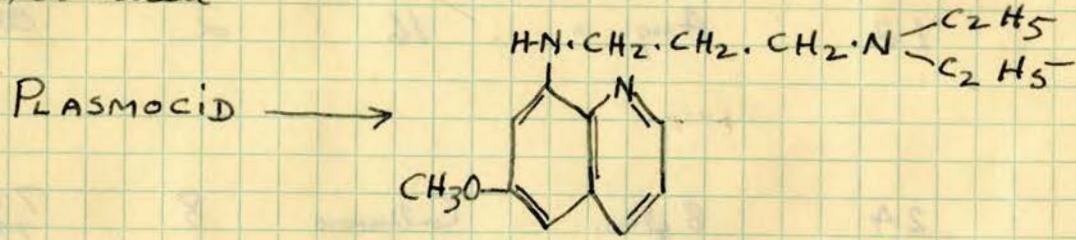
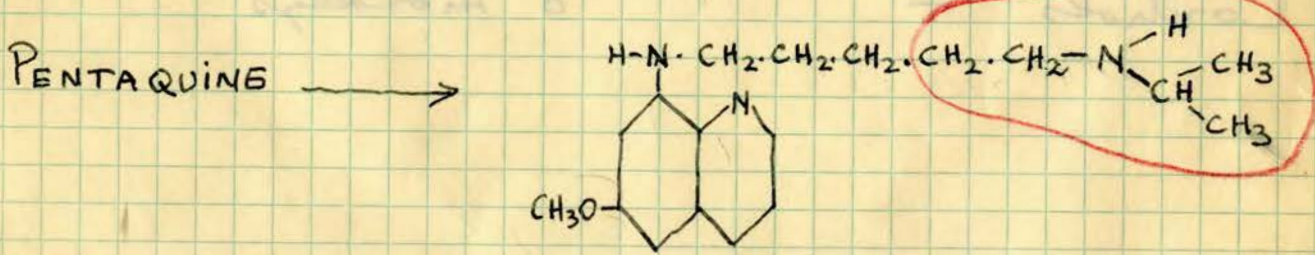
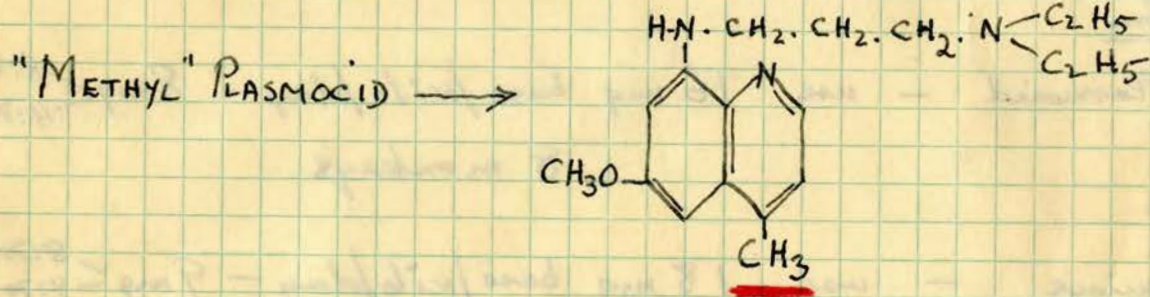


Effect on Experimental Poliomyelitis in Monkeys of "Toxic" Doses of 6-methoxy, 8-aminoquinoline Compounds Related to Plasmocid but Deprived of Neurotoxicity by Two Different Modifications in Structural Formula.



PENTAQUINE
METHYL
PLASMOCID

COMPOUNDS TO BE TESTED



STANDARD B & P "NOTEBOOK"

L.H. Schmidt's Data on Toxicity in Monkeys

| <u>Compound</u> | <u>Total dose per kilo/day</u> mg. base | <u>Individual Doses</u> mg. base | <u>No. of days administ.</u> | <u>No. of monkeys</u> | <u>Result</u> |
|------------------------|--|-------------------------------------|------------------------------|-----------------------|---|
| "Methyl" Plasmoicid | 48 | 16 q. 8hrs | 3 | 1 | Dead 4 th day |
| | 24 | 8 " " | continuous | 2 | 1 dead 13 th day 1 sick + killed 16 th day |
| | 12 | 4mg. " | 16 | 2 | OK. for 16 days |
| Pentaquine | 24 | 8 q. 8hrs. | Continuous | 8 | 7 died between 7 th + 18 th days |
| | 12 | 4mg 8hrs | 14 to 21 | 10 | Only 1 died in 9 days |

Proposed Plan

"Methyl" Plasmoicid - use 16 mg base/kilo/day - 8mg $\begin{matrix} \swarrow 8:30 AM \\ \searrow 4:30 PM \end{matrix}$
8 monkeys

Pentaquine - use 18 mg base/kilo/day - 9mg $\begin{matrix} \swarrow 8:30 AM \\ \searrow 4:30 PM \end{matrix}$
12 monkeys

