

# Passage of French Neurotropic Yellow Fever Virus

OCT 12 1950

Purpose - to provide fresh virus for testing susceptibility or resistance of PRI mice for comparison with their established resistance to the 17-D derivative strain

Virus - Received to-day by air mail, spec. delivery (unrefrigerated, 24 hours in transit, from [redacted], I.H.D., Rockefeller Inst., N.Y.C. two ampoules - marked SV 42 - SEP 29 '48 - of lyophilized virus - 250<sup>th</sup> passage.

One ampoule stored in req. refrigerator

Other reconstituted with 0.5cc of sterile dist. H<sub>2</sub>O and 0.03cc inoculated i.c.e.r. into each of 10 Maxfield (Swiss) mice, about 8-10 Gm - average weight. (2:30 PM)

## Passage 251:

1 2 3 4 5 6 7

1	D					
2	-	-	-	CNS		
3	-	-	-	CNS		
4	-	-	-	CNS		
5	-	-	-	CNS		
6	-	-	-	CNS		
7	-	-	-	CNS	D	
8	-	-	-	CNS	P <sub>2</sub>	D
9	-	-	-	CNS	P <sub>2</sub>	D
10	-	-	-	CNS	P <sub>2</sub>	D

HAR - 10/16 - titred in PRI + SWISS 3 amps of 2090-B  
BAP 000

French Neurotropic

French Neurotropic Yellow Fever Virus in PRI Mice OCT 16 1950

PURPOSE - To determine the effect of the French neurotropic strain of yellow fever virus on PRI mice which are resistant to the 17-D strain of yellow fever.

VIRUS - Passage 251 material from 4 mice, inoculated 10/12/50, showing CNS signs 10/16/50. Brain of 4 mice removed + ground to 20% in NRS. 2000 SN diluted in 10% R55 for this test + remainder of centrifuged 20% suspension frozen (3 ampoules @ 1.5-2cc each)  
 of vial - B - -  
 BAP-000

MICE - 3-4 week old PRI - weaned 10/16/50  
~~8-10 week old PRI~~  
 4-5 week old Wilbster-Swiss (controls).

PRI MICE

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\* - all mice ruffled

FRENCH NEUROTROPIC YELLOW FEVER IN PRI

PRI MICE

OCT 16 1950

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\* all mice suffled

\*\* Mouse 10 of  $10^5$  has pyogenic infection of hind paw  
10/30 Mice 6, 7, 4 & 8 exhibit - pyogenic inflamm. lesions of extremities

PRI MICE

10<sup>-7</sup>

9/10

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Has sutured 10/30 - BAP-000

10<sup>-8</sup>

4/10

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10/30 - Examination to-day revealed that mice were sick - no definite cars signs.

The presence of the severe purulent inflammatory lesions in the extremities of mice in the 10<sup>-5</sup> box suggests that some spontaneous bacterial infection might be responsible.

(CONTROLS OVER)





STANDARD B & P "NOTEAR"

Passage of French Anthonipai Yellow Fever Virus

NOV 17 1950

PASS 252

PURPOSE - To provide fresh virus for retesting susceptibility or resistance of PRI mice to this virus.

VIRUS - French Anthonipai Yellow fever virus - Passage 251 of 10/16/50. Frozen as 2090 in NRS

MICE - 8-10 gram Muffield albinos

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4	-	-	-	(M)	
5	-	-	-	(M)	D
6	-	-	-	(M)	D
7	-	-	-	(M)	D
8	-	-	-	(M)	D
9	-	-	-	(M)	D
10	-	-	-	(M)	D

HAR 11/21 & titred in mgt + PRI MICE BAP-006  
lamp Frozen 15-1-1 as 2090 in NRS

STANDARD B & P "NOTEAR"

FRENCH NEUROTROPIC YELLOW FEVER VIRUS IN PRI  
(REPEAT TEST)

NOV 21 1950

PURPOSE - to determine the effect of French yellow fever virus on PRI mice.

VIRUS - French neurotropic yellow fever virus pass 252 of 11/20/50 diluted in 10% RSI for the titration & 1 amp page p-1-1. ~ 20% susp in NRS.

MICE - 3-4 week old PRI mice  
8-10 year mayfield albinos (controls).

PRI MICE

10<sup>-1</sup>

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10<sup>-2</sup>

\* P<sub>3</sub> Han 10/28/50 - ground as 20% in NRS. <sup>titrated in SIRS</sup> <sub>passed in NRS</sub> - BAP-D

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6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

10<sup>-7</sup>

	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
1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

\* Ruffled  
p? - Quercus? or Partial Paralysis





Titration of French Nemotopic Yellow Fever  
Virus from PRI M#1 - 10<sup>-2</sup> of 11/21/50

NOV 28 1950

PURPOSE - to determine titer of virus in brains of PRI mouse inoculated with French Nemotopic yellow fever virus. Mouse was paralyzed 11/28/50 - 7 days after being inoculated with 10<sup>-2</sup> dilution of the virus.

VIRUS - PRI M#1 10<sup>-2</sup>, inoculated with French Nemotopic yellow fever virus Pass 252-11/21, showing paralysis 11/28 was sacrificed. Brain + spinal cord removed + found as 2090 in NRS. Dilutions for titration prepared in 1090 RSS. Remainder of 2090 frozen B-1-1 BAP-0

MICE - 4-5 week old Webster Swiss.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	
10 <sup>-3</sup>	1	-	-	W	P	P	P	P	D												
	2	-	-	-	-	-	P	P	D												
	3	-	-	-	-	-	?	D													
	4	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10 <sup>-4</sup>	1	D																			
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10 <sup>-5</sup>	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10 <sup>-6</sup>	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10 <sup>-7</sup>	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10 <sup>-8</sup>	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

\* MISSING

French West African Yellow Fever Virus  
 from PRI in PRI.

