg = 10 units (or 10 mg of former)

DOSAGE: - 10 units per day in saline (pH 3.8) per hamster - or 2.74 mg/day. ACTH made up in PSS at PH 3.8 so that each ml contains 10 units or 2.74 mg. Administered 3 X daily at 8 A.M., 4 P.M, and 12 M for eight days in doses of 0.3 ml, 0.3 ml and 0.4 ml as follows

Injection	-3 JAN 11 1952
"	-2 JAN 12 1952
"	-1 JAN 13 1952
JAN 14 1952 "	0 - CORTISONE GROUPS A, B, G - VIRUS ALL BUT D
"	+1 JAN 15 1952
	+2 JAN 16 1952
	+3 JAN 17 1952
	+4 JAN 18 1952

CORTISONE: Cortisone acetate Merck - Lot # 01C 1634
25 mg/ml

VIRUS: Lansing virus - Pool VI of 2/5/51

BREEDING AND LABORATORY MALE HAMSTERS 1/11/57

CORTISONE (5 mg) ONCE I.M. — LANSING - 0.05 ml OF 1:100 I. CER.

2 NP

CORTISONE VIRUS

A

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
420		20	23	25	28	28	29	25																										
						P	T	D																										2
421		14	18	19	24	24	25	24	23	25																								
						–	–	–	D																									5
422		15	19	21	24	22	23	21	21	23	20	19	20	18	14	13	11																
						–	–	–	–	–	?	P	P	P	P	P	D																	7
423		17	19	21	25	25	27	26																										
						–	P	D																										2
424		17	19	23	26	26	26	25	25	28	25	22																						
						–	–	–	h	P	D																							5
Bleed 425		16	18	21	24	25	27	27	27	28	29	28	30	32	32	35	36	38	39	41	43	46	46	51	53	55	57	59	60	62	64	65	67	68
						–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
262 426		14	17	17	22	22	23	21																										
						–	P	P	D																										2
427		19	22	24	28	27	29	29	28	29	22																							
						–	–	–	–	T	D																							5
266 428		14	18	21	23	24	25	25	24	25	26	26	26	24	20	19	16	15	14	13														
						–	–	–	–	–	–	–	?	P	P	P	P	P	P	P	P	D													9
429		18	23	25	29	29	30	29	30																									
						–	–	–	D																									4
430		13	17	19	23	23	25	24																										
						–	P	D																										2
Bleed 431		21	24	25	29	28	30	28	30	31	32	31	33	35	36	39	41	43	44	47	49	50	51	55	57	61	62	63	66	67	68	68	70	72
						–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
432		11	15	16	20	20	22	23	22	24	22	18	17	15	12																			
						–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	D													5
433		18	24	26	28	29	31	30	32	32	28	26																						
						–	–	–	P	P	D																								4
434		17	20	22	27	27	29	30	29	30	29																							
						–	–	–	?	P	D																								5
435		17	21	23	26	25	27	27	23	20																								
						–	–	h	Cons	h	D																								3
436		18	20	23	26	26	27	27	25	27	27	27																						
						–	–	?	–	?	P	D																							6
437		13	16	19	22	23	24	24	20																									
						–	–	P	P	D																									3
438		17	21	23	25	25	26	26	26	27	24																							
						–	–	–	–	–	D																								6
439		15	18	20	24	23	25	26	25	27	25	25	22	19	16																			
						–	–	–	–	?	?	P	P	P	P	D																			7

AVERAGE WEIGHT 16.2 P 21 25.1 25 26.5 25.8 25.6 26.8 25.7 24.6 24.6 23 23 21.6 26.5 26 32 32 33 33 34 44 43 49 53 55 58 59.5 61 63 64.5 66 66.5 68.5 70

% P, CNS, D 0 20 30 35 65 75 85 85 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90

% DEAD 0 5 20 30 40 55 70 70 75 80 80 85 85 85 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90 90

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23

BREEDING AND LABORATORY MALE HAMSTERS

2NP
2P

ACTH – 3X DAILY FOR 8 DAYS (10 units per day) S.C. – CORTISONE – 5mg ONCE ONLY – I.M. ON 4TH DAY – LANSING 1:100 ON 4TH DAY

B

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	
*440		16	19	19	22	22	24	24	24	24	25	24	23	23	21	22	22	23	24	25	24	23	19	15										
						–	–	–	–	–	–	–	?	P	P	P	P	PP	P	P	P	W	P	W	P	W	D								10
*499		44	15	16	16	20	18	19	21	22	23	21	21	21	21	22	21	23	24	25	27	28	30	31	33	35	36	37	37	38	40	38	41	42	44	44
						–	–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	6
		44	2	17	20	20	23	22	23	24	22																							
						–	–	P	P	D																									3
		44	3	19	21	22	25	23	26	24																								
						–	P	←D																											2
		44	4	16	18	20	21	20	22	23	24	25	25	25	25	24	22	24	22	21	21	21	18	16										
						–	–	–	–	–	–	–	P	P	P	P	P	P	P	P	D															8
		44	5	14	17	18	21	20	22	23	22	21	17																					
						–	–	←h	←h	P	T	D																								3
		44	6	20	22	22	23	23	25	22	25	26	26	25	24	24	24	25	27	29	31	32	34	35	36	38	40	41	42	43	45	46	48	50	51	52
						–	–	–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	6
		44	7	15	17	17	21	20	22	23	23	24	24	21	18	16	14																	
						–	–	–	–	–	?	W	P	P	P	T	P	D																		7
		44	8	15	19	20	23	21	25	25																								
						–	–	P	P	←D																										3
		44	9	20	22	23	25	24	25	25	26	27	27	27	27	27	26	26	25	25	26	27	26	24										
						–	–	–	–	–	–	–	–	P	P	P	P	P	P	P	D															9
		45	0	16	22	22	25	24	27	28	27	26	27	27	26	23	22	26	23															
						–	–	–	–	–	–	–	?	–	–	–	D																			12
		45	1	16	19	20	22	22	24	25	24	25	25	24	24	21	20	21	21	21	21	24	21	22	22	21	21	19						
						–	–	–	–	–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	D							8
		45	2	11	15	15	18	17	19	20	20	22	22	22	22	23	22	23	25	25	27	27	28	27	29	29	29	29	29	32	34	36	36	36	32	36	38
						–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
		45	3	14	18	17	20	18	21																									
						–	D																											2
		45	4	12	16	16	19	18	19	21	22	22	19	15																				
						–	–	–	–	SAL	T	SAL	D																							5
x	455		15	19	19	22	22	24	25																									
						–	–	D																											3
		45	6	11	15	16	17	17	19	18																								
						–	P	P	←D																											2
x	457		16	21	21	23	22	22	25	25	26	27	27	26	26	24	21	22	22	23	26	23	20	19	18	15	19	16	19						
						–	–	–	–	–	–	–	P	P	P	P	P	P	P	P	P	P	P	W	P	W	–	–	D						9
		45	8	18	21	22	25	25	27	28	28	29	29	31	32	33	34	38	40	42	45	47	49	51	54	56	56	56	58	56	56	58	59	61	63	67	65
						–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
		45	9	11	14	14	18	17	19	20	18																							
						–	–	CNS	←D																											3
AVERAGE WEIGHT		15.2	18	5	18.9	21	20.8	22	22	23.4	23.6	24.5	24.1	24.0	24.4	23.5	22.5	25.2	25.1	26.2	27.6	28.3	27.6	27.7	30	30.2	33	33.6	31.2	42.1	44.7	44.7	46	54.7	49.5	49.7
																																		46
% R, CNS, D						0	15	40	40	45	55	60	70	80	85	85	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	90	5.9
						0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23							
% DEAD						15	30	35	35	40	45	45	45	50	50	55	55	55	55	55	55	65	65	70	75	75	80	80	80	80	80	80	80	80		

* Substituted for #441 which died on morning of 5th – Given Cortisone + Lansing 1:100 with rest of this group

BREEDING AND LABORATORY MALE HAMSTERS

1/11/52

ACTH - 3X DAILY FOR 8 DAYS (10 units per day) S.C - LANSING VIRUS - 1:100 ON 4th DAY

7 WP
4 TP
3 P

C

HAMSTER NO	A-3-2-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
12 ✓460	21	24	25	27	29	31	33	35	33	36	40	44	46	48	52	53	48	45	46	47	49	47	46	52	52	57	59	62	57	61	62	66	67
		–	–	–	–	–	–	–	–	–	–	SAL	SAL	–	I	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
461	18	21	22	25	25	28	29	31	33	25	21	19	17	15																
5		–	–	–	T	T	P	T	P	T	PRED																			
462	18	22	22	25	25	27	28	29	29	31	31	30	28	28	29	29	30	32	33	31	32	28	25	28	26	25	27	27	25	23	21
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	?	TY	TY	TY	–	–	–	S	S	D
✓463	15	18	18	21	22	25	25	27	26	20	20	20	19	22	24	26	26	27	31	30	31	29	26	29	28	34	35	38	35	38	38	45	47
4		–	–	–	SAL	SAL	SAL	P	P	P	P	P	P	P	P	P	P	P	P	W	W	W	–	–	–	P	P	P	P			
464	16	19	21	22	23	25	26	25	22	18	15																			
4		–	–	?	P	P	P	P	P	P	D																			
~~465~~	19	23	22	26	26	29	30	31	34	35	37	41	43	44	47	50	52	54	57	59	60	58	60	62	66	68	69	71	68	71	72	74	79
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
3 3 1 ~~466~~	17	19	21	24	23	26	28	29	32	32	31	32	33	34	37	38	41	43	45	46	48	46	46	51	62	52	55	56	52	54	56	58	60
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
✓~~467~~	18	19	22	25	24	27	28	29	31	32	33	35	37	39	42	44	46	49	49	50	49	47	49	53	54	56	58	60	55	58	60	63	63
7		–	–	–	–	–	P	P	P	P	W	W	W	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
✓~~468~~	15	18	18	20	20	23	23	25	26	29	30	33	35	35	37	37	41	43	43	45	46	44	46	47	48	48	49	50	46	51	54	50	63
9		–	–	–	–	–	–	P	P	P	P	P	P	W	P	W	P	W	P	P	P	W	W	–	–	–	–	W	W				
✓469	15	18	19	22	22	25	26	27	28	29	27	26	30	32	36	36	39	44	46	50	51	47	49	63	55	52	58	60	56	57	59	62	64
5		–	–	–	P	P	P	W	P	W	P	W	P	P	P	P	P	P	P	P	W	W	W	W	W	W	–	–	W	W			
470	19	22	24	26	27	30	31	33	34	35	35	32	29	25	23	21															
8		–	–	–	–	–	?	P	P	P	P	P	P	P	P	D															
✓471	18	21	22	25	26	29	29	31	34	36	38	41	43	46	49	50	54	56	58	59	58	56	58	62	64	65	68	67	66	67	68	69	69
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
3 4 2 ~~471~~ ~~472~~	17	20	21	24	25	28	29	32	34	36	38	42	45	47	51	54	57	58	60	59	58	54	58	61	62	62	66	69	62	61	63	74	75
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
473	20	23	24	28	28	31	28	27	26	23	21	18	21	21	23	23	24	22	20	20											
4		–	–	?	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	D											
D ✓474	15	17	18	20	20	22	23	24	25	24	23	23	27	28	32	33	35	37	40	41	42	38	37	40	40	45	45	48	43	46	46	53	55
4		–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
D ~~475~~	17	22	22	26	26	29	31	32	34	34	33	30	29	29	31	31	32	33	33	36	37	36	38	42	44	45	46	47	44	47	48	49	49
4		–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
~~476~~	17	19	21	24	24	26	27	28	29	31	33	35	37	39	43	45	48	49	51	54	55	52	52	56	55	56	57	58	56	58	60	60	62
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
~~477~~	21	23	25	27	26	29	30	30	32	33	34	37	40	41	44	46	49	50	51	49	49	46	45	49	51	50	53	56	53	53	56	59	61
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
5.8 ✓478	23	25	26	29	29	32	33	34	36	38	40	43	46	49	52	53	56	58	60	61	58	56	58	61	62	60	64	63	60	62	65	65	66
		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
4 479	20	22	24	27	27	31	33	33	36	33	30	28	25	22	20																
10		–	–	–	P	P	P	P	P	P	P	P	P	P	P	D															
AVERAGE WEIGHT	17.9	20.7	21.8	24.7	24.8	27.6	28.9	29.5	30.7	30.6	29.6	32.0	33.1	33.8	35.7	33.9	34.3	34.3	37.1	45.1	46.1	44.8	46.6	46.6	49.1	50.6	52.9	53.9	55.6	57.8	53.8	56.0	56.5	62.1
% P, CNS, D		0	0	0	30	40	40	45	50	55	55	55	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	63	63
% DEAD		0	0	0	0	0	5	5	10	10	15	20	20	20	20	25	25	25	25	25	25	25	25	25	25	25	25	26	26				