Controls - 8 monkeys

METHYL PLASMOCID AND PENTAQUINE

Exp. I

2/17-49

| GROUP | MONKEY | WEIGHT | | mg Base 2x DAY | c.c. STOCK SOLUTION | c.c. Distil WATER | Weight: 2-26-48 (10.9) | | |
|--|---------|----------|-------|-------------------|------------------------|----------------------|------------------------|-------|---------|
| | | POUNDS | GRAMS | | | | GM. | Diff. | PERCENT |
| I CONTROLS ONLY VIRUS | 1240 ✓ | 4 (7) | 1812 | | | | 1812 | 0 | |
| | 1241 ✓ | 7.5 | 3387 | | | | 3171 | -216 | -6.3 |
| | 1242 ✓ | 7.25 (8) | 3274 | | | | 3171 | -103 | -3.1 |
| | 1243 ✓ | 5.75 (7) | 2603 | | | | 2491 | -112 | -4.3 |
| | 1244 ✓ | 4.5 (7) | 2038 | | | | 2265 | +227 | +11.1 |
| | 1245 ✓ | 5.25 (6) | 2378 | | | | 2944 | +566 | +23.8 |
| | 1246 ✓ | 6.5 (7) | 2944 | | | | 2718 | -226 | -7.6 |
| 1247 ✓ | 6. (12) | 2718 | | | | 2604 | -114 | -4.1 | |
| II METHYL PLASMOCID 16 mg BASE/R day VIRUS | 1248 ✓ | 5.5 | 2491 | 19.9 | 2. | 18 | | | |
| | 1249 ✓ | 6.25 | 2831 | 22.6 | 2.3 | 17.7 | 2378 | -453 | -16.0 |
| | 1250 ✓ | 4.75 | 2150 | 17.2 | 1.7 | 18.3 | | | |
| | 1251 ✓ | 6.75 | 3056 | 24.5 | 2.5 | 17.5 | 2604 | -452 | -14.7 |
| | 1252 ✓ | 4.5 | 2038 | 16.3 | 1.6 | 18.4 | | | |
| | 1253 ✓ | 7.25 | 3274 | 26.2 | 2.6 | 17.4 | 2718 | -556 | -16.9 |
| | 1254 ✓ | 5.25 | 2378 | 19.0 | 1.9 | 18.1 | | | |
| 1255 ✓ | 5.25 | 2378 | 19.0 | 1.9 | 18.1 | | | | |
| III PENTAQUINE 18 mg BASE/R day VIRUS | 1256 ✓ | 7.25 | 3274 | 29.4 | 2.9 | 17.1 | 2718 | -556 | -16.9 |
| | 1257 ✓ | 6.5 | 2944 | 26.5 | 2.6 | 17.4 | 2265 | -679 | -23.6 |
| | 1258 ✓ | 5.5 | 2491 | 22.4 | 2.2 | 17.8 | | | |
| | 1259 ✓ | 5.75 | 2603 | 23.4 | 2.3 | 17.7 | 2038 | -565 | -21.7 |
| | 1260 ✓ | 6.5 | 2944 | 26.5 | 2.7 | 17.3 | 1925 | -1019 | -34.6 |
| | 1261 ✓ | 5. | 2265 | 20.4 | 2. | 18. | 2151 | -114 | -5.0 |
| | 1262 ✓ | 5.5 | 2491 | 22.4 | 2.2 | 17.8 | 2038 | -453 | -18.1 |
| | 1263 ✓ | 6.75 | 3056 | 27.5 | 2.8 | 17.2 | 2491 | -565 | -17.5 |
| | 1264 ✓ | 7. | 3161 | 29.4 | 2.8 | 17.2 | 2812 | -349 | -11.0 |
| | 1265 ✓ | 7.5 | 3387 | 30.4 | 3. | 17. | 2718 | -669 | -19.7 |
| | 1266 ✓ | 4.5 | 2038 | 18.3 | 1.8 | 18.2 | 1472 | -566 | -27.7 |
| | 1267 ✓ | 6.75 | 3056 | 27.5 | 2.8 | 17.2 | | | |

- N.C. 41 - A Methyl Plasmoacid (dihydrochloride)
Base content: 80.2% - Lot of 7-5-46.
- S.N. 13276 - Pentaquine (monophosphate)
Base content: 75.5% - Batch P-4N.
- Stock Solutions:
For Methyl Plasmoacid = 1.247 GM DRUG IN 100 c.c. D. WATER
= 10 mg BASE/c.c.
For Pentaquine = 1324 GM. DRUG IN 100 c.c. D. WATER
= 10 mg BASE/c.c. (Cover for Virus)

FEB 21 1949

— [redacted] Virus (Vial #4 - same as used in previous expt - B-8-4) used. 0.5 cc of 1:5 (20%) + 49.5 cc of saline → 1:500

Ice injected into right "thalamic" region beginning with 1267 and working back to controls.

Rh 1255 not inoculated because it appeared terminal - died under observation 3 hrs. later.

Rh: 1240

CONTROL

FEB 17 1949

only virus



DATE: FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10 11 12 13 14

FEB - 20 - O.K.

1" 21 - O.K.

" 22 - O.K.

" 23 - O.K.

" 24 - O.K.

" 25 - AM. Excited - tremor on shoulder and arms.

" 26 - AM. Tremor on head, shoulders and arms.

PM - marked tremor and excitement.

27 - AM - tremor - excited.

PM - very severe tremor. No paralysis.