NOV 28 1950

PURPOSE - To determine whether material from infected  
 PRI mice, showing signs, will cause an apparent  
 infection in PRI mice (most of which are resistant  
 to the virus when it is prepared in susceptible  
 Swiss mouse brain.)

VIRUS - PRI mouse # 1 -  $10^{-2}$ , inoculated = French  
 West African Yellow Fever Virus Pan 252 11/21/50 -  
 showing paralysis 11/28/50, harvested 11/28/50 +  
 brain + cord suspension used in this test + for  
 titration in Swiss mice. (See Protocol of titration).  
 Remains of 2090 prep B-1-1  
 BAP-000

MICE - 10 PRI mice 3-4 wks old.

$10^{-1}$

	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		
1	-	-	-	-	-	?	-	-	?	W	W	P	D																	
2	-	-	-	-	-	-	-	-	-	W	W	W	D																	
3	-	-	-	-	-	-	-	-	-	?	?	??	?	W	W	W	?	-	-	-	-	-	-	-	-	-	-	-	-	
4	-	-	-	-	-	-	-	-	-	-	-	-	-	W	W	?	-	-	-	-	-	-	-	-	-	-	-	-	-	
5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

Box missing

# Effect of French Neurotropic Yellow Fever Virus on F<sub>1</sub> and Backcross Mice.

Purpose - The French neurotropic yellow fever virus, despite a low level of multiplication in PRI mice nevertheless paralyzes and kills a certain proportion of them - more with smaller initial inocula than with larger ones. This suggests the possibility that the CNS of different mice varies with regard to vulnerability by the "French" virus. Is this variation also on a genetic basis? If so is it inherited as a dominant <sup>in which case</sup> all F<sub>2</sub> mice or a recessive when the PRI mice are bred with Swiss?

Mice - These were bred for tests with 17-D virus, but were in excess of the numbers needed. They vary in age as indicated in the protocols.

Virus - Passage 252 frozen in B-1-1 since 11/21/50 20% susp. in heated undil. rabbit serum. Fresh virus titered 10<sup>-7.6</sup>. Dilutions prepared in 10% rabbit serum saline, kept in ice water during inoculation.

## Summary

Type of Mouse	Inoculum	No. of Mice	No. with CNS or paralysis	No. dead
Swiss - 6wk	10 <sup>-1</sup>	10	6	10 - 100%
	10 <sup>-6</sup>	10	10	9 -
PRI - 5wk	10 <sup>-1</sup>	10	6	5 } 45%
" - old ♀	"	10	4	
" - 5wk	10 <sup>-6</sup>	10	8	8 } 50%
	10 <sup>-6</sup>	10	3	
F <sub>1</sub>	10 <sup>-1</sup>	35	30	
	10 <sup>-6</sup>	35	31	
<u>Backcross</u> PRI ♀ + F <sub>1</sub> ♂ (S + R)	10 <sup>-1</sup>	20	13	
	10 <sup>-6</sup>	17	17	



F1 Mice - 10-6 French Neurotropic Y.F.

FEB 9 1951

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

Box H	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
	-	-	-	-	?	-	-	-	W	W	PP	D																
Rq + S $\sigma$ <sup>+</sup>	-	-	-	-	-	-	-	-	-	W	W	D																
born 12/27	-	-	-	-	-	-	-	-	-	-	W	PP	D															
	-	-	-	-	-	-	-	-	-	-	W	PP	D															
	-	-	-	-	-	-	-	-	-	-	W	PP	D															
	-	-	-	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Box I	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
	-	-	-	-	-	-	-	-	-	D																		
Rq + S $\sigma$ <sup>+</sup>	-	-	-	-	-	-	-	-	-	W	PP	D																
born 1/17/51	-	-	-	-	-	-	-	-	-	?	?	D																
5 mice in orig. litter																												

Box J	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
	-	-	-	-	-	*D																						
	-	-	-	-	-	*D																						
Large $\sigma$	-	-	-	-	-	-	*D																					
from various litters	-	-	-	-	-	-	-	D																				
	-	-	-	-	-	-	-	D																				
	-	-	-	-	-	-	-	as W D																				
(fighting)	-	-	-	-	-	-	-	as W PP D																				
	-	-	-	-	-	-	-	? W W D																				
	-	-	-	-	-	-	-	? W D																				
	-	-	-	-	-	-	-	-	-	?	PP D																	

Box K	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
	(D)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	-	(*D)																				
Large $\sigma$	-	-	-	-	-	-	-	-	PP D																			
from various litters	-	-	-	-	-	-	-	-	W D																			
	-	-	-	-	-	-	-	-	as P <sub>2</sub> D																			
	-	-	-	-	-	-	-	-	as PP <sub>2</sub> D																			
	-	-	-	-	-	-	-	-	? (CN) PP D																			
	-	-	-	-	-	-	-	-	? (CN) PP D																			

Box L	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
	(D)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rq + S $\sigma$ <sup>+</sup>	-	-	-	-	-	-	-	-	?	PP D																		
born 11/6/50	-	-	-	-	-	-	-	-	-	W PP D																		
one litter	-	-	-	-	-	-	-	-	-	W PP P <sub>2</sub> P <sub>2</sub> D																		
	-	-	-	-	-	-	-	-	-	W PP PP P <sub>2</sub> D																		
	-	-	-	-	-	-	-	-	-	? (CN) PP P <sub>2</sub> D																		

\* MICE FIGHTING; BADLY CHAWED  
~~AND FIGHTING~~







Of French Hemotropic Yellow Fever Virus  
in F<sub>1</sub> mice

MAR 23 1951

PURPOSE - To determine effect of this virus on large F<sub>1</sub> mice.