8 BREEDING AND LABORATORY MALE HAMSTERS (480-487)
12 MAXFIELD MALE HAMSTERS (488-499)

ACTH ONLY — 3x DAILY FOR 8 DAYS — S.C

D

ACTH 1/4/52

Bleed 3

HAMSTER NO.	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
480	20	23	25	28	29	32	33	36	37	40	43	46	52	53	58	60	63	65	66	68	69	64	68	71	71	73	75	75	73	75	77	78	77
✓52 ~~487~~	23	27	28	32	33	35	37	38	40	42	44	47	51	53	55	58	62	62	65	67	68	62	68	69	74	76	79	81	78	80	81	83	82
✓ 482	15	18	20	22	23	25	27	28	30	30	32	36	41	42	47	49	51	54	58	58	61	55	61	62	64	67	68	70	68	69	70	71	69
✓63 483	16	18	19	22	23	26	27	28	30	32	35	37	41	43	46	48	52	53	56	57	59	52	59	62	66	66	71	73	73	74	76	75	75
✓76 484	20	23	25	28	29	30	32	33	35	37	38	41	45	47	50	52	55	57	58	59	62	57	62	64	65	65	68	69	69	70	71	73	69
✓485	18	22	23	27	28	31	33	35	35	38	40	43	47	51	55	58	62	64	68	68	71	65	69	72	74	76	76	78	77	77	79	80	78
✓486	19	22	23	26	27	29	30	31	33	36	38	41	44	45	60	63	55	58	60	62	63	58	61	62	64	65	65	65	64	65	66	68	68
✓487	15	21	21	24	25	27	29	29	32	33	36	38	44	44	49	51	54	57	62	60	64	59	63	65	68	69	71	72	74	72	74	72	69
✓49 ~~488~~	20	18	20	23	25	27	30	32	34	35	38	40	43	45	49	52	54	56	61	62	64	59	64	66	68	69	73	75	76	75	75	77	75
37✓ 489	15	17	19	22	24	26	28	29	32	34	36	38	42	44	47	49	53	54	57	60	61	57	61	64	68	70	70	70	73	71	73	74	74
55 ~~490~~	19	15	18	22	23	25	27	28	31	33	35	37	41	42	45	48	51	51	58	61	62	53	55	55	56	58	60	62	65	65	64	65	67	65
✓ 491	14	17	19	23	24	26	27	28	31	34	36	39	43	44	50	52	55	58	61	63	66	61	65	70	71	73	75	79	77	78	79	78	76
✓105 492	16	18	21	24	26	28	31	32	35	38	41	44	48	51	56	57	63	64	67	71	73	66	71	73	76	76	78	82	77	77	79	80	77
89 ~~493~~	15	17	19	23	25	26	29	31	33	35	37	40	43	43	49	49	52	53	59	60	62	56	61	63	66	68	68	70	68	70	70	71	70
Dead 1 day 494	17	17	20	23	24	26	29	29	31	33	36	38	42	46	47	50	54	55	59	61	63	56	62	64	66	69	70	73	74	74	76	76	76
Dead 2 days 495	16	15	19	20	22	24	25	26	28	31	33	36	39	41	45	48	52	56	58	58	59	55	60	61	64	67	67	67	66	67	66	68	67
496	16	19	21	24	25	27	29	30	32	34	36	41	43	44	48	50	54	53	59	61	64	61	65	65	67	66	68	70	68	68	69	69	67
Dead 497	13	16	18	20	22	24	24	26	27	29	31	34	38	39	43	45	49	50	53	55	54	64	49	51	53	56	59	61	61	62	62	63	64	63
183 ~~498~~	13	16	18	21	22	24	25	27	28	31	33	35	38	42	45	48	52	53	56	58	61	55	61	60	62	63	64	66	66	67	69	72	71
499	12	15	16	20	19	Transferred to B as substitute for 441 which died on inoculation 4 Jan 52																											
AV. SCALE WEIGHT		16.6	18.7	20.6	23.8	24.1	27.2	29.0	30.3	32.3	34.5	36.7	39.5	43.4	45.2	47.1	51.4	54.8	56.4	60.0	61.6	63.0	59.3	62.4	64.3	66.7	68.6	69.9	71.6	70.9	71.3	73.2	73.4	72
% P. CNS. D						0	0	0	0	0	0	0	0	0																			
% DEAD						0	0	0	0	0	0	0	0	0																			

ACTH

1720 LAKEVIEW HAMSTER COLONY MALE HAMSTERS (500-517) 1/11/52

LANSING VIRUS ONLY — 0.05 ml OF 1:100 I. CER.

E 1/14/52

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
500	16				19	21	25	26	27	31	29	26	22	18																			
501	18				21	22	19	16																									
~~32~~ 502	14				17	18	22	24	25	29	31	35	37	39	40	43	45	48	51	53	55	56	58	60	64	66	68	71	74	74	74	71	>67
dead ✓ 503	18				22	23	26	28	31	34	37		32	33	36	40	42	44	47	48	52	52	53	56	58	58	58	60	59	54	50	45	40	38	36
✓ 504	16				18	20	24	24	24	23	24	26	26	26	27	30	30	32	31	28	24	23	24	25	27	27	28	29	30	31	30	28	28	26
505	15				16	17	21	20	18	18	16	13																					
506	17				18	21	24	27	25	28	29	30																					
507	17				20	23	26	28	33	36	39	41	44	39	33	30	26																
✓ 508	17				19	21	26	26	28	30	32	34	35	37	37	41	43	45	46	45	43	41	39	38	40	45	45	46	44	41	39	36	36	34
509	17				20	21	24	26	28	32	34	36	37	39	42	44	47	48	49	52	54	55	53	53	54	54	56	56	56	62	62	58	58	57	53
✓ 510	15				17	19	22	24	23	24	23	22	23	24	25	26	27	26	26	25	24	27	28	29	32	33	34	36	37	37	34	32	34	33
✓ 511	15				17	19	22	24	26	28	31	33	34	35	37	40	44	47	50	53	56	59	60	64	69	71	73	76	78	80	79	81	84	84
~~38~~ 512	16				17	19	23	25	28	31	32	30	27	26	26	26	27	29	33	34	37	40	42	45	47	49	50	51	53	54	56	54	57	60
~~513~~ ✓	17				20	21	25	26	31	34	36	39	42	44	45	48	51	54	55	59	61	64	65	68	69	73	75	77	79	78	78	78	79	77
✓ 514	14				16	18	22	23	24	28	31		29	29	32	35	36	40	41	43	47	49	49	53	52	57	54	58	61	61	61	63	64	64
✓ 515	17				21	21	25	26	28	29	30	32	33	36	38	42	43	45	47	49	50	52	52	53	53	54	53	51	50	49	52	52	52	51
✓ 516	15				16	18	21	22	20	21	21	22	21	24	26	29	32	34	37	39	42	45	47	45	48	51	54	57	58	59	60	60	61	62
517	12				10																												
✓ 518	19	18	19	22	22	26	28	32	35	39	41	44	48	50	53	56	59	61	62	66	66	63	66	63	63	63	65	66	66	66	68	68	70
✓ 519	15	14	14	14	14	15	15	16	17	18	20	20	22	24	27	29	31	32	30	33	35	39	41	43	46	46	48	49	52	54	51	53	56
AVERAGE WEIGHT	16.0				18.0	19.9	23.2	24.1	25.9	28.2	29.5	30.0	31.8	32.4	34.5	36.9	39.2	41.5	43.1	44.2	45.4	44.2	43.9	44.9	44.7	45.1	45.3	45.4	45.6	46.7	46.7	47.2	46.5	46.5
% P, CNS, D					0	10	26	32	32	37	42	42	53	53	53	53	53	53	53	58	58	58	58	58	58	58	58	63	63	63	63	63		
% DEAD					0	0	5	5	5	5	16	16	21	21	21	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26	26
					0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21								