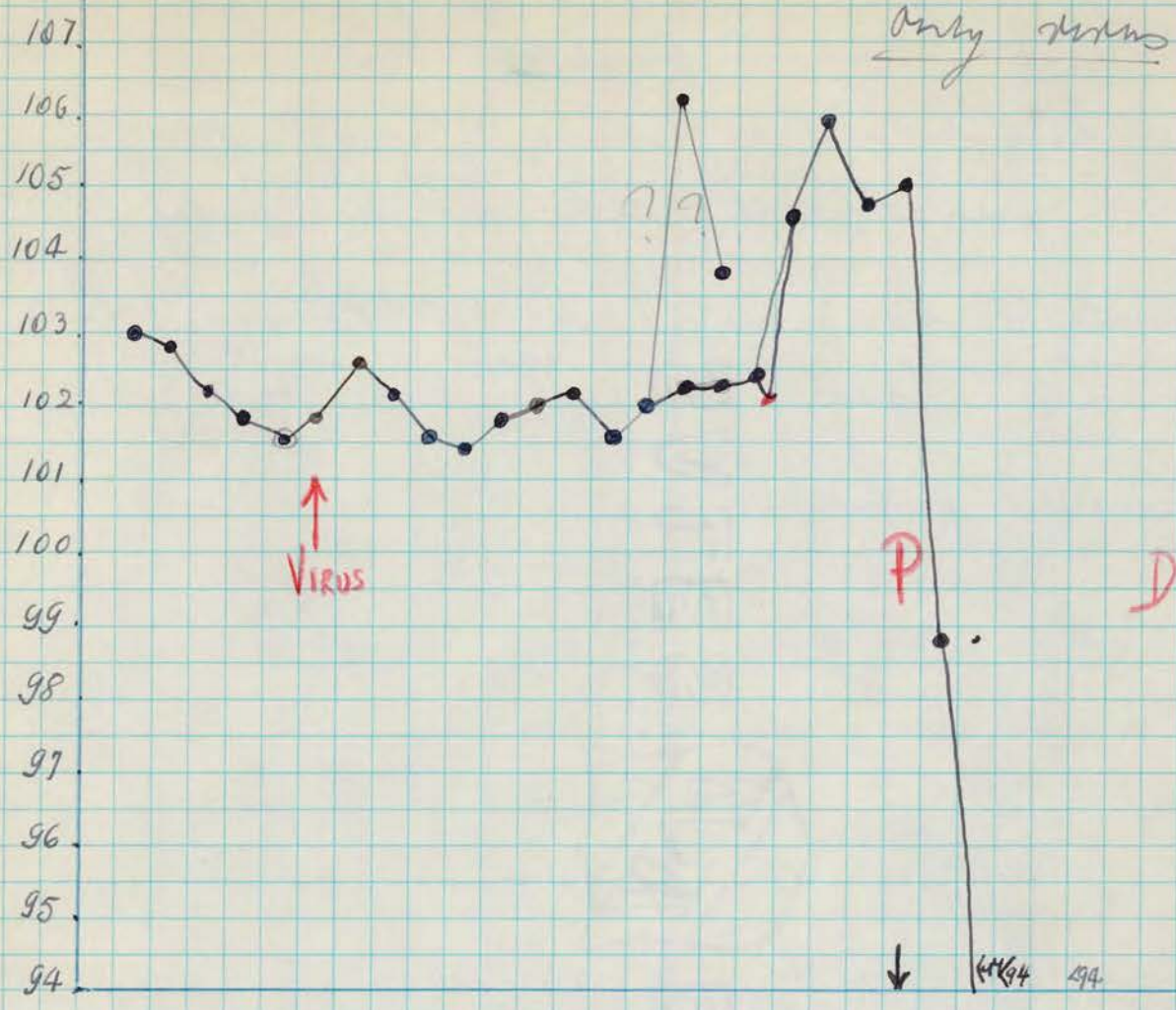
28 - AM. Tremor still very severe. Right facial paralysis. Partial paralysis right leg up.

MARCH.

- 1 - AM - Almost complete
paralysis both arms
fingers still marked
facial paralysis in right side
weakened on left.
- PM - Partial all four extremi-
ties more marked on upper
still with tremor, sits up.
- " 2 - AM - Same condition.
PM - Same condition.
- " 3 - AM - Partial paralysis on all
four extremities - sits up.
Tremor still noticeable.
- " 4 -
- " 5 - No tremor. Partial para-
lysis all four extremities
can sit up.
- " 6 - Sits up. Same condition.
- " 7 - Same as of yesterday.
- " 8 - Same; facial still present
- " 14 - Same condition. -
- " 15 - Same condition. -
- " 16 - Same condition. -

24.

Only signs



| DATE: FEB | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | | | | | |
|-----------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |

FEB. 20 - O.K.

- n 21 - O.K.
- n 22 - O.K.
- n 23 - O.K.
- n 24 - O.K.
- n 25 - AM - O.K.
- n 26 - O.K.
- n 27 - O.K. PM: O.K.
- n 28 - O.K.

MARCH. 1 - AM - O.K.
- PM - O.K.

- n 2 - AM - O.K.
- PM - O.K.
- n 3 - AM: O.K.
- n 4 - OK
- n 5 - OK
- n 6 - AM: Excited. Temp 5PM - 102.1; No signs
- n 7 - Excited
- n 8 - Excited - no paralysis

(over)

3-9 - AM. Easily fatigued + weakness of legs evident
but no definite paralysis

P.M. - Definite partial paralysis of lower extremities
- cannot get back into cage except with
great difficulty; falls over when pushed.

3-10 Complete flaccid paralysis of both lowers + back,
partial uppers - lies on floor - cannot raise
himself - can move head, very alert

3-11 Same

3-12 Completely prostrate

3-14 Completely prostrate.