MICE - 5 types + weight of F<sub>1</sub> mice as described below.  
PRI mice as described below  
SWISS mice as described below

VIRUS - Passage 252 frozen in B-1-1 since 11/21/50 2090  
map in NRS. 10<sup>-1</sup> Dilution prepared in 1090 RSS.  
0.03 cc 10<sup>-1</sup> I.c.h.

<u>TYPE OF MOUSE</u>	<u>AVG. WEIGHT</u>	<u>NO OF MICE</u>
A) F <sub>1</sub> ♀ (CR♀ x S♂)	22.8 grams	8
B) F <sub>1</sub> ♀ (CR♀ x S♂)	24.1 grams	8
C) F <sub>1</sub> ♀ (CR♀ x S♂)	27.0 grams	5
D) F <sub>1</sub> ♂ (CR♀ x S♂)	28.6 grams	3
E) F <sub>1</sub> ♀ (S♀ x R♂)	27.4 grams	9
F) F <sub>1</sub> ♀ (S♀ x R♂)	26.6 grams	9
G) F <sub>1</sub> ♂ (S♀ x R♂)	28.3 grams	7
H) PRI ♀	28.4 grams	10
I) PRI ♀	30.5 grams	10
J) CH. SWISS ♂	22.1 grams	7
K) CH. SWISS ♀	26.3 grams	10
L) MAX-SWISS ♀	29.5 grams	7

MAR 23 1951

**A**  
F<sub>1</sub> ♀ (R♀ x S♂)  
22.89 grams =  
AVG. WT.

	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
1	-	-	-	-	? D																							
2	-	-	-	-	-	ww D																						
3	-	-	-	-	-	cn)(cn)(cn) D																						
4	-	-	-	-	-	? cn)(cn)(cn) D																						
5	-	-	-	-	-	ww ? ? ?																						
6	-	-	-	-	-	? ?																						
7	-	-	-	-	-																							
8	-	-	-	-	-																							

**B**  
F<sub>1</sub> ♀ (R♀ x S♂)  
24.19 grams =  
AVG. WT.

1	-	-	-	-	-	cn) D																						
2	-	-	-	-	-	cn) D																						
3	-	-	-	-	-	cn) D																						
4	-	-	-	-	-	ww D																						
5	-	-	-	-	-	ww D																						
6	-	-	-	-	-	cn) D																						
7	-	-	-	-	-	cn)(cn) ? cn) D																						
8	-	-	-	-	-	cn)(cn) ? P: D																						

**C**  
F<sub>1</sub> ♀ (R♀ x S♂)  
27.09 grams =  
AVG. WT.

1	-	-	-	-	-	cn)(cn)(cn)(cn) D																						
2	-	-	-	-	-	w cn)(cn)(cn) D																						
3	-	-	-	-	-	w cn) ? ? cn) D																						
4	-	-	-	-	-	? ? ? ? ?																						
5	-	-	-	-	-	? ? ?																						

**D**  
F<sub>1</sub> ♂ (R♀ x S♂)  
28.6 =  
AVG. WT.

1	-	-	-	-	-	? ? ? ? ? ?																						
2	-	-	-	-	-	? ?																						
3	-	-	-	-	-																							

**E**  
F<sub>1</sub> ♀ (S♀ x R♂)  
AVG. WT = 27.4

1	-	-	-	-	-	D																						
2	-	-	-	-	-	cn) PP D																						
3	-	-	-	-	-	cn) PP D																						
4	-	-	-	-	-	ww PP D																						
5	-	-	-	-	-	ww ww PP PP D																						
6	-	-	-	-	-	cn) ? ?																						
7	-	-	-	-	-	? ?																						
8	-	-	-	-	-																							
9	-	-	-	-	-																							

**F**  
F<sub>1</sub> ♀ (S♀ x R♂)  
AVG. WT = 26.6

1	-	-	-	-	-	ww D																						
2	-	-	-	-	-	ww D																						
3	-	-	-	-	-	? PP D																						
4	-	-	-	-	-	? ww D																						
5	-	-	-	-	-	? ww PP PP PP D																						
6	-	-	-	-	-	cn) ? ?																						
7	-	-	-	-	-	? ?																						
8	-	-	-	-	-																							
9	-	-	-	-	-																							

♀ Total 26  
39 66.7%

G  
F<sub>1</sub> ♂ (S♀ x R)

	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	
	1	-	-	-	-	W	D																						
	2	-	-	-	-	D																							
	3	-	-	-	-	D																							
	4	-	-	-	-	W	D																						
	5	-	-	-	-	D																							
Avg. WT. =	6	-	-	-	-	D																							
28.39g	7	-	-	-	-	D																							

H  
PRI ♀

	1	-	-	-	-	?	?	D																					
	2	-	-	-	-	?	?	D	W	W	W	?	?																
	3	-	-	-	-	?	?	D	W	W	W	?	?																
	4	-	-	-	-	?	?	D	W	W	W	?	?																
	5	-	-	-	-	?	?	D	W	W	W	?	?																
	6	-	-	-	-	?	?	D	W	W	W	?	?																
	7	-	-	-	-	?	?	D	W	W	W	?	?																
Avg. WT. =	8	-	-	-	-	?	?	D	W	W	W	?	?																
28.49g	9	-	-	-	-	?	?	D	W	W	W	?	?																
	10	-	-	-	-	?	?	D	W	W	W	?	?																