BREEDING AND LABORATORY

LAKEVIEW HAMSTER COLONY FEMALE HAMSTERS 1/11/52

LANSING ONLY — 1:100 — I. CER - 0.05 ml

10 NP
5 P

F

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
✓ 520	17				20	21	24	24	25	24	25	26	26	29	30	33	35	38	37	40	41	42	42	43	45	47	49	49	52	53	64	54	55	56
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
*521	17			I	19	22	25	23	28	31	33	31	28	25	22	21	18	16																
					-	-	-	-	-	-	P	P	P	P	P	P	P	P	D															
✓ ✓ 522	15				17	18	21	21	26	27	29	24	23	27	27	31	33	36	39	41	43	47	46	52	54	57	56	59	61	63	62	62	64	65
					-	-	-	P	-	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
523	19				21	22	26	25	28	30	29	26	25	25	26	27	27	26	23	21	18													
				4	-	-	-	P	P	P	P	P	P	P	P	P	P	P	P	P	P	D												
524	16				18	19	23	21	24	26	27	28	30	32	34	36	39	42	42	44	44	46	47	50	52	54	57	58	62	62	59	57	58	46
					-	-	-	-	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
3014 * 525	19			5	21	23	26	27	31	33	33	33	31	30	32	34	34	37	36	38	41	42	42	44	45	46	46	48	51	51	50	50	51	60
					-	-	-	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
526	17			4	20	22	25	24	28	29	30	27	24	24	22	25	25	26	28	28	26	24	23	22	23	23	22							
					-	-	-	-	-	-	?	P	P	P	P	P	P	P	P	P	P	D													
✓ ✓ 527	19			8	22	24	27	26	30	32	34	36	38	41	43	46	48	52	53	56	58	60	57	58	59	61	61	61	63	66	63	64	64	
					-	-	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
✓ ✓ * 528	16			3	19	20	24	22	28	30	34	37	38	41	43	46	48	51	53	55	56	58	58	61	66	68	68	68	72	75	73	72	71	72
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
✓ ✓ 529	16				18	19	23	24	29	31	34	38	40	43	45	48	50	53	53	57	58	59	58	65	66	69	71	74	79	78	77	81	83	84
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
✓ ✓ 530	17				20	20	24	25	27	29	32	34	36	39	42	45	46	49	50	52	52	54	55	57	57	56	57	59	61	61	57	52	54	49
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
✓ ✓ 531	16				18	20	24	22	26	29	33	36	39	42	45	48	51	56	55	58	59	63	64	67	69	71	72	75	78	78	79	81	83	83
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
✓ ✓ 532	19				22	23	27	28	32	35	36	38	40	43	45	49	52	55	56	59	60	63	62	65	66	66	69	72	75	77	77	75	75	74	72
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
533	17				18																												
					D																												
3052 * 534	17				19	21	24	23	27	25	27	28	26	31	32	34	36	40	38	42	43	46	46	49	50	51	55	56	55	57	58	56	58	60	59
					-	?	?	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
535	19				21	22	25	25	29	28	24	19	18	17	14																			
				5	-	-	-	-	T	T	T	T	T	D																				
✓ ✓ 536	17				20	21	25	24	27	27	28	27	27	28	29	32	32	33	33	32	30	29	28	27	31	33	34	33	33	32	31	33	34	37
					-	-	-	-	?	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
537	16				19	20	22	24	26																									
				3	-	-	P	D																										
✓ ✓ 538	17				18	20	24	22	27	29	33	36	39	42	43	46	49	53	53	54	56	59	61	65	63	64	62	55	55	55	56	60	62	64
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
339 ✓ 539	15				17	19	22	21	25	28	31	32	36	37	39	42	43	46	46	50	51	53	54	56	51	61	61	62	67	66	66	65	67	71
				4	-	-	-	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
✓ ✓ 540	15				18	19	22	21	26	30	32	34	37	39	42	45	48	52	55	57	59	61	63	68	68	72	73	76	79	81	79	81	82	83
					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
AVERAGE WT	17.0				19.3	20.7	24.0	23.6	27.4	29.1	30.1	31.1	31.6	33.6	34.4	34.4	38.2	39.6	42.2	44.1	46.1	46.3	46.3	50.3	50.5	53.0	53.0	54.0	56.0	56.3	57.0	60.3	62.8	63.8	62.6	62.3	64.0	63.6
46 / 10 = 4.6					0	0																															
% P, CNS, D							15	30	40	40	45	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
% DEAD							0	5	5	5	5	5	10	10	10	15	15	15	20	20	20	20	20	20	25	25	25	25	25	25	25							

STANDARD B&P "NOEAR"

STANDARD B&P "NOEAR"

D 2/23/52

D 2/24/52

G

LAKEVIEW HAMSTER COLONY FEMALE HAMSTERS 1/11/52

CORTISONE – 5 MG. ONCE I.M. – LANSING VIRUS – 1:100 – I.CER.

HAMSTER NO.	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
541	20				22	22	23	23	24	24	25	23	22	21	18		17		15		14	12											
	12				–	–	–	–	–	–	–				?		?		?		APH	APH	D										
542	16				17	18	20	20	21	19	21	19	18	18	17	19	22	23	25		27	28	30	31	33	34	33	34	32	32	30	28	25	27	28
	6				–	–	–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
543	16				18	18	21	20	21	21	22	21	20	23	24	26	28	31	33	35	36	39	41	44	45	45	46	46	46	46	46	46	48	48
	21				–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	P	P	P	P	P	P	P	P	P	P
544	15				17	18	20	20	21	21	18																						
	5				–	–	–	–	P	P	D																						
545	19				22	22	24	24	21	16																							
	4				–	–	–	CNS	D																								
546	16				17	17	19	19	16																								
	3				–	–	P	D																									
547	22				25	24	27	26	27	27	28	24	21	20	17	16	14																
	6				–	–	–	–	–	SAL	P	P	P	P	P	P	P	D																
548	18				19	19	20	21	21	21	22	19	16																				
	7				–	–	–	–	–	?	T	ED																						
549	23				24	25	28	28	29	28	30	23	21																				
	6				–	–	–	–	–	SAL	CNS	D																						
550	18				20	20	22	21	22																								
	4				–	–	–	D																									
*551	19				20	21	22	22	22	21	22	19	18	20	21	22	25	27	27	29	30	32	31	32	32	32	32	31	30	29	28	25	25
	5				–	–	?	?	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	D
552	17				21	22	23	24	24	24	22	19	17	16	14																		
	6				–	–	–	–	–	P	P	P	P	P	P	D																		
553	17				19	19	22	22	21	22	24	26	25	26	20	19	18		18	18	16	17	14										
	10				–	–	–	–	–	–	–	?	P	P	W	W	W	–	W	D														
554	17				19	19	20	21	21	21	21	18	17	17	18	20	21	22	23	23	26	28	28	32	34	35	37	39	41	41	40	43	44	42
	4				–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
555	17				20	20	22	21	22	23	22	21	18	17	14	14	12	10															
	8				–	–	–	–	–	–	P	P	P	P	P	D																		
556	17				18	19	22	22	23	22	22	22	22	22	26	27	29	33	36	38	40	42	45	46	51	52	57	58	60	62	62	63	66	66
	7				–	–	–	–	–	–	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
557	20				21	22	24	24	26	25	24	19																					
	6				–	–	–	–	–	–	T	D																						
*558	18				20	21	22	22	22	22	22	20																					
	6				–	–	–	–	–	–	D																							
559	16				18	19	21	20	21	21	21	20	18	16																			
	7				–	–	–	–	–	–	–	P	P	P	D																			
560	15				18	18	20	20	21	19	20	17	14	13	12	12																	
	7				–	–	–	–	–	?	APH	APH	APH	P	P	D																			
561	15				17	18	20	21	19																								
	3				–	–	SAL P	D																									
562	17				20	20	20	20	19	17	16																						
	3				–	–	h→	h→	T→	D																							
AVERAGE WT.	17.6				19.6	20.0	21.9	21.8	22.	21.5	22	22	20.6	19.0	19.4	18.3	19.4	20.8	22.6	25.1	25	29	26	31	33	35	34	38	38	37	38	41	41.	41.
					T46=46																												
					22																												
% P, CNS, D					0	0	14	27	36	64	82	86	86	91	91	91	95	95	95	95	95	95	95	95	95	100	100	100	100	100	100	100	100	
% DEAD					0	0	0	14	18	32	41	45	50	55	55	59	64	68	73	73	73	77	77	77	77	77	77	77	77	77	77	77	77	82

NORMAL ADRENALS	DEVIATION FROM MEAN	(DEVIATION FROM MEAN)^2	ACTH TREATED ADRENAL	DEVIATION FROM MEAN	(DEVIATION FROM MEAN)^2
12.3	+0.32	0.1024	19.4	+0.76	0.5776
11.8	−0.18	0.0324	17.0	−1.64	2.6896
12.6	+0.62	0.3844	16.4	−2.24	5.0176
8.9	−3.08	9.4864	21.0	+2.36	5.5696
14.3	+2.32	5.3824	19.4	+0.76	0.5776
SUM 59.9	0	15.3880	93.20	0	14.8320
MEAN 11.98		3.0776	18.64		2.9664

STANDARD DEVIATION $= \sqrt{\frac{3.0776}{4}} = \sqrt{0.7694} = 0.877$

STANDARD ERROR $= \frac{0.877}{\sqrt{5}} = \frac{0.877}{2.236} = 0.392$

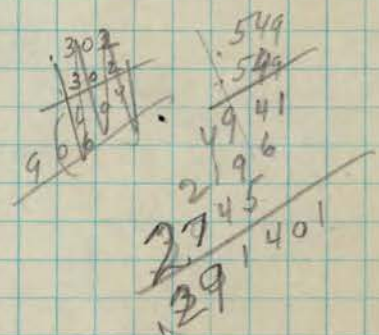
S.D $= \sqrt{\frac{2.9664}{4}} = \sqrt{0.7416} = 0.861$

S.E. $= \frac{0.861}{\sqrt{5}} = \frac{0.861}{2.236} = 0.385$

STANDARD ERROR OF THE DIFFERENCE $= \sqrt{\frac{(SD_1)^2}{n_1} + \frac{(SD_2)^2}{n_2}} = \sqrt{\frac{(.877)^2}{5} + \frac{(.861)^2}{5}} = \sqrt{\frac{.769}{5} + \frac{.741}{5}} = \sqrt{.302} = 0.549$

Means differ by 6.66 mg which is more than twice as great as the standard error of the difference ∴ the increase in adrenal weight may be considered significant

The difference in means is 12.1 times greater than the standard error.



THE EFFECT OF ACTH ON POLIOMYELITIS INFECTION IN HAMSTERS OF DIFFERENT AGES.

APR 18 1952

PURPOSE:

In the experiment of January 11, 1952 ACTH failed to have any effect on poliomyelitis in baby hamsters (14-18 grams). It was also found that ACTH did not produce a loss of weight or cessation of growth as might be expected if the adrenal cortex was being stimulated to produce cortisone. It seemed possible that the ACTH was inactive or that there was a lack of the biological response to the heterologous ACTH (bovine origin).

When the ACTH was assayed by the adrenal hypertrophy method in hamsters slightly older it was found that during the period of administration (3 day; 10 units daily) saline inoculated controls gained an average of 6.2 ~~grams~~ grams more than ACTH-treated hamsters which gained 5.6 grams during this period. Furthermore ACTH produced hypertrophy of the adrenals in the ACTH-treated group.