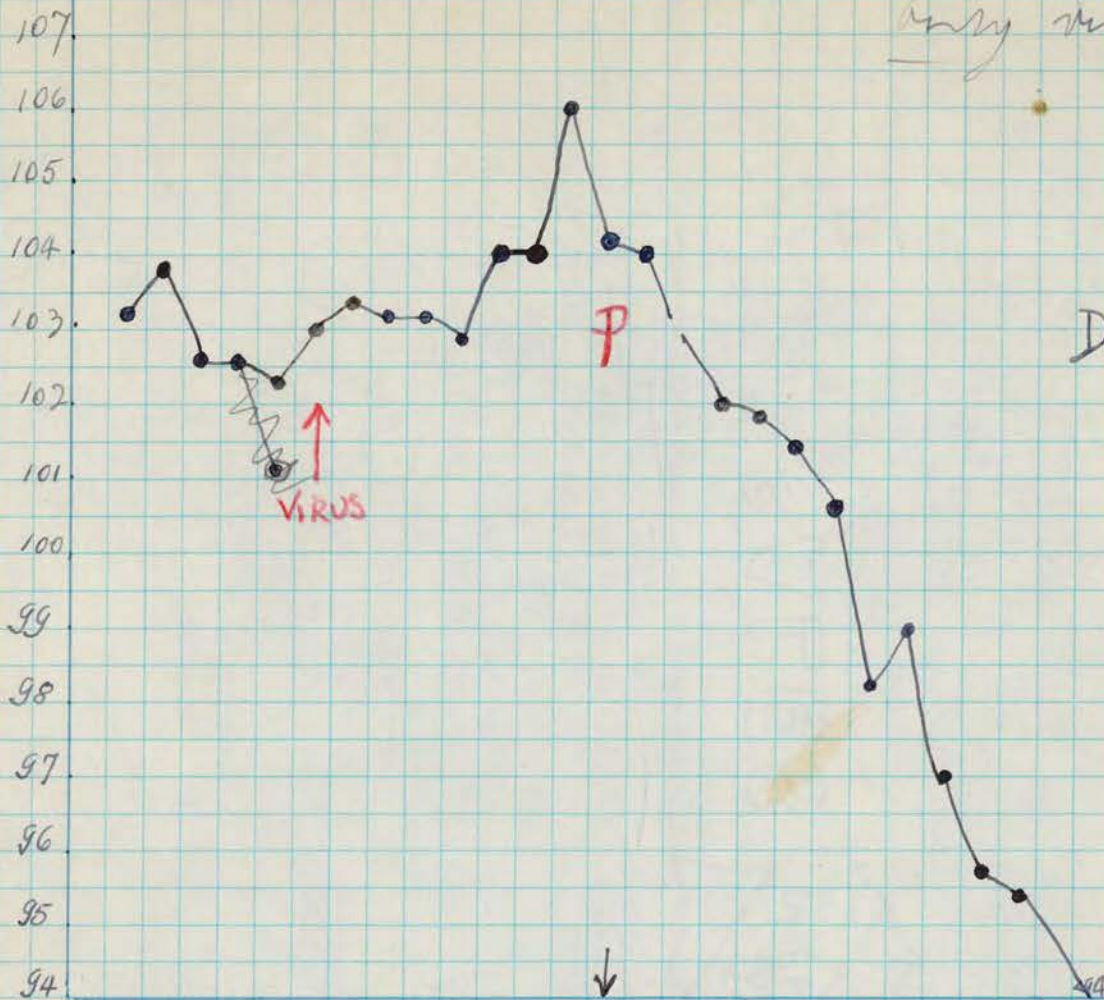
3-15 Same - Very weak.

3-16 AM - Dead - Unrecorded.

Rh. 1242

CONTROL - FEB 17 1949

only virus



DATE: FEB: 10 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10 11 12 13 14

FEB 20 - O.K.

- n 21 - O.K.
- n 22 - O.K.
- n 23 - O.K.
- n 24 - O.K.
- n 25 - AM - O.K.
- n 26 - O.K.
- n 27 - Excited (?) PM: O.K.
- n 28 - O.K.

MARCH 1 - AM Partial paralysis left upper.
 Pt tremors on head and shoulders.
 PM - Partial paralysis both upper.

n 2 - AM - Partial paralysis all four extremities
 more advanced on uppers.
 has down.
 PM - Complete Paralysis upper and
 left lower. Partial on right
 lower, and Back + neck.

MARCH

2 - 3 PM. Prostate but about
Complete quadruplets.

" 3 - AM - Same condition.