I  
PRI ♀

	1	-	-	-	-	?	?	CM	PP	D																			
	2	-	-	-	-	?	?	CM	CM	D																			
	3	-	-	-	-	?	?	?	?	PP	D																		
	4	-	-	-	-	?	?	?	?	PP	D																		
	5	-	-	-	-	?	?	?	?	PP	D																		
	6	-	-	-	-	?	?	?	?	PP	D																		
	7	-	-	-	-	?	?	?	?	PP	D																		
Avg. WT. =	8	-	-	-	-	?	?	?	?	PP	D																		
30.5	9	-	-	-	-	?	?	?	?	PP	D																		
	10	-	-	-	-	?	?	?	?	PP	D																		

Strain of Mice	No. tested	No. <sup>cases</sup> dead	%
Swiss	24	24	100
PRI	20	4	20
F <sub>1</sub>	49	29	60

Suscept.  
AA (aa)  
PRI  
PRI  
PRI  
♀  
x  
♂

MAR 23 1951

	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	
J CH-SWISS ♂	1	-	-	cnj	D																								
	2	-	-	cnj	D																								
	3	-	-	cnj	D																								
	4	-	-	?	D																								
	5	-	-	?	D																								
AVG. WT = 22.1	6	-	-	cnj	D																								
	7	-	-	?	P <sub>2</sub> D																								

K CH-SWISS ♀	1	-	-	?	cnj	D
	2	-	-	?	D	
	3	-	-	?	D	
	4	-	-	-	cnj	D
	5	-	-	-	cnj	D
	6	-	-	-	cnj	D
	7	-	-	-	cnj	D
	8	-	-	-	cnj	D
	9	-	-	-	cnj	D
	10	-	-	-	cnj	D

L MAX SWISS ♀	1	-	-	PP	D	
	2	-	-	PP	D	
	3	-	-	?	D	
	4	-	-	?	D	
	5	-	-	-	P <sub>2</sub> D	
	6	-	-	-	cnj	D
	7	-	-	-	cnj	D

AVG. WT = 29.5

French Neurotropic Yellow Fever Virus  
in old PRI ♂

APR 29 1951

PURPOSE - To obtain PRI ♂ mice resistant to French neurotropic yellow fever virus for subsequent breeding = PRI ♀ + Swiss ♀.

VIRUS - French neurotropic virus of 11/21/50 - Pass 252 - B-1-1  
2090 - NRS. Dilution prepared - 1090 R55.  
0.03 cc 10<sup>-1</sup> I.C.H.

MICE - OLD PRI Males.

	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	
1	-	-	-	-	CND																								
2	-	-	-	-	-	-	-	CND																					
3	-	-	-	-	-	-	-	CND																					
4	-	-	-	-	-	-	-	WD																					
5	-	-	-	-	-	-	-	WD																					
6	-	-	-	-	-	-	-	CND																					
7	-	-	-	-	-	-	-	CND																					
8	-	-	-	-	-	-	-	WD																					
9	-	-	-	-	-	-	-	PR.P.P.P.P.D																					
10	-	-	-	-	-	-	-	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
11	-	-	-	-	-	-	-	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
12	-	-	-	-	-	-	-	CND	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W	W
13	-	-	-	-	-	-	-	?	W	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
14	-	-	-	-	-	-	-	W	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
15	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
16	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
17	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
18	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
19	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
20	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
21	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
22	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
23	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
24	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
25	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
26	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
27	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
28	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
29	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
30	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
31	-	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?

Mated =  
PRI ♀  
+  
W-SWISS ♀  
5/25/51

9/31 = 29%

French Nemotopie

4-29

C.H. albino

@ 7 weeks old

	1	2	3	4	5	6
1	-	-	-	?	CMS	}
2	-	-	-	?	CMS	
3	-	-	-	?	CMS	
4	-	-	-	?	CMS	
5	-	-	-	?	CMS	
6	-	-	-	-	CMS	D
7	-	-	-	-	CMS	D
8	-	-	-	-	CMS	D
9	-	-	-	-	CMS	D
10	-	-	-	-	CMS	D

Passage 253  
 Han 5/4/51 - Davis guinea 2070 - NRS + 5 samples  
 of 2000 SN frozen. B-1-1 DAP-000



JUL 16 1951

Situation of French N. neurotypic Yellow Fever from 4 DAY PRI M # 1, # 2, # 3

PURPOSE - To determine the level of multiplication of this virus in the brain & end of PRI MICE.

VIRUS Cerebr. & Brain of 3 PRI mice, inoculated 7/12/51 with French neurotypic yellow fever 10^-2 I.C.A., harvested & ground individually in HRS 10%. 1090 RSS used for distribution. (MICE SHOWED NO CNS SIGNS) M # 1 BAP - 000 M # 2 BAP - 000 M # 3 BAP - 000

MICE - 3-4 week old W-Swiss.