This test is therefore being carried out to determine if ACTH when given to older hamsters will produce an increased susceptibility as a correlation with the effect on weight of body and adrenals.

PROCEDURE:

Hamsters were divided into the following groups:

A = 20 ♂ 14-18 GM - NORMAL UNTREATED - WEIGHT CONTROL
B = 20 ♂ 34-38 GM - NORMAL UNTREATED - WEIGHT CONTROLS
C = 20 ♂ 14-18 GM - ACTH ONLY
D = 20 ♂ 34-38 GM - ACTH ONLY
E = 20 ♂ 14-18 GM - LANSING 1:100 ONLY
F = 20 ♂ 34-38 GM - LANSING 1:100 ONLY
G = 20 ♂ 14-18 GM - ACTH + LANSING 1:100
H = 20 ♂ 38-38 GM - ACTH + LANSING 1:100

ACTH was administered three times daily at 8 hour intervals for 8 days. Each hamster received 10 units daily in equally divided doses. Animals were weighed daily. At the end of 8 days 5 animals from each group, except those receiving virus or virus + ACTH was sacrificed and their adrenals, spleens, thymus, liver were removed and weighed.

ACTH: Armour adrenocorticotrophic hormone of porcine origin. Lot # 146R-S3. 2 grams. The 2 grams were dissolved in saline-HCl and the volume made up to 729.9 ml Each ml contained 2.74 mg of ACTH which was equivalent to 10 units of Armour LA-1-A standard per ml.
Each hamster received 0.3 ml (3 units) at 8 AM. and 4 PM and 0.4 ml (4 units) at 12 M for 8 days - given S.C.
PH = 3.66

HAMSTERS: Laboriem hamster Colony hamsters
80 ♂ hamsters weighing 14-18 grams
80 ♂ hamsters weighing 34-38 grams

VIRUS: Lansing Virus. Pool JII of 2/11/52.
10% suspension in saline & centrifuged 10 minds at 2000 rpm

STANDARD B & P "NOTEAR"
STANDARD B & P "NO

APR 18 1952

NORMAL UNTREATED MALE HAMSTERS (20)

WEIGHT CONTROLS (10-18 GRAMS) - AVE = 12.9

A

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
					0	1	2	3	4	5	6	7	8																				
563		12	12	15	17	21	23	25	27	31	32																						
564		13	17	19	22	25	27	30	33	37	36																						
565		12	15	18	21	24	26	30	33	36	38																						
566		14	18	20	23	26	28	33	36	39	38																						
567		15	18	21	25	27	30	34	36	41	42																						
64	568	15	17	21	24	27	28	32	35	38	45	46	46	49	52	55	58	62	65	69	78	74	76	80	80	82	82	86	89	88	88	89	90	93
	569	13	16	18	22	22	24	27	28	33	36	38	44	42	44	46	48	51	53	55	57	60	59	60	62	64	66	68	71	66	71	71	74	74
	570	13	15	18	21	24	26	30	32	37	41	43	44	44	49	49	52	55	57	60	62	64	65	66	69	71	72	75	76	78	74	78	80	81	83
	571	13	14	18	21	25	27	31	33	38	43	46	50	53	56	61	64	67	71	73	77	77	81	85	85	88	92	93	94	90	93	93	95	96
	572	13	15	18	22	25	27	31	34	38	43	46	49	52	55	59	63	67	69	72	75	75	79	83	84	86	87	91	93	89	94	95	97	99
73	573	12	14	17	21	24	25	29	32	36	40	42	44	46	49	52	54	59	60	63	66	69	72	74	74	76	75	77	81	75	80	81	83	85
85	574	13	14	17	19	23	25	28	31	35	40	41	44	47	50	54	58	61	64	67	70	73	75	77	77	78	81	82	87	82	86	86	88	91
	575	13	17	18	23	25	27	32	33	37	41	43	45	49	51	55	57	61	63	66	68	68	72	75	76	78	77	78	76	72	75	76	77	81
	576	14	17	19	22	25	Dead																										
282	577	13	15	17	21	23	25	29	32	36	40	42	43	47	49	52	54	56	59	62	64	65	67	70	71	73	75	76	80	78	81	84	84	87
62	578	12	13	16	20	22	25	27	28	33	35	37	39	42	44	46	47	49	51	53	56	55	56	55	58	59	63	64	65	61	65	66	68	70
	579	12	14	17	21	23	25	28	29	33	36	39	43	45	47	50	52	55	57	59	61	65	66	67	69	70	73	74	75	72	75	77	79	82
48	580	12	14	17	20	23	25	29	31	35	40	44	44	41	46	48	50	50	51	53	56	58	58	59	61	62	63	65	67	61	67	67	70	72
535	581	11	10	13	15	18	20	23	25	28	32	34	35	38	40	42	45	48	48	51	55	55	55	56	58	60	63	64	66	67	63	66	68	69	70
	582	13	16	19	22	26	28	31	34	38	42	45	46	49	52	55	59	62	66	69	72	74	73	76	75	78	82	85	84	80	83	85	86	89
AVERAGE WEIGHT		12.9	15.1	17.8	21.1	23.9	25.8	29.4	31.7	35.7	39.9	41.8	43.7	46.3	48.8	51.9	53.8	57.5	60.5	62.4	65.2	66.6	68.2	70.5	71.6	73.5	75.0	77.2	79.0	78.2	79.8	81.5	83.7

% P, CNS, D

% DEAD

NORMAL UNTREATED MALE HAMSTERS (20)

WEIGHT CONTROLS — 28-39 GRAMS (AVE = 32.1)

B

HAMSTER NO	A -3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
583	34	38	40	43	45	46	48	49	52	50																						
584	30	30	36	38	40	41	45	46	50	50																						
585	30	34	36	38	41	41	45	46	50	50																						
586	34	38	42	45	49	50	54	55	60	60																						
587	35	39	42	45	47	48	52	54	57	56																						
✓ 588	35	38	41	45	47	48	52	53	57	62	64	66	69	71	74	76	77	80	81	82	85	87	89	91	92	95	96	97	99	100	101	104
✓ ✓ 589	24	30	32	35	39	41	45	47	51	55	59	60	64	65	66	68	69	71	73	73	76	76	77	78	80	81	83	83	86	86	87	91
188 ~~590~~	34	38	40	44	46	48	51	54	57	60	65	66	69	72	74	76	78	82	84	84	86	89	92	93	95	95	97	99	95	101	101	104
✓ 591	31	34	38	42	44	46	49	52	55	59	61	63	65	67	68	70	72	74	74	74	78	80	81	81	84	84	85	86	83	87	86	88
✓ 592	35	39	41	44	47	48	52	53	57	62	64	66	69	71	74	76	78	81	83	84	86	87	89	90	92	91	94	95	91	96	97	98
✓ 593	38	41	43	46	47	48	52	53	57	61	64	66	69	71	74	77	78	80	84	86	90	90	94	97	97	99	99	100	97	103	101	104
✓ 594	34	37	40	44	44	46	50	51	55	59	61	63	66	66	68	72	74	76	78	80	80	82	86	86	87	89	92	91	93	90	94	94
✓ 595	32	33	39	40	41	43	46	49	51	55	56	58	60	60	62	62	63	64	65	64	67	68	69	70	72	72	74	75	71	76	77	78
✓ 596	25	28	31	34	35	34	36	36	40	43	44	46	47	49	51	54	54	56	57	58	59	61	63	62	65	65	66	66	63	67	68	69
✓ ✓ 597	33	36	39	42	44	45	48	49	52	55	57	59	60	62	64	67	67	68	71	71	73	74	76	78	79	79	79	81	79	84	84	86
598	36	40	Transferred to F (664)																													
102 ~~599~~	30	34	36	38	40	42	44	46	48	52	55	55	56	58	60	63	64	66	66	67	65	67	69	69	71	71	72	73	74	70	76	77
✓ 600	33	36	38	42	43	46	50	50	54	56	59	60	62	62	64	64	64	66	66	67	67	67	70	73	70	73	74	75	74	71	76	77
✓ 601	26	31	32	35	36	38	42	44	46	50	51	51	56	57	61	64	65	67	69	71	72	75	77	78	80	81	82	83	80	86	86	88
✓ ✓ 602	32	35	38	41	43	44	47	49	52	55	58	58	60	62	66	68	69	71	73	73	75	78	80	83	84	83	83	84	80	83	84	85
AVERAGE WEIGHT	32.1	35.5	38.4	41.1	43.1	44.4	47.8	49.3	52.7	55.1	57.4	59.7	62.1	64.0	66.6	68.4	69.2	71.7	73.4	73.7	75.7	77.3	79.0	80.6	82.3	83.1	83.9	85.0	81.6	86.7	87.0	88.8	89.5

% P, CNS, D

% DEAD

APR 18 1952

ACTH - 3X DAILY FOR 8 DAYS (10 UNITS PER DAY) - S.C.

C

NO VIRUS

20 ♂ HAMSTERS - 12-17 GMS - AVERAGE = 12.6

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
603		12	13	15	18	21	21	24	25	28	29																						
604		12	12	13	16	18	19	21	23	25	27																						
605		12	14	15	17	20	21	24	25	28	29																						
606		13	13	15	17	19	20	23	24	25	27																						
607		12	14	15	18	21	21	24	25	28	30																						
608		12	12	14	16	19	20	23	24	25	28	31	34	38	42	43	47	49	51	65	58	59	61	62	65	66	67	70	73	70	75	77	79	78
46. 609		11	12	13	14	17	17	20	21	23	24	27	29	33	35	38	40	42	44	47	50	52	53	56	56	59	54	58	60	58	60	61	62	63
610		13	15	16	19	21	22	26	28	32	34	38	43	44	47	49	52	55	58	62	64	68	70	72	73	75	77	78	80	78	82	84	84	88
611		12	13	15	17	20	22	24	26	28	30	34	37	40	42	45	48	50	52	64	68	58	69	62	64	65	67	69	72	69	75	77	79	80
612		12	13	15	16	19	19	22	24	27	29	32	34	37	39	43	45	45	47	48	50	52	54	55	57	59	58	60	63	61	63	67	68	69
✓ 613		14	16	18	21	23	23	26	27	30	32	35	37	41	43	45	46	48	48	50	53	55	57	59	62	62	67	68	69	65	71	73	75	77
98. 614		13	15	16	18	19	20	23	24	27	30	34	37	39	40	41	45	47	50	52	55	57	60	63	62	65	65	67	69	69	71	73	75	76
✓ 615		15	17	19	22	24	24	26	27	30	33	36	38	41	44	47	48	51	52	54	56	58	59	63	64	66	66	69	71	68	74	76	77	78
616		11	12	14	16	18	20	22	23	26	28	32	34	37	39	41	44	48	50	53	56	57	59	60	61	63	64	65	68	65	71	70	73	73
350 617		13	14	16	18	20	21	23	25	28	30	33	36	39	42	44	47	51	53	55	58	61	63	67	68	69	72	75	78	74	79	82	82	85
78. 618		13	14	15	17	21	21	24	25	27	29	33	35	37	39	42	44	46	49	51	54	56	58	61	63	65	63	64	67	63	69	71	73	74
619		13	13	15	17	19	20	23	24	27	29	32	34	37	39	41	44	44	46	48	57	54	56	58	60	60	63	64	66	66	67	72	74	77
620		13	14	16	18	20	20	23	24	26	28	31	32	34	37	40	41	43	45	48	52	53	55	57	57	58	59	61	63	60	64	65	67	68
621		13	14	15	17	20	20	23	24	27	29	33	35	38	41	44	46	49	52	54	58	60	61	63	66	67	68	70	71	70	74	74	77	78
622		12	14	16	18	21	21	24	24	26	29	32	37	39	42	45	47	51	53	57	61	63	67	68	71	73	75	76	78	76	80	82	84	85
AVERAGE WEIGHT		12.6	13.7	15.3	17.5	20.0	20.6	23.4	24.6	27.7	29.2	32.8	35.4	38.2	40.7	43.2	45.6	48.0	50.1	52.7	55.8	57.6	59.6	61.8	63.2	65.0	65.7	67.7	70.0	67.4	71.9	73.6	75.2	76.6
% P, CNS, D																																	
% DEAD																																	