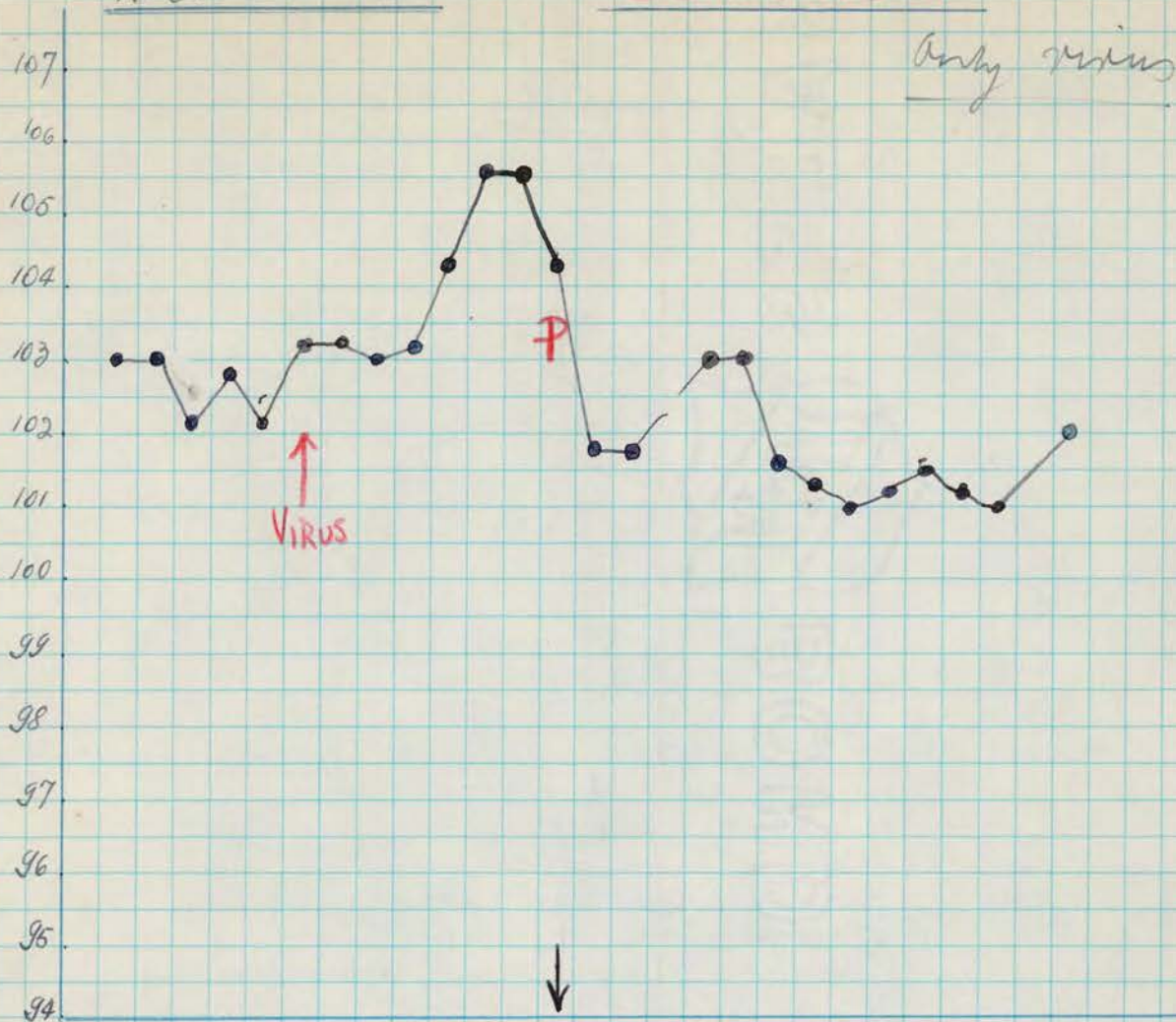
" 4 -

" 5 - Same condition

" 6 - Same as yesterday.

" 7 - Same as before.

" 14 - 2 PM - dead - no signs
of scanning.



DATE: FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10 11 12 13 14

FEB - 20 - O.K.

" 21 - O.K.

" 22 - O.K.

" 23 - O.K.

" 24 - O.K.

" 25 - Excited.

" 26 - Excited.

" 27 - Piliomotor on shoulders - Excited.
PM: same.

" 28 - AM. Excited.

MARCH 1 - AM Complete flaccid paralysis
on right lower.
PM - + partial paralysis left
lower.

" 2 - AM. Complete paralysis both lowers -
Partial P. left upper + back
hiss down. Piliomotor on head + shoulders
PM - Same concentration

MARCH. 3 - AM: his down: complete flaccid paralysis both lower and left upper. No paralysis on right upper and neck. Back paralyzed.

" 5 - Same condition

" 6 - Can sit up. Move right arm and somewhat his left arm in neck and superior part of the back, works better than yesterday did.

" 7 - Same condition.

" 14 - Same condition. Can move head and right arm. Very little work on his left arm.

" 15 - Same condition.

" 16 - Same as yesterday.

" 21 - It is noticeable a good improvement on 4 extremities.

" 22 - Same condition.

APRIL 2 - Same condition.

" 11 - Can sit up. Important improvement on upper and lower. No neck paralysis.

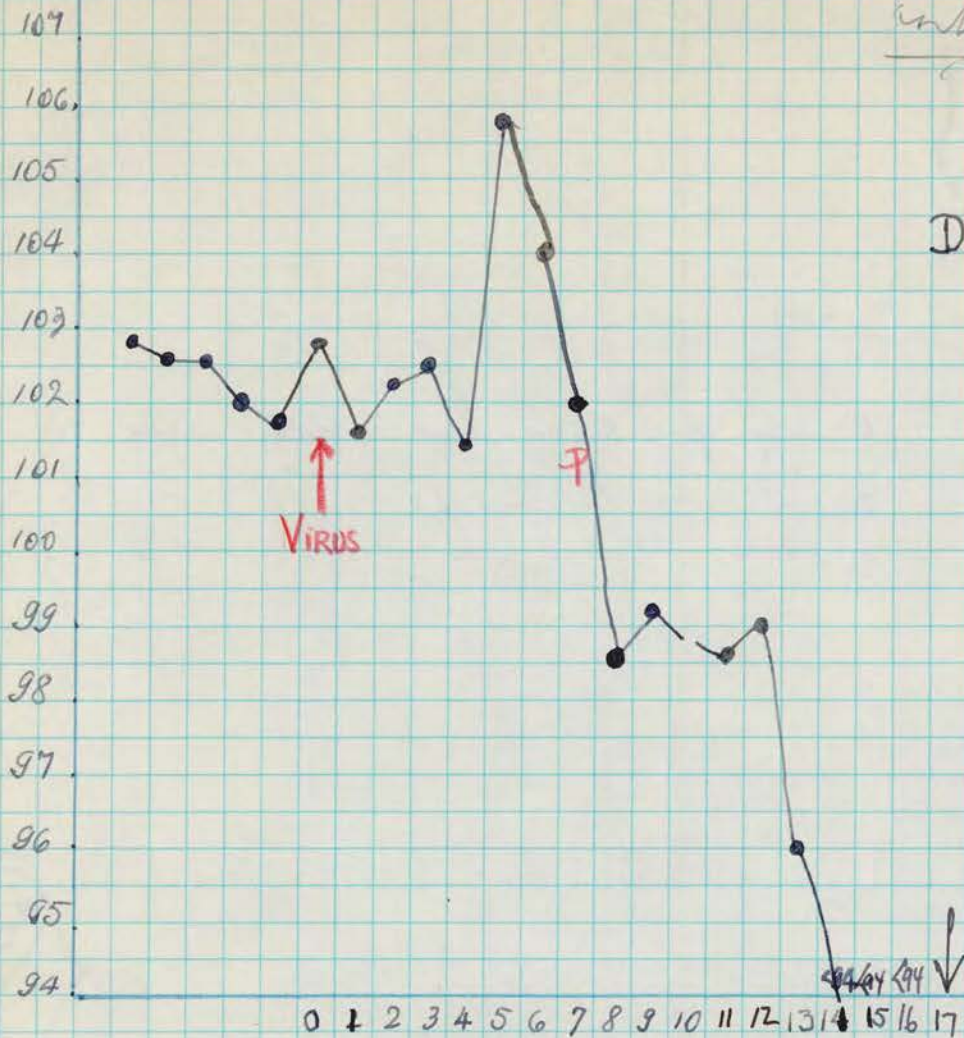
E 4.