From 4 day PRI M # 1 - 4.2

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
$10^{-1}$	1	-	-	-	D																	
	2	-	-	-	D																	
	3	-	-	-	D																	
	4	-	-	-	(CN)	D																
	5	-	-	-	(CN)	D																
$10^{-2}$	1	-	?	D																		
	2	-	-	-	D																	
	3	-	-	-	(CN)	D																
	4	-	-	-	(CN)	D																
	5	-	-	-	(CN)	D																
$10^{-3}$	1	-	-	-	(CN)	D																
	2	-	-	-	(CN)	D																
	3	-	-	-	?	D																
	4	-	-	-	?	D																
	5	-	-	-	-	D																
$10^{-4}$	1	-	-	-	-	D																
	2	-	-	-	-	D																
	3	-	-	-	-	(CN)	D															
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$10^{-5}$	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
$10^{-6}$	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

4.2

















Genetic Basis of Special Susceptibility of Nervous System to Damage  
at Low Levels of Viral Multiplication

Outline of Breeding Experiment to Determine  
Genetic Aspects of Factor which  
Renders Mice Susceptible to French  
Neurotropic Virus (Yellow Fever) at  
Low level of Multiplication

1. Inoculate 30 old PRI males with  $4\frac{1}{2} \times 10^6$   
French Neurotropic Yellow Fever Virus
2. Save Completely resistant Males.
3. Breed PRI ♀ + Resistant PRI ♂  
Then Individual PRI ♀ + their litters to be  
tested with F. N. Y. F. virus  
Try for 20 such ♀ - (2♀ + 1♂ per box)
4. Breed Swiss ♀ + Resistant PRI ♂  
as under 3

FRENCH NEUROTROPIC YELLOW FEVER VIRUS

JUL 25 1951

IN W-SWISS MOTHERS + PROGENY (W-SWISS ♀ x FR. N.Y.F. RES. PRI ♂)

VIRUS - French neurotropic yellow fever virus of 5/4/51 - 20% in NRS  
10-1 in 1090 RSS used for this test. B-1-1

MICE - W-SWISS ♀s, + their litters (described below), which were bred = French neurotropic yellow fever resistant PRI males.  
@ 6wk old PRI + @ 6wk old W-Swiss (controls)

	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
SWISS MOTHER	-	-	-	D																								
Litter of 8-6/14/51 (S♀ x Res. PRI ♂)	1 ♂	-	-	-	-	-	CNS ?	?	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2 ♂	-	-	-	-	-	CNS ?	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4 ♀	-	-	-	-	-	CNS	CNS	?	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	5 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

	1	2	3	4	5	6
SWISS MOTHER	-	-	-	D		
Litter of 8-6/15 (S♀ x Res. PRI ♂)	1 ♀	-	-	(W) D		
	2 ♂	-	-	-	CNS D	
	3 ♀	-	-	-	-	D
	4 ♀	-	-	-	CNS	CNS D
	5 ♂	-	-	-	-	CNS D
	6 ♂	-	-	-	-	CNS D

	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
SWISS MOTHER	-	-	-	D																								
Litter of 5-6/16 (S♀ x Res. PRI ♂)	1 ♀	-	-	-	-	?	?	?	?	-	-	*	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

	1	2	3	4	5	6	7
SWISS MOTHER	-	-	-	-	CNS D		
Litter of 7-6/18 (S♀ x Res. PRI ♂)	1 ♀	-	-	-	-	CNS Pr. D	
	2 ♀	-	-	-	-	? CNS D	
	3 ♀	-	-	-	-	? CNS	CNS D *
	4 ♀	-	-	-	-	-	-
	5 ♂	-	-	-	-	CNS	CNS D
	6 ♂	-	-	-	-	-	? (W) CNS D
	7 ♂	-	-	-	-	-	-

\* Boxes cleaned 8/1/51 by Preston Mupke; mice from box of 6/18 mixed = mice of 6/16. (Box of 6/18 empty - discarded).

W- SWISS Controls

10<sup>-1</sup>

	1	2	3	4	5
1	D				
2	-	-	-	D	
3	-	-	-	CMS D	
4	-	-	-	CMS D	
5	-	-	-	CMS D	
6	-	-	-	CMS D	
7	-	-	-	CMS D	
8	-	-	-	CMS D	
9	-	-	-	CMS D	
10	-	-	-	CMS PP D	

PRI Controls

10<sup>-1</sup>

	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	
1	-	-	-	-	-	-	?	CMS D																					
2	-	-	-	-	-	-	?	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	D
3	-	-	-	-	-	-	?	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS	CMS
4	-	-	-	-	-	-	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?	?
5	-	-	-	-	-	-	?																						
6	-	-	-	-	-	-																							
7	-	-	-	-	-	-																							
8	-	-	-	-	-	-																							
9	-	-	-	-	-	-																							
10	-	-	-	-	-	-																							

If mother dies - two possibilities on hypothesis of single dominant gene for susceptibility

$$S_r + r_r = S_r + r_r = 50\% \text{ resistant}$$

$$S_s + r_r = S_r + S_r = 100\% \text{ die}$$

If mother survives - then:

$$r_r + r_r = r_r - \text{all should survive}$$

IN PRI MOTHERS + PROGENY (PRI ♀ x F. N.Y.F. RES. PRI ♂)

VIRUS - French Neurotropic Yellow Fever virus of 5/4/51 - 20% - NRS-B-1-1  
10<sup>-1</sup> in 1090 RSS used in this test

MICE - PRI females, & their litter described below, which  
were bred = French neurotropic yellow fever resistant  
PRI males.  
- @ 6 wk old PRI + @ 1 wk old W-Swiss (control)