↑ ACTH ↑

ACTH ONLY - 3X DAILY FOR 8 DAYS (10 UNITS PER DAY) - S.C.

D

20 ♂ HAMSTERS - 32-42 GMS - AVERAGE = 33.0

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
623	37	42	43	44	46	45	47	49	51	52																							
624	34	38	38	40	41	41	44	44	47	49																							
625	33	37	37	38	39	40	43	44	44	46																							
626	36	41	43	44	45	45	48	50	54	56																							
627	33	36	37	37	38	38	41	42	45	47	52	52	56	58	61	65	68	69	72	74	76	78	80	81	83	85	86	86	85	90	87	90	93
628	34	37	38	40	42	42	45	46	50	52	55	57	60	62	65	68	70	72	74	77	78	80	82	85	85	87	88	90	89	95	95	96	94
629	30	32	34	35	37	37	39	40	43	46	48	51	52	56	57	59	62	62	65	66	67	69	69	72	74	75	76	77	74	81	82	84	86
630	32	35	36	37	39	38	41	41	44	47																							
631	33	37	38	40	41	42	45	46	50	53	58	59	63	67	69	73	78	78	81	84	87	88	90	92	94	93	96	96	95	98	99	101	102
632	31	36	35	37	38	39	42	44	47	52	56	57	61	63	67	70	73	74	76	80	81	84	86	87	88	91	92	93	91	97	99	100	102
633	33	36	37	39	41	40	44	44	47	50	53	54	55	59	61	63	64	64	66	68	70	72	74	75	77	78	80	79	78	82	85	85	87
634	34	38	38	39	41	41	44	45	48	51	54	57	59	62	66	68	70	72	75	78	81	82	83	87	88	89	91	89	86	93	91	94	96
635	32	36	38	38	40	40	44	45	48	51	55	56	58	60	63	67	68	69	70	71	74	77	78	81	83	84	87	85	89	88	88	94	92
636	32	33	37	37	39	39	42	44	46	49	52	55	55	58	60	63	63	67	67	66	67	70	73	75	75	78	77	77	79	78	81	82	84	86
637	34	37	38	40	42	41	45	46	48	51	54	56	59	61	65	67	70	71	74	77	78	81	81	84	85	86	87	86	85	89	88	89	90
638	33	36	36	37	38	38	42	41	43	45	49	57	54	56	59	61	63	64	66	66	68	69	71	73	75	76	79	81	81	80	86	86	88	88
639	33	35	37	38	40	39	42	43	46	49	52	54	55	57	60	62	65	64	66	66	69	71	73	76	77	79	82	83	45	81	86	89	90	93
640	31	35	34	37	38	38	39	40	43	46	49	51	53	56	59	63	67	67	71	73	76	79	80	83	85	87	89	90	87	93	94	95	97
641	33	36	36	37	38	38	42	43	46	49	51	54	56	56	57	60	61	64	64	67	68	71	72	73	75	77	80	81	82	79	84	86	88	88
642	31	32	37	37	38	38	41	43	45	48	51	52	54	57	61	63	66	66	68	70	72	74	76	75	78	80	81	82	78	84	85	87	88

AVERAGE WEIGHT 35. 36.2 37.4 38.6 40.1 39.9 43.0 44.0 46.8 48.4 45.6 54.4 56.8 59.4 62.4 64.8 67.6 68.2 70.4 72.6 74.7 76.8 78.4 80.2 82.0 83.5 85.1 86.3 83.2 87.4 89.0 90.6 91.8

↑ ACTH ↑

% P, CNS, D

% DEAD

#613 has no tag. painted yellow on Belly.

Brunton Longs Bait Shop

#602 no tag (not painted)

#584 has tag

5-5-52

Painted yellow

#613 no tag painted in BX

#615 no tag in BIX

5-5-52

78 Has no tag in cage painted

5-16-52

APR 18 1952

STANDARD

LANSING VIRUS ONLY – 0.05 ML OF 1:100 E. COLI

20 ♂ HAMSTERS – 13-17 GMS. – AVERAGE = 13.2

STANDARD B&P "NOTEAR"

HAMSTER NO	A	-3	-2	-1	0 (4/21)	1	2	3	4	5 (4/26)	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
643	15	16	21	26	28	30	29	28	27	29	30	32	34	38	40	43	47	47	51	52	55	56	59	60	61	63	65	64	60	64	58	56	57
644	14	15	20	24	27	28	31	32	38	41	44	45	46	45	45	48	51	51	53	53	57	59	60	64	65	67	68	67	64	70	71	73	74
645	14	15	19	23	26	27	28	29	33	36	36	36	39	42	45	47	50	54	56	57	60	64	64	67	69	70	71	73	74	78	79	80	81
646	14	16	21	25	28	29	31	33	34	32	30	29	31	32	34	36	38	39	39	36	41	43	45	47	48	50	49	49	45	50	48	50	48
647	12	13	16	18	21	23	24	25	25	25	26	27	31	34	37	40	44	44	45	47	49	51	54	55	55	57	58	60	60	57	58	58	59	61
648	12	13	17	19	22	25	25	26	28	28	31	33	36	41	43	44	44	45	45	47	49	51	52	55	57	59	60	62	63	61	64	65	67	68
649	12	13	17	20	18	22	24	25	27	28	30	32	36	38	41	45	48	51	55	58	61	64	66	68	70	71	71	71	69	76	77	79	80
650	13	14	19	22	25	27	29	30	33	36	37	38	42	44	48	49	51	53	55	55	57	58	59	61	63	63	63	61	60	59	57	58	59
651	12	13	15	18	20	22	21	17		16																							
652	13	16	20	24	25	27	29	30	31	29	26	26	25	27	28	30	32	33	35	37	38	38	41	44	45	46	47	48	45	51	52	52	54
653	15	17	22	27	28	31	33	36	39	42	45	48	52	56	58	62	66	67	70	74	75	77	79	82	84	83	84	83	80	86	89	90	91
654	12	14	17	21	24	26	26	27	26	27	27	30	32	34	35	38	41	41	45	47	48	48	51	52	54	55	57	58	56	58	59	61	62
655	12	13	17	21	24	25	27	29	34	37	41	43	46	48	48	43																	
656	12	14	17	20	22	24	26	28	31	35	37	38	40	41	44	46	51	51	53	56	60	61	66	68	70	71	74	74	70	79	81	83	85
657	12	14	18	21	22	24	26	28	29	32	35	37	40	43	46	49	53	54	58	61	63	64	68	69	71	73	75	76	72	77	79	81	82
658	14	15	19	24	26	28	31	33	31	30	28	29	31	34	36	38	40	40	41	40	41	44	43	45	48	44	43	41	39	37	35	33	31
659	16	14	20	24	26	28	30	32	36	40	43	45	49	53	55	58	62	63	66	67	70	73	76	78	80	80	83	84	80	86	89	91	92
660	12	14	18	23	25	26	28	27	26	26	23	22	23	26	28	31	33	33	34	37	37	38	40	41	43	42	43	44	41	44	44	46	44
661	14	16	19	24	27	28	31	33	36	40	43	44	48	50	52	57	61	63	66	66	67	67	69	65	65	68	70	69	67	71	74	75	76
662	14	14	19	22	24	25	27	27	28	29	29	32	35	39	40	43	44	44	44	46	47	45	44	43	43	46	47	46	46	48	45	49	49
AVERAGE WEIGHT	13.2	14.4	18.6	22.3	24.4	26.3	27.8	28.8	32.2	32.8	33.7	36.4	37.6	40.2	42.2	44.5	47.6	48.6	50.7	52.2	54.1	55.6	57.6	59.3	61.0	61.6	62.8	62.2	59.2	63.4	64.2	64.6	66.7
% P, CNS, D					0	5	25	30	30	30	30	30	30	30	30	35	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40	45	45
% DEAD					0	0	0	0	0	5	5	5	5	5	5	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	15	15

VIRUS

+ autopsied immediately or dead – Cadaver – cerebellum, stem and cord and brain removed – external hyperemia, thick

STANDARD

LANSING VIRUS ONLY — 0.05 ML OF 1:100 I. CER.