Rh. 1244

CONTROL.

FEB 17 1949

early virus



DATE FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB 20 O.K.

- " 21 - O.K.
- " 22 - O.K.
- " 23 - O.K.
- " 24 - O.K.
- " 25 - M.O. K
- " 26 - bilumofax.
- " 27 - O.K. PM: O.K.

" 28 - Partial paralysis lower and right upper.

MARCH 1 - AM Partial paralysis all four extremities - lies down. Eat.
PM - Same condition - Cannot sit up.

" 2 - AM - Partial P upper - Partial paralysis lower and back - lies down.
PM - Complete flaccid quadriplegia + Back and neck muscles only vertical.

MARCH 3 AM - No myasthenia
Complete flaccid paralysis
on left upper and lower. Par-
tial paralysis on right upper
and lower. Back and neck
paralyzed -
his down.

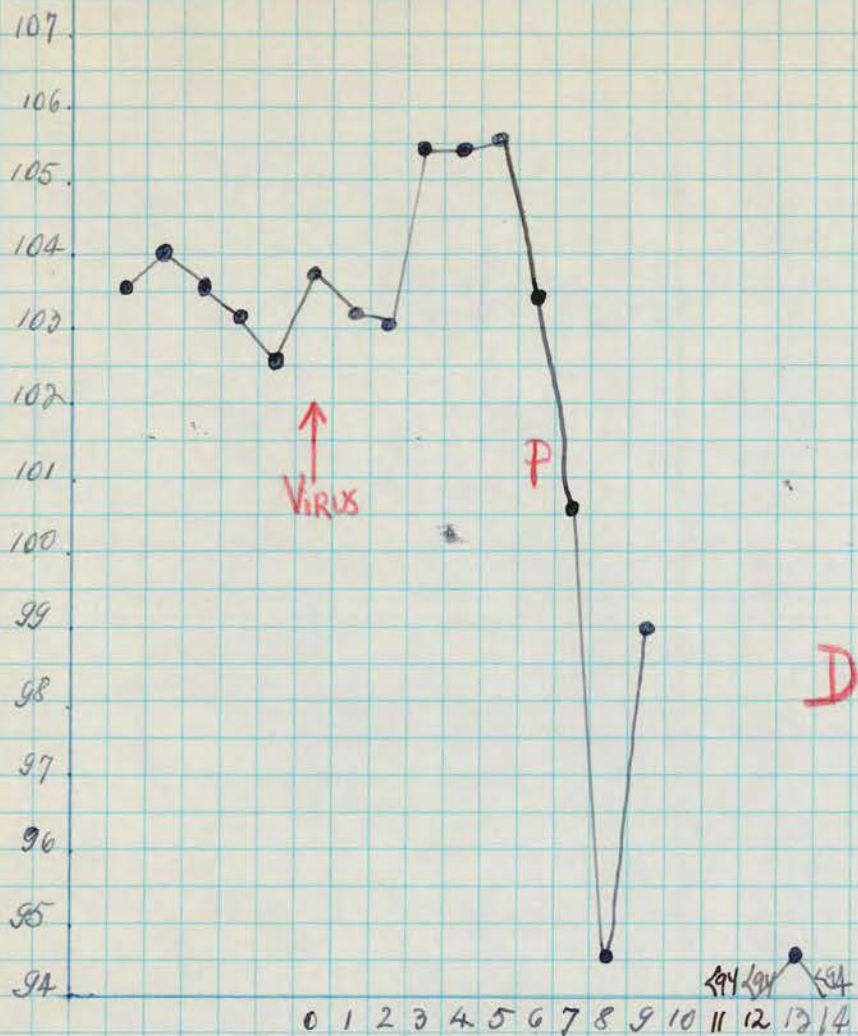
| | | |
|---|------|----------------------------------|
| " | 5 - | Move head and right hand. |
| " | 6 - | Same condition |
| " | 7 - | More prostration |
| " | 8 - | Barely breathing but still alive |
| " | 9 - | " " " " |
| " | 10 - | Dead - discarded |

Rh 1245

CONTROL

FEB 17 1949

only virus



DATE: FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7

FEB 20 - O.K.

- " 21 - O.K.
- " 22 - O.K.
- " 23 - O.K.
- " 24 - O.K.

" 25 - AM Excited.

" 26 - AM: Tremor on head

" 27 - 8 AM: Partial paralysis left lower limb, weakness on both arms.

12 - Partial paralysis all four extremities and face.

PM: Prostrate - Cannot sit up. Paralysis more advanced.

" 28 - AM Prostrate. Complete paralysis of extremities and back, otherwise alert, eat.

MARCH 1 - AM Prostrate. Neck also paralyzed.

MARCH 1 - PM - Prostrate. does not eat.

" 2 - AM - Prostrate " " "

" 3 - AM - Prostrate " " "

" 5 - Same condition
Tries to eat.