		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				
	PRI MOTHER	-	-	-	-	-	-	-	?	?	?	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-	-				
Litter of 8 - 6/16/51 (R ♀ x Res. R ♂)	1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	-	-	-	-	-	-	-	-	-	-	-	-				
	2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	3 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	5 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	6 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	7 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	8 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	PRI MOTHER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
Litter of 7 - 6/16/51 (R ♀ x Res. R ♂)	1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	3 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	4 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	5 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	6 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	7 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	PRI MOTHER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Litter of 6 - 6/17/51 (R ♀ x Res. R ♂)	1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	4 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	5 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	6 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	PRI MOTHER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Litter of 6 - 6/18/51 (R ♀ x Res. R ♂)	1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	PRI MOTHER	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Litter of 3 - 6/18/51 (R ♀ x Res. R ♂)	1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	2 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Mothers dead - 7/18 - 3 litters

13/39 - 7 litters











AUG 13 1951

FRENCH NEUROTROPIC YELLOW FEVER VIRUS vN

W-SWISS MOTHERS + PROGENY (W-Swiss ♀ x Fr. N. Y. F. Res. PRI ♂)

VIRUS - French neurotropic yellow fever virus of 5/4/51 - 20% in N.R.S. - B-1-1  
 10<sup>-1</sup> in 10% R.S.S. used for this test

MICE - W-Swiss ♀'s and their litters (described below) which were bred c̄ French neurotropic yellow fever resistant ♂'s.

@ 4-5 wk. old P.R.I. and 4-5 wk old Swiss controls.

	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
MOTHER	-	-	-	W	D																							
Litter of 9-7/51	♀ 1	-	-	-	W	W	P	P	P	P	D																	
	♀ 2	-	-	-	W	W	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	♀ 3	-	-	-	-	-	-	-	-	-	2	=	W	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
(S-♀ x Res. PRI ♂)	♀ 4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	♂ 5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	♂ 6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	♂ 7	-	-	-	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	♂ 8	-	-	-	-	-	-	W	2	2	-	-	-	-	-	-	-	-	-	-	-	-	2	2	-	-	-	-

	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
MOTHER	-	-	-	PP	D																							
Litter of 11-8/1	♀ 1	-	-	2	2	2	2	W	W	W	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	♀ 2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	♀ 3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
(S-♀ x Res. PRI ♂)	♂ 4	-	-	-	-	-	-	2	W	W	W	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP	PP
	♂ 5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	♂ 6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

W-SWISS CONTROLS - 10<sup>-1</sup>

	1	2	3	4	5
1	-	-	D		
2	-	-	D		
3	-	-	PP	D	
4	-	-	W	D	
5	-	-	W	D	
6	-	-	W	W	D
7	-	-	W	W	D
8	-	-	2	W	D
9	-	-	-	W	D
10	-	-	-	W	D

STANDARD B & P "NOTEAR"





Reaction of PRI Mice of KnownParentage to French Neurotropic Yellow Fever Virus

Purpose - This test was set up in the hope of finding offspring both of whose parents are susceptible to the virus - to find out whether 100% of such offspring would then succumb.

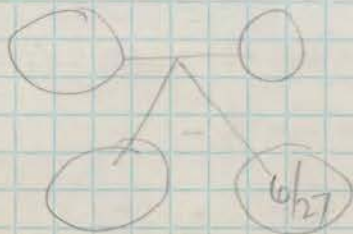
Breeding of Mice - Individual males & females were bred and their litters preserved and marked - all were tested simultaneously. The parents had holes punched in their ears for identification.

Virus - Passage of French Neurotropic - 0.03cc of  $10^7$  rec.

Parents and offspring inoculated simultaneously.

		D	CNS	
<u>One parent died</u>	No. 31	- 0/4	1/4	One susc. = aa aa + AA = all resist aa + Aa = Aa + aa = 50% susc. 8/27 = 30%
	" 81	- 4/12	6/12	
	" 82	- 4/15	6/15	
		8/31	13/31	

<u>Both parents survived</u>	No. 13	- 3/11	4 families all resistant could be Aa + AA or AA + AA  3 families with 6/27 or 22.2% could be: Aa + Aa = AA + 2Aa + aa or 25% suscept.
	" 17	- 0/4	
	" 23	- 0/15	
	" 36	- 1/8	
	" 86	- 0/5	
	" 88	- 2/8	
	" 90	- 0/3	
		6/54	





FRENCH NEUROTROPIC YELLOW FEVER  
IN PRI FAMILIES

DEC 5 1951

LITTER # & DATE	VIRUS No	SEX	DAYS AFTER INOCULATION																			MORTALITY		
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19		20	21
LITTER #36 1st LITTER OF 8/20/51	10 <sup>-1</sup>	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	PP
		2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	PP
		3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	PP
LITTER #36 2nd LITTER OF 9/20/51	10 <sup>-1</sup>	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	WP
		2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	WP
		3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	WP
LITTER #81 1st LITTER OF 8/12/51	10 <sup>-1</sup>	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	W
		2 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	W
		3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	W
LITTER #81 2nd LITTER OF 9/13/51	10 <sup>-1</sup>	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		1 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	D
		2 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	D
		3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	D
LITTER #82 1st LITTER OF 8/13/51	10 <sup>-1</sup>	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		1 ♀	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		2 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	D
		3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	D
LITTER #82 2nd LITTER OF 9/18/51	10 <sup>-1</sup>	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
		F	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		1 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	PP
		2 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	PP
		3 ♂	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	PP