F

20 ♂ HAMSTERS — 29-41 GMS — AVERAGE = 31.2

HAMSTER NO	A -3 -2 -1	0 (4/21)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
663	26	30	34	35	39	40	40	43	47	51	52	55	58	59	63	65	67	65	65	69	71	72	74	75	77	77	78	75	77	75	77	79
664	36	40	44	46	50	53	51	50	55	59	60	62	64	68	68	64	67	69	65	64	69	63	68	72	73	79	81	85	81	86	81	84	86
665	29	32	35	35	39	41	40	40	43	47	52	53	57	58	60	62	64	66	64	64	69	72	73	75	77	78	79	81	79	82	76	80	81
666	28	32	36	39	42	43	41	40	39	—	—	F	PP	D																			
667	31	29	36	38	41	43	43	42	47	49	52	54	57	60	61	63	65	63	60	60	64	65	64	65	67	69	69	71	69	72	68	72	73
668	32	35	38	41	45	46	44	41	47	52	55	57	59	60	61	63	64	67	63	63	68	70	69	72	74	73	94	74	70	75	70	74	74
669	35	39	43	45	49	49	49	48	53	58	60	63	67	68	72	75	78	81	80	81	85	88	88	92	92	96	95	98	97	99	95	99	101
670	32	32	37	39	41	44	42	41	45	47	45	42	41	39	39	40	42	43	39	38	44	43	43	46	47	46	47	46	44	47	46	48	49
671	30	35	40	42	44	46	46	45	51	54	57	55	52	48	44	45	46	47	45	47	49	52	52	55	59	59	61	59	57	60	54	58	60
672	35	40	44	47	51	53	52	52	57	60	62	62	61	63	65	67	71	73	70	71	77	80	82	83	85	86	84	86	83	88	82	86	87
673	29	33	37	38	41	42	41	41	43	43	45	47	50	53	55	60	63	65	62	64	69	71	73	74	76	77	77	79	75	80	73	78	80
674	37	40	44	46	49	51	48	—	—	—	—	F	PP	D																			
675	28	32	36	39	41	42	43	42	46	46	47	49	52	55	57	61	64	67	66	68	71	72	72	75	76	77	79	79	74	79	76	79	81
676	32	35	40	41	45	46	46	45	50	52	53	55	55	57	58	61	63	65	63	62	65	66	64	67	69	68	68	68	65	70	67	70	72
677	37	41	45	47	51	53	53	53	57	61	61	57	51	48	—	—	—	—	—	—	PP	PD											
678	31	35	39	42	45	47	43	41	41	38	35	32	28	25	23	22	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
679	32	36	38	42	45	47	45	44	50	53	55	52	50	46	41	38	38	39	37	34	40	41	44	47	49	48	51	51	48	53	50	53	52
680	27	32	35	35	37	39	36	31	—	—	—	F	FF	D																			
681	31	35	38	40	41	44	37	35	34	—	—	—	?	PP	D																		
682	28	33	36	40	43	45	43	43	47	52	57	58	62	65	68	71	75	77	76	76	81	85	87	89	91	92	93	95	93	99	92	96	99
AVERAGE WEIGHT	31	34	33	38	40	40	44	44	45	45	45	47	47	51	51	52	52	54	52	52	53	53	53	54	54	55	54	57.0	56	61	61	62	63
% P, CNS, D	0	0	10	20	25	35	35	45	55	55	55	55	55	55	55	55	55	55	55	60	60	60	60	60	60	60	60	60	60	60	60	60	60
% DEAD	0	0	5	15	20	20	20	20	20	25	25	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30

VIRUS

Dead stick

Control - cerebellum, stomach and spinal cord used for injection

APR 18 1952

ACTH - 3X DAILY FOR 8 DAYS (10 UNITS PER DAY) - S.C. - LANSING VIRUS - 0.05 ML OF 1:100 ON 4TH DAY - ICER

G

20 ♂ HAMSTERS - 11-17 GMS. - AVERAGE = 13.6

HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
87-643		12	11	15	17	18	21	21	22	25	25	27	28	31	33	37	37	39	42	44	46	47	49	51	53	55	53	54	54	53	56	57	59	61
684		14	15	19	20	21	22	22	22	22	24	26	25	26	29	33	34	34	36	37	36	35	31	29	28	26	23							
685		14	16	18	20	21	22	23	25	26	25	26	27	29	33	35	37	39	41	44	46	48	51	53	54	56	59	61	61	60	63	65	67	66
686		15	16	19	20	23	22	23	22	22	21	22	22	24	26	28	30	32	34	35	37	38	41	44	44	48	47	49	50	48	52	53	55	58
687		12	11	14	16	17	19	21	22	24	25	27	28	29	31	33	34	36	38	38	39	41	43	44	46	47	50	51	52	53	56	58	59	59
688		16	17	20	22	24	25	26	25	23	22	20	20	20	22	22	21	19	18	16														
689		13	14	17	18	20	21	20																										
690		16	13	18	20	22	22	21	23	25	26	29	31	33	36	39	41	42	42	43	45	47	49	51	52	54	55	57	59	62	64	62	64	65
691		14	16	19	21	22	23	24	24	24	25	26	27	27	30	32	35	36	35	35	35	37	41	43	45	48	49	50	51	48	67	53	58	58
692		13	15	14	20	21	22	24	23	20																								
693		13	14	17	18	20	22	22	20	18	17	16	14	15	15	16	17	18	19	18	18	18	18	17	18	17	15	14	15	14	15	14	15	
694		13	15	19	20	21	22	23	24	23	22	22	23	23	25	26	28	30	32	33	36	38	39	42	44	45	47	48	50	51	53	56	57	58	59
695		12	13	16	17	18	19	20	19	17	15	14	14	14	15	14	15	15	15	15	16	17	16	17	17	16	17	16	16	14	15	15	15	15
696		12	14	16	18	20	21	21	20	19	16	15	13																					
697		13	16	17	18	18	18	19	17	16	15																							
698		15	16	20	21	23																												
699		14	16	19	21	22	23	23	23	22	23	23	24	26	27	29	31	33	33	34	36	35	37	38	39	40	40	41	41	38	43	43	45	47
700		15	17	19	22	23	24	26	27	29	32	36	37	39	42	44	47	48	50	52	55	57	58	60	61	63	64	66	67	65	68	69	71	73
567		01	13	14	18	18	20	21	23	24	25	28	29	32	34	37	40	42	44	46	48	51	53	56	58	58	61	64	65	66	64	69	68	69	69
702			13	13	18	18	20	22	22	23	25	27	29	32	34	37	39	43	45	48	49	52	53	56	59	61	63	63	66	67	62	69	71	73	74
AVERAGE WEIGHT		13.6	14.6	17.8	19.3	20.7	21.6	22.3	22.5	22.5	22.8	23.9	24.2	25.3	27.1	29.2	31.2	32.5	34.1	35.3	36.2	39.2	40.3	42.0	43.3	44.4	45.7	46.2	49.2	50.4	48.7	52.5	52.6	54.2	58.6
% P, CNS, D						0	2	1	4	7	6	3	6	8	6	8	6	8	6	8	6	8	6	8	6	8	7	4	7	9	7	9	7	9	7	9	7	9	7	9	7	9
% DEAD						0	0	5	11	11	16	16	21	21	21	21	21	21	21	26	26	26	26	26	26	26	32	32	32	32	32	32	37	

ACTH

VIRUS

ACTH - 3X DAILY FOR 8 DAYS (10 UNITS PER DAY) - S.C.)
+ LANSING VIRUS — 0.05 ML OF 1:100 ON 4th DAY.

20 ♂ HAMSTERS — —39 GMS — AVERAGE = 31.2

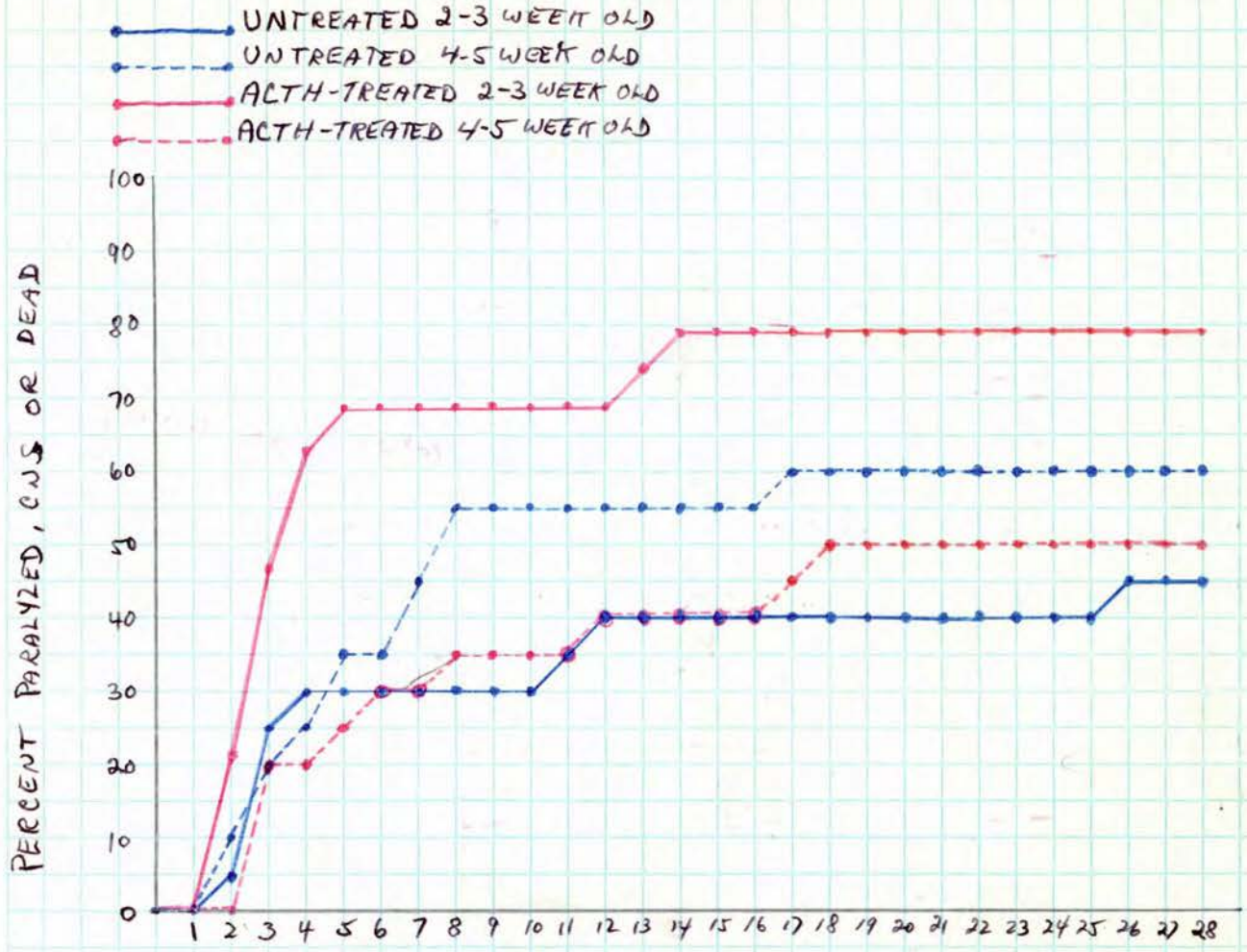
HAMSTER NO	A	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
703		32	36	36	39	38	39	41	37																								
									PP	D																							
3																																	
✓49	~~Ent~~	30	30	35	37	37	38	40	42	41	45	48	50	51	52	53	54	54	55	56	59	61	63	66	69	71	72	75	75	71	76	81	81	83
✓ 79	705	32	35	37	38	40	42	43	44	47	51	53	54	56	60	62	65	66	69	68	70	70	73	76	78	80	82	84	84	85	89	89	92	92
✓	706	31	34	35	35	35	35	36	36	36	38	40	43	42	42	44	44	47	51	51	52	49	51	52	51	52	50	50	49	42	50	55	55	57
18																								P	P	P	P	P	P	P	P	P	P
✓	707	29	34	36	37	37	37	38	38	44	48	49	50	51	52	55	55	57	60	61	62	63	68	68	72	74	75	74	76	72	79	82	83	83
✓	708	33	29	33	35	34	35	36	37	40	42	44	45	47	48	50	51	51	51	50	51	52	54	56	57	59	62	63	64	61	68	70	67	
12																	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	
✓	709	32	34	34	35	35	37	38	38	40	41	42	44	43	44	46	45	46	46	46	49	51	54	56	57	59	60	62	64	60	67	68	70	70
✓	✓ 710	32	31	35	35	36	37	39	40	42	45	46	49	52	55	59	61	63	65	65	68	71	72	75	77	80	81	83	83	83	88	90	91	93
✓	711	33	36	37	39	39	39	41	41	43	47	49	51	51	51	50	48	47	46	45	46	48	51	53	54	56	58	60	62	59	64	66	69	67
	712	33	37	37	39	40	41	43	44	46	51																						
6										D																							
	713	36	39	41	42	43	43	44	45	46	50	53	51	45	42	38	36																
																CNS	CNS	E→h	E→h	E→h	E→h	D											
8																																	
✓ 75	~~714~~	33	36	37	40	38	41	42	44	46	50	52	54	56	60	62	64	67	70	69	71	72	77	79	80	82	83	85	86	88	89	92	93	95
✓	715	27	30	31	30	32	32	33	33	32	32	34	35	36	39	42	43	45	46	48	51	52	53	53	55	57	56	54	53	50	55	56	58	58
17																					P	P	P	P	P	P	P	P	P	P	P	P	P	
✓ 89	716	27	30	31	33	34	35	36	36	38	41	44	45	46	48	51	53	55	57	59	63	64	66	68	69	71	72	73	72	70	75	76	78	77
	717	33	36	36	37	37	35	36	37	36	32																						
5										PP	D																						
✓ 52	~~718~~	29	32	32	35	35	35	37	39	42	44	48	49	51	53	56	57	60	61	60	63	64	67	69	70	71	73	74	74	76	79	81	83	84
	719	29	33	34	35	35	35	37	36																								
3										P	D																						
✓	720	27	30	29	31	31	32	33	33	35	37	40	42	42	44	46	47	48	50	51	53	55	57	58	59	61	63	64	66	66	68	70	72	72
	721	31	35	36	38	38	38	40	33	29																							
3										P	P	P	P	D																			
✓	722	35	38	39	42	41	41	42	41	40	39	37	36	35	37	36	38	35	35	36	37	37	39	41	43	45	46	39	35	32	36	37	38	42
3										P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P