" 6 - Same condition

" 7 - Same condition - Alive at 9 AM

Dead at 10 AM

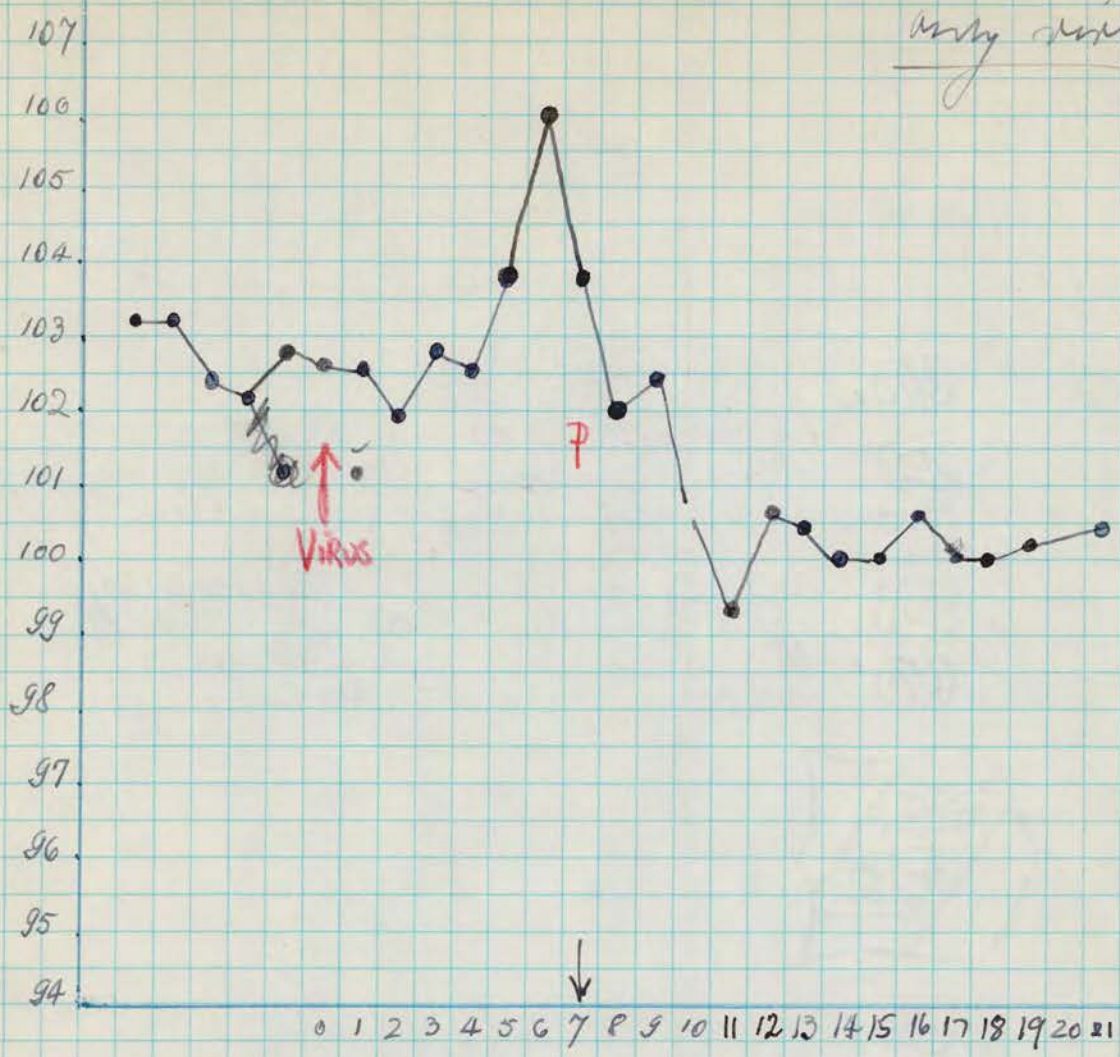
Discarded

Rh 1246

CONTROL

FEB 17 1949

body temp



DATE FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10 11 12 13 14

FEB 20 - O.K.

- " 21 - O.K.
- " 22 - O.K.
- " 23 - O.K.
- " 24 - O.K.
- " 25 - O.K.
- " 26 - O.K.

" 27 - Excited - Pilomotor.
PM: Same.

" 28 - Complete paralysis left lower. Partial paralysis right lower.

MARCH 1 - AM Complete paralysis both lower
PM - Partial paralysis ~~lower~~ up.

" 2 - AM - Complete paralysis both lower and left upper. Partial paralysis on right upper and back. LHS down.

" 2 - PM - Same condition - Not sick paralysis

MARCH 3 AM - Complete placid paralysis
on all four extremities and
back - neck not paralyzed. Eat.

" 5 - Same condition.

" 6 - Same as before.

" 7 - Same as yesterday.

" 14 - Same condition.

" 15 - Same condition.

" 16 - Same as yesterday.

" 21 - It is not least an improvement
on both upper and neck.

" 22 - Same condition.