\* Arthritis



Resistant PRI Male - French Neurotropic

PRI Mother	Offspring	♂	PRI Control
○	♀, ♀, ♀, ♂, ♂, ♂, ♂, ♂	2/8	0/10
○		0/5	2/10
○	♀ ♀ ♀, ♂ ♂ ♂	0/6	"
○			
○	♀ ♀ ♀ ♀ ♀, ♂ ♂ ♂	2/8	
○	♀, ♀, ♀, ♂ ♂ ♂ ♂	2/7	
○	♀ ♀	0/2	
○	♀, ♂ <sup>13</sup> , ♂	1/3	2/10
○	♀ <sup>9</sup> , ♀ <sup>10</sup> , ♀ ♀, ♂, ♂, ♂	2/7	
○	♀ <sup>7</sup> ♀ <sup>8</sup> ♀ <sup>10</sup> ♀ ♀, ♂ <sup>9</sup> ♂ <sup>8</sup>	5/7	
○	♀ ♀ ♀ ♀, ♂	0/5	
10		24% 14/58	3/30
D9	♀ (8, 8, 10), ♂ (8, 0, 0)	4/6	
D8	♀ (10, 14, 0) ♂ (0/5)	2/8	2/10
D9	♂ (9, 0, 0, 0)	1/4	
		38.9% 7/18	

PR I controls

Swiss

9/13/51

0/10

10/10

If resistance <sup>to French</sup> were recessive then the genetic formula for all resistants would be aa and crossing resistants - should yield all resistant which did not happen

Let A = cell damage susc - dom.  
a = " " resist - recess

Resist = aa  
Susc = Aa  
" = AA

If ~~resistance~~ is dominant then formula can be AA or Aa + crossing resistants should yield a certain proportion of susceptibles, but less than random breeding

If resistant ♀ = aa  
" ♂ = aa

F<sub>2</sub> = aa all resist

Let A = <sup>que for</sup> cell dam resist = dom  
a = " " susc = recess

Aa + Aa = AA + aa + 2Aa

then resist = AA or Aa  
Susapt = aa

If resist ♀ is AA }  
+ resist ♂ " AA } then all are resist

If resist ♀ is Aa }  
" ♂ is AA } then AA + Aa - all resist

If resist ♀ is Aa }  
" ♂ is Aa } then AA + Aa + aa → 25% susc

Resistant PRI Male +

Offspring

~~Results~~

Swiss Mother

♀

♂

Total

4

0/2

0/3

0/5

4

3/3 (5,6,6)

3/3 (7,7,9)

6/6

4

0/2

1/3 (7)

1/5

5

3/4 (8,8,11)

2/3 (10,13)

5/7

5

1/2 (8)

1/3 (9)

2/5

5

1/6 (7)

2/2 (7,8)

3/8

Miss

4/4 (4,5,5,5)

3/3 (4,4,5)

7/7?

5

2/6 (9,26)

0/2

2/8

5

0/3

0/3

0/6

9 mothers

14/32

12/25

26/57 (45.6%)

aa

Assume

Most or all swiss are recessive for cell damage

Susc ♀ = aa

Resist ♂ = Aa

Aa + aa = 50% sus

Susc ♀ = aa

+ Resist ♂ + AA

Aa + Aa - all resist

AA + aa

Random PRI population may be expected to have aa, Aa and AA

aa = Susc.

Susc.

Resist

25% are aa + aa = 10      0

50% are Aa + aa = 5      5  
 Aa + aa = 5      5

25% are AA + aa = 0      10  
 20      20 = 20/40

10 / 30 = 33.3

Random bred PRI - 3/30 = 10%

Resist ♀ PRI × Resist ♂ PRI = 14/58 = 24% } not signif

Suscept ♀ PRI × Resist ♂ PRI = 7/18 = 38.9%

Swiss ♀ × " " = 26/57 = 45.6%

If majority of PRI are heterozygous as regards cell vulnerability + A = gene for resist then gen. const. would be Aa

Aa × Aa = AA + Aa + Aa + aa or only 25% suscept

If Swiss are homozygous for vulnerability, i.e. aa

Relative Susceptibility of PRI + F<sub>1</sub> (Swiss x PRI)  
 French Neurotropic  
 Using 10<sup>-1</sup> virus

Group	Observed			Expected	
	Died	Survived	Total	D	S
PRI	29 <sup>(24%)</sup>	92	121	52	69
F <sub>1</sub>	59 <sup>(70%)</sup>	25	84	36	48
	<u>88<sup>(43%)</sup></u>	<u>117</u>	<u>205</u>		

$$\chi^2 = \frac{[(92 \times 59) - (29 \times 25)]^2 \times 205^{\log 2.31175}}{121 \times 84 \times 88 \times 117} = \frac{\log 9.65649}{\log 8.01974} = 1.63675$$

92	29	4.7
59	25	4.7
<u>828</u>	<u>145</u>	<u>329</u>
460	58	188
<u>5428</u>	<u>725</u>	<u>22,090,000</u>
725		
<u>4,703</u>		

$$\chi^2 = 44$$

$$P = <$$

$$= 3.67237$$

$$3.67237$$

$$\frac{7.34474}{2.31175} = 22,120,000$$

$$2.31175$$

$$9.65649$$

$$2.08279$$

$$1.92428$$

$$1.94448$$

$$2.06819$$

$$8.01974$$

PRI 14/40

4/20

8/31

3/30

29/121 (24%)

F<sub>1</sub> 30/35

29/49

59/84 (70%)