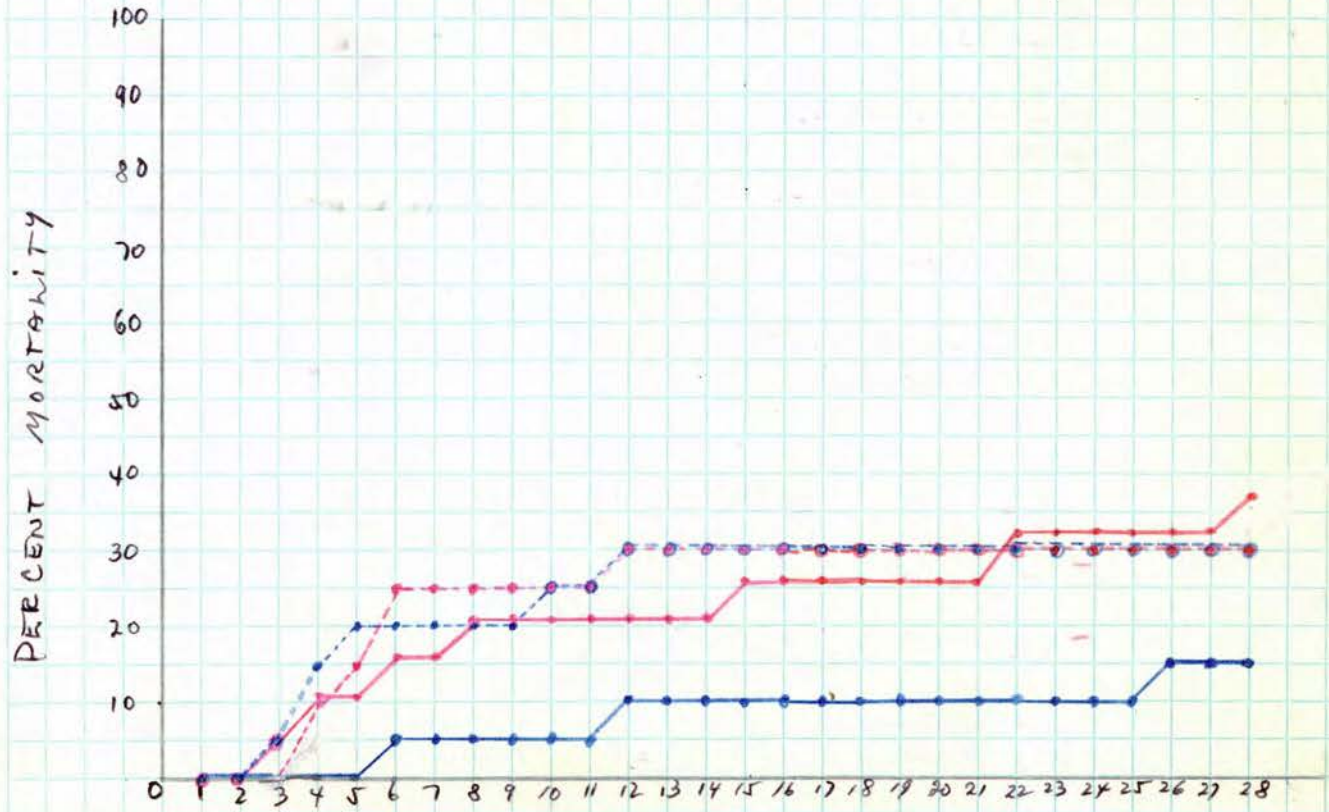
AVERAGE WEIGHT 31.2 33.7 35 36.6 36.8 37.4 38.8 38.7 40.1 43.1 45 44.6 47.0 48.4 50.6 50.7 52.9 54.4 54.6 56.7 57.7 60.3 62.1 63.6 65.5 66.6 62.1 62.7 66.5 70. 72.1 73.7 77.1

ACTH ↑ VIRUS ↑

%P, CNS, D	0	0	20	20	25	30	30	35	35	35	35	40	40	40	40	40	45	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
%DEAD	0	0	0	10	15	25	25	25	25	25	25	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30

EFFECT OF ACTH INOCULATED 3 TIMES DAILY FOR 8 DAYS (10 UNITS DAILY) ON SUSCEPTIBILITY OF 2-3 WEEK OLD AND 4-5 WEEK OLD HAMSTERS TO LANSING VIRUS (1:100)





J. Pharmacy and Pharmacol., 1952, 4, 37

The Effects of Cortisone and Adrenocorticotrophic Hormone on Poliomyelitis and on Other Virus Infections

[redacted]

From The Pharmacological Laboratories, School of Pharmacy, University of London

Received November 4, 1951

There is growing evidence that under certain circumstances cortisone reduces the resistance of animals to bacterial infections; thus the infection becomes more intense after cortisone in experimental tuberculosis, syphilis, and pneumococcal septicaemia. There is also evidence that cortisone has a similar action in some virus infections. Schwartzmann found that cortisone had an accelerating action on poliomyelitis in mice when the virus was inoculated intracerebrally. In addition, golden hamsters, Mesocricetus auratus, which normally are highly resistant to intracerebral inoculation with Lansing types of poliomyelitis virus, were found to become highly susceptible to this route of infection when MEF_1 poliomyelitis virus was injected intracerebrally.

Experiments on Poliomyelitis in Mice

Experiment 1. 30 mice were inoculated intracerebrally with 0.03 ml. of a suspension containing approximately 100 ID50 doses of MEF1 poliomyelitis virus. 10 mice were left as controls: a second group of 10 mice was given 5 mg. of cortisone acetate 2 hours, and again 19 hours, after the intracerebral injection of virus: a third group of 10 mice received 5 mg. of ACTH intramuscularly 2 hours before being injected with the virus; 5 mg. of cortisone acetate was then injected intramuscularly 2 hours after the injection of the virus and the same dose was repeated 19 hours after the injection of virus. The average period from inoculation of virus to death is shown in Table I.

TABLE I

Number of mice	Treatment	Average period from inoculation to death days	Percentage mortality
10	Control	12.3 ± 3.2	90
10	ACTH and Cortisone	6.4 ± 2.6	100
10	Cortisone	7.5 ± 2.2	100

Experiment 2. A similar experiment was carried out with 30 mice, 15 mice being used as control and 15 receiving cortisone alone in the dosage as before. The results were similar: the controls died in an average of 14.2 days while the cortisone-treated mice died in an average of 6.2 days. One curious fact was that whereas the cortisone was invariably injected intramuscularly into the hind leg, paralysis almost always occurred in the front legs, thus showing that the paralysis was not due to the trauma occasioned by the cortisone injection.

Experiment 3. In this experiment ACTH alone was used. 40 mice were inoculated intracerebrally with 0.03 ml. of approximately 50 LD50 doses of MEF1 poliomyelitis virus in a suspension of mouse cord in saline solution. 20 mice were given 5 mg. of ACTH intramuscularly 2 hours before being injected with the poliomyelitis virus and again with the same dose 22 hours after injection of the virus. The average period from inoculation to death was 10.2 days in the control mice and 9.8 days in the ACTH-treated mice. Of the ACTH-treated mice half were dead by the seventh day after

infection, whereas of the control mice half were dead only by the tenth day after infection. Thereafter the ACTH-treated mice showed a slight retardation and 2 mice survived the observation period of 25 days. The effect of ACTH on the poliomyelitis infection was not therefore very noticeable.

Experiment 4. The experimental results described suggested that cortisone in some way reduced the resistance of the central nervous system to poliomyelitis virus once it had gained entrance to the central nervous system. This reduced resistance might be due to a change in the nervous system whereby paralysis and death occurred in the presence of a smaller amount of virus than was required to produce paralysis in the normal mouse or to the more rapid multiplication of virus in the spinal cord.