# PRI Mice

	D	S	Total
R♀ x R♂	14	44	58
S♀ x R♂	7	11	18
	<u>21</u>	<u>55</u>	<u>76</u>

$$\frac{[(44 \times 7) - (14 \times 11)]^2 \times 76}{58 \times 18 \times 21 \times 55} = \frac{\log 6.25585}{\log 6.08128} = 0.17457$$

$$\chi^2 = 1.5$$

44	14
<u>7</u>	<u>11</u>
308	154
<u>154</u>	<u>154</u>
154	

1.76343
1.25527
1.32222
1.74036
<u>6.08128</u>

2.18752
2.18752
<u>1.88081</u>
6.25585

Ⓐ PRI Resist ♂ x PRI Resist ♀

VS  
Ⓑ PRI " " x Swiss ♀

	D	S	Total
A	14	44	58
B	26	31	57
	<u>40</u>	<u>75</u>	<u>115</u>

$$\frac{[(44 \times 26) - (31 \times 14)]^2 \times 115}{58 \times 57 \times 40 \times 75} = \frac{\log 7.76322}{\log 6.99642}$$

$$\log .76680$$

$$\chi^2 = 5.981$$

4-5-52

# Breeding Experiments for Resistance to French Neurotropic Yellow Fever Virus

These data include test of Dec 5, 1951

I. PRI x PRI - both parents resistant -  $\frac{20}{112} = 18\%$

9 litters - all mice well - 0/45

9 litters - mixed -  $\frac{20}{67} = 30\%$

If one assumes that a single factor determines cell vulnerability and that the gene for high vulnerability is recessive (r) and for low vulnerability, dominant (R), then a resistant mouse may have the genetic formula of either RR or Rr and the results of the possible matings should be as follows:

$Rr + Rr = RR + \overset{2Rr}{rr} = \frac{25}{50}\%$  should be susceptible

$RR + Rr = RR + Rr =$  all should be resistant

$RR + RR = RR + RR =$  all should be resistant

Since ~~only~~ 30 per cent of the mixed litters were susceptible, the data are ~~not~~ in accord with the hypothesis that a single factor determines cell vulnerability.

II Resistant PRI x Susceptible PRI =  $\frac{15}{49} = 31\%$

Possible matings:

$Rr + rr = Rr + rr = 50\%$  susceptible

$RR + rr = Rr + Rr =$  all should be resistant

Actually - 1 litter - all resistant - 0/4

7 litters - mixed -  $\frac{15}{45} = 33.3\%$

III Resistant PRI x Swiss Q =  $\frac{26}{57} = 46\%$

$Rr + rr = 50\%$  susceptible | 2 litters - all resistant - 0/11

$RR + rr =$  all resistant | 7 litters - mixed =  $\frac{26}{46} = 56.5\%$

(over)

# Statistical Significance of Differences

	D	S	Total
Res. PRI x PRI resist	20	92	112
Res. PRI x Swiss	<u>26</u>	<u>31</u>	<u>57</u>
	46	123	169

$$\chi^2 = \frac{[(92 \times 26) - (31 \times 20)]^2}{112 \times 57 \times 46 \times 123} = \frac{\log 8.72433}{\log 7.55776} = \log 1.16657 = 14.7$$

3.24822  
3.24822  
2.22789  
8.72433

2.04922  
2.08991  
1.75587  
1.66276  
7.55776

$$\sqrt{14.7} = 3.8$$

$$P = 0.000145$$

	D	S	Total
Res. PRI x PRI resist.	20	92	112
Sus: " x " "	<u>15</u>	<u>34</u>	<u>49</u>
	35	126	161

$$\chi^2 = \frac{[(92 \times 15) - (34 \times 20)]^2}{112 \times 49 \times 35 \times 126} = \frac{\log 7.89703}{\log 7.39386} = 3.19$$

2.84510  
2.84510  
2.20683  
7.89703

2.04922  
2.10037  
1.69020  
1.54407  
7.39386

$$P = 0.07$$

not significant

Assuming single <sup>recessive</sup> factor for cell vulnerability and Swiss mice as "rr" then ~~the~~ mating with random PRI <sup>with 24% Suscep</sup> should

yield: rr + rr = all susceptible - 24% of progeny  
 rr + Rr = mixed progeny - 50% susceptible - 50% resistant  
 rr + RR = all resistant <sup>or 76%</sup> - 38% suscep

Excluding PRI mice of "RR" constitution - one would expect 62% ~~24%~~ of progeny to be susceptible. If the number of "RR" mice is small - the 70% observed incidence is a fairly close fit

# Significance of Backcross Mortality

	Died	S	Total
Unselected PRI	29	92	121
Backcross	<u>12</u>	<u>8</u>	<u>20</u>
	41	100	141

$$\chi^2 = \frac{[(92 \times 12) - (29 \times 8)]^2 \times 141}{121 \times 20 \times 41 \times 100}$$

$$\chi^2 = 10.8$$

$$\sqrt{\chi^2} = 3.29$$

$$P = 0.001$$

$$\begin{array}{r} 92 \\ \underline{12} \\ 184 \\ \underline{92} \\ 1104 \\ \underline{232} \\ 872 \end{array}$$

$$\begin{array}{r} 29 \\ \underline{8} \\ 232 \end{array}$$

$$\begin{array}{r} 2.94052 \\ 2.94052 \\ \underline{2.14922} \\ 8.83026 \\ \underline{6.99660} \\ 1.03366 \\ .51683 \end{array}$$

$$2420 \times 4100$$

$$\begin{array}{r} 3.38382 \\ \underline{3.61278} \\ 6.99660 \end{array}$$

$$\begin{array}{r} 90 \quad (31) \\ \underline{62} \quad 29 \\ 280 \\ 279 \end{array}$$