In order to throw light on this point 6 mice were each injected intramuscularly in the right leg with 5.0 mg. of cortisone in 0.5 ml. of saline solution: 6 control mice were similarly given an intramuscular injection of 0.5 ml. of saline solution. 2 hours later the 6 cortisone-treated and the 6 control mice were injected with 0.03 ml. of 50 MLD50 of MEF1 poliomyelitis virus in the form of a saline suspension of mouse cord. 18 hours later on the following day the cortisone-treated group were again injected with 5.0 mg. of cortisone in 0.5 ml. of saline solution and the control mice received 0.5 ml. of saline solution. 24 hours after the original injection of cortisone 3 mice from the cortisone-infected and 3 from the saline-treated mice were killed. Their cervical and lumbar cords were dissected out. The 3 cervical cords were weighed together and ground up to form a 1 in 10 suspension in physiological saline solution: the 3 lumbar cords were similarly treated. Dilutions of the 1 in 10 suspensions in saline solution were diluted so as to provide suspensions of 1 in 100, 1 in 200, and 1 in 400. Batches of 4 mice were then inoculated intracerebrally with 0.03 ml. of each dilution of cervical cord and of each dilution of lumbar cord. 48 hours after the original injection of cortisone the remaining 3 mice in each batch were killed and suspensions of their cervical and lumbar cords were prepared as before, batches of mice receiving 0.03 ml. of each dilution as before. The period from intracerebral inoculation to death is shown in Table II: mice were observed for 25 days; S signifies survival for this period.

TABLE II

Period of Survival of Mice in Days after Intracerebral Inoculation of Cords From Cortisone-Treated and From Normal Mice Infected with Poliomyelitis (MEF1 Strain)

Dilution of cord suspension	Cords from cortisone-treated mice killed after		Cords from saline-treated mice killed after	
	24 hours	48 hours	24 hours	48 hours
Cervical cord:				
1 in 10 ..	9,14,15,16	9,10,10,16	S,S,S,S	22, S,S,S
1 in 100 ..	4, 9,13,14	6,10,11,20	S,S,S,S	S, S,S,S
1 in 200 ..	16,20,20, S	9,11,11,13	S,S,S,S	S, S,S,S
1 in 400 ..	13,17, S, S	11,11,13, S	S,S,S,S	S, S,S,S
Lumbar cord:				
1 in 10 ..	22, S, S, S	6,15,13, S	S,S,S,S	S, S,S,S
1 in 100 ..	S, S, S, S	S, S, S, S	S,S,S,S	S, S,S,S
1 in 200 ..	S, S, S, S	S, S, S, S	S,S,S,S	S, S,S,S
1 in 400 ..	S, S, S, S	S, S, S, S	S,S,S,S	S, S,S,S

S = Survival.

The evidence thus shows that poliomyelitis virus was present in cervical cords even 24 hours after intracerebral inoculation of suspensions of cervical cord from mice inoculated with MEF1 poliomyelitis and treated with cortisone whereas no virus was present in the cervical cords of mice similarly infected with MEF1 virus but injected intramuscularly with saline solution only. This difference between cortisone-treated and saline-treated mice is even more marked when the cervical and lumbar cords were removed from mice 48 hours after injection of MEF1 virus.

The evidence thus suggests that cortisone increases the rate of multiplication of poliomyelitis virus in the spinal cord of mice. Cultures from the heart blood and brains of cortisone-treated mice showed no evidence of bacterial infection.

Experiments in mice using 5-pregnene-3-β-ol-20-one, in the same dosage as with cortisone, showed no effect in accelerating the development of poliomyelitis.

Experiments on Poliomyelitis in Golden Hamsters

Even more striking than the effect of cortisone on MEF1 poliomyelitis virus infection in mice were the results obtained by Schwartzman in the golden hamster (Mesocricetus auratus). The experiments here recorded were carriedout with the Lansing strain of poliomyelitis. This strain in mice is normally rather less active than the MEF1 virus and the intervals between inoculation and death of a batch of mice show a more irregular distribution. From time to time batches of golden hamsters have been inoculated intracerebrally with the Lansing strain of poliomyelitis virus: no symptoms have been seen and the animals have survived.

10 half-grown golden hamsters were inoculated intracerebrally with 0.05 ml. of a 1 in 20 suspension in saline solution of mouse cord infected with the Lansing strain of poliomyelitis virus. 5 of the hamsters were injected intramuscularly in the hind leg with 5 mg. of cortisone acetate in 0.5 ml. of physiological saline solution: the same dose of cortisone was injected intramuscularly 3 hours after the intracerebral injection of the poliomyelitis virus. 5 control hamsters were given intramuscular injections of physiological saline solution. Of the control hamsters 1 died within3 hours as a result of the shock of inoculation. Of the cortisone-treated hamsters, 1 became paralyzed after 3 days, 1 after 8 days, 1 after 11 days and 1 after 28 days. The fifth hamster survived. The control hamsters were observed for the 35 days without symptoms. Just as was described by Schwartzman, the cortisone-treated hamsters at the same time as they developed paralysis were seen to have hunched backs, ruffled fur and conjunctivitis. As in the case of mice, paralysis first appeared in the front legs.

Cultures of heart blood from the paralyzed hamsters were bacteriologically sterile. In order to be quite certain that an encephalo-myocarditis virus was not being carried over together with the Lansing poliomyelitis virus suspensions 1 in 5, 1 in 50 and 1 in 200 of the spinal cords from paralyzed mice were mixed with normal rabbit serum and with rabbit serum containing immune bodies against Columbia SK virus. Mice were then injected intracerebrally with 0.03 ml. of the various suspensions. There was no difference in the time at which the two series of mice developed paralysis and died: in other words the Columbia SK immune serum had not action on the virus present in the cord suspensions which was therefore not a virus of the encephalo-myocarditis group.

One point of considerable interest was in the histological appearances of the cords from hamsters which had developed paralysis as a result of cortisone treatment. The anterior horn cells in the cervical cord especially showed widespread necrosis but there was remarkably little round cell or neuroglial reaction in the neighbourhood of the degenerate neurones. As no material was available for comparison from normal hamsters inoculated with the Lansing virus 6 young hamsters were injected intracerebrally with 0.05 ml. of a 1 in 10 suspension in saline of spinal cord from mice paralyzed by the MEF1 virus. 2 of these hamsters became paralyz

the MEF1 virus. 2 of these hamsters became paralyzed in 18 and 24 days after inoculatipn: histological examination of their spinal cords showed a much more intense reaction round the anterior horn cells.

Experiments with Other Viruses

A small number of experiments were carried out with other viruses to determine the effects of cortisone.

Rift Valley Fever Virus. The viscerotropic strain of this virus when inoculated intraperitoneally into mice causes diffuse necrosis of the liver. 2 experiments were carried out. 20 mice were injected intramuscularly with 5 mg. of cortisone acetate: 2 hours a later these 20 mice and 24 controls were inoculated intraperitoneally with 0.1 ml. of dilutions of mouse blood infected with Rift Valley fever virus. The cortisone treated mice were given a further intramuscular injection of 5 mg. of cortisone 3 hours after the intraperitoneal injection of the virus. The period from inoculation to death is shown in Table III.

TABLE III

Mice Inoculated Intraperitoneally with Rift Valley Fever Virus

Dilution of blood	Time in days from infection to death	
	Control mice	Cortisone-treated mice
10^{-1}	2, 2, 2, 2	2, 2, 2, 2
10^{-4}	3, 3, 4, 5	2, 2, 2, 2
10^{-5}	3, 3, 4, 5	2, 2, 2, 2
10^{-6}	3, 4, 4, 5	2, 2, 2, 2
10^{-7}	S, S, S, S	3, 3, 3, 3
10^{-8}	S, S, S, S	5, 5, 6, S

S = Survival

It will be seen thatthe infection in the cortisone-treated mice was much more rapid than in the control mice. Histological examination of the livers of the cortisone-treated mice, dying in 48 hours after an injection of 0.1 ml. of blood diluted 10^{-6} showed a diffuse liver necrosis with margination of the nuclear chromatin and acidophilic intranuclear inclusions entirely comparable to that seen in mice inoculated with infected blood diluted 10^{-1}.

Coxsackie Virus. Evidence has been obtained that young adult mice which show only a very slight multiplication of Coxsackie Virus in the muscles, when injected with cortisone exhibit a much more intense production of virus.

Encephalo-myocarditis Viruses. The Columbia SK Virus when inoculated intraperitoneally into mice gives rise to viraemia followed by the production of encephalitis and myocarditis. When cortisone-treated and control mice are inoculated intraperitoneally with dilutions of Columbia SK virus it is again found that the cortisone-treated mice exhibit a rapid infection after inoculation with dilutions of infected mouse brain which kill normal mice only after a dealy of 4 to 5 days.

Discussion

The evidence obtained with poliomyelitis viruses of the Lansing type, with Rift Valley fever virus, with Coxsackie viruses, and with encephalo-myocarditis virus (Columbia SK and Senger Viruses) all points to the fact that cortisone and ACTH permit a more rapid multiplication of these viruses. How exactly this increased virus multiplication occurs is not known although there is a suggestion that the tissue reaction of the host to infection is in some way inhibited. This effect on the tissue reactivity is not specific to any one tissue; Kass et al. found that in mice infected with influenza virus (a dilution of 10^{-5} intranasally) and treated with cortisone, 10 of 10 mice died in an average of 6.5 days: only 6 of 10 control mice died in an average of 8.5 days. In the survivors after 12 days the lung lesions were not extensive. Kligman et al, similarly found that when 5 mg. of cortisone was injected daily into guinea-pigs for 2 days and vaccinia virus was then inoculated intradermally the lesions were more intense in the cortisone-treated animals than in normal guinea-pigs.

Conclusions

1. Treatment of mice infected with poliomyelitis virus by cortisone early in the infection results in a more rapid onset of paralysis and death than in control mice untreated by cortisone.

2./ The evidence suggests that there is more rapid multiplication of virus in the cervical cord of cortisone-treated mice.

3. Injections of ACTH early in infection produce early paralysis and death in some mice but the effect is less marked than with cortisone.

4. Golden hamsters infected with Lansing poliomyelitis are highly resistant but if cortisone is injected at the time of infection the majority develop paralysis and die. This infection is due to poliomyelitis virus and not to an intercurrent infection.

5. There is evidence that cortisone increases the rate of multiplication and hence the rapidity and severity of symptoms in mice infected with the viruses of Rift Valley fever, encephalomyocarditis (Columbia SK) and Coxsackie (type A).

The cortisone used in this work was provided from a generous gift made jointly to the Medical Research Council and the Nuffield Foundation by Merck and Co., Inc. We wish to expressour gratitude for this gift. One of us (G.M.F.) is in receipt of an expenses grant from the Medical Research Council.