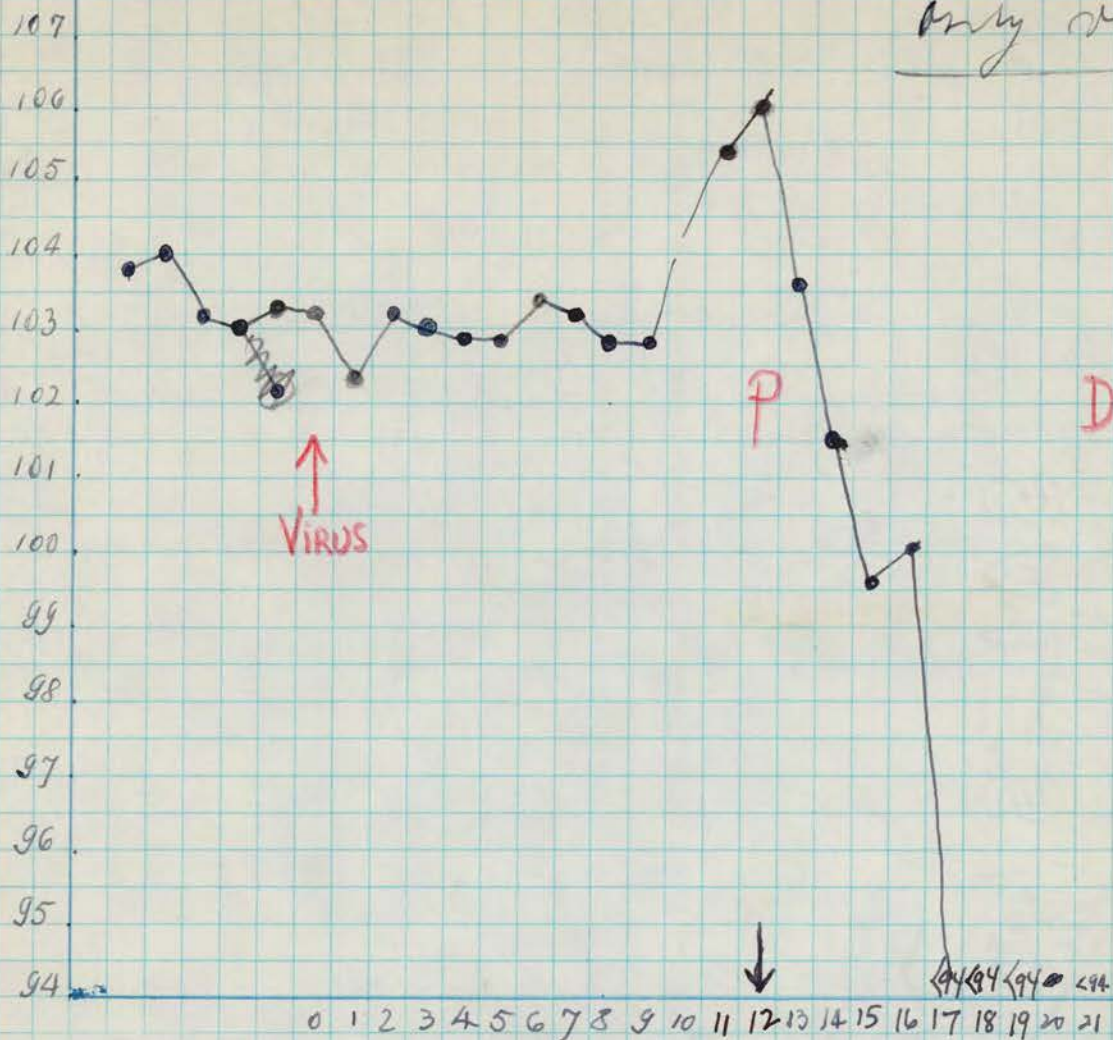
APRIL 11 - Almost complete recovery
on upper neck and back.
Almost complete paralysis
on lower. - bus down.

Rh 1247

CONTROL

FEB 17 1949

only virus



DATA FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10 11 12 13 14

FEB 20 - O.K.

- " 21 - O.K.
- " 22 - O.K.
- " 23 - O.K.
- " 24 - O.K.
- " 25 - O.K.
- " 26 - O.K.
- " 27 - O.K. PM: O.K.
- " 28 - AM - O.K.

MARCH 1 - AM - O.K. -
PM - O.K. -

" 2 - AM - O.K.
PM - O.K.

" 3 - AM - excited. Pilomotor on head, shoulder and arms.

" 4 - Tremor
" 5 - Mapped tremor on head (over) pilomotor - Back paralyzed

March 5 - Uncontrollable, continued shaking of head
Marked ataxia, and partial
paralysis back, arms & legs

" 6 - AM. The paralysis is more
marked on right upper and
lower. Back paralyzed.
Still tumor on head.

" 7 - Still tumor on head.
Partial paralysis in all four
extremities. - almost complete
on right arm, back and
neck paralyzed. -

" 8 Prostrate

" 14 - 2 PM. ~~Dead~~
Dead, no rigor - discarded. -

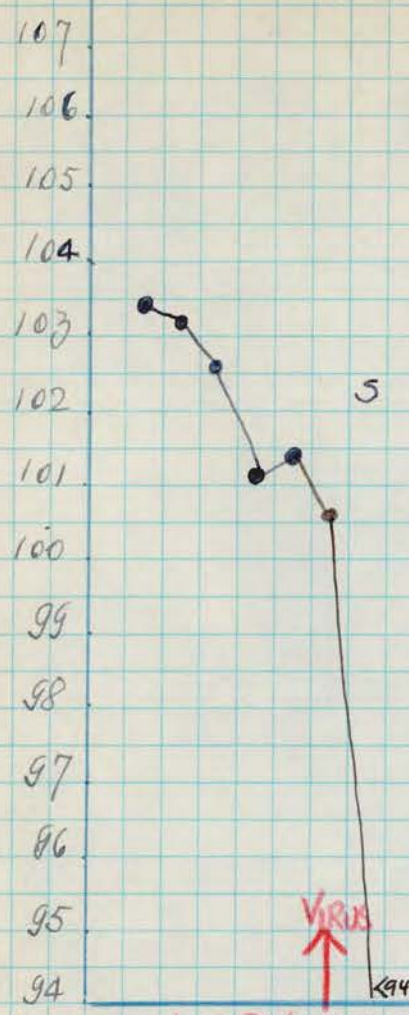
Rh 1248

FEB 17 1949

METHYL PLASMOCID - 8mg Base /K / 2 x a Day
16mg BASE / DAY

E.T. (collected tissue)

Total Base: 5 Days = 80 mg / B / K



1 2 3 4 0 1 2 3 4 5 6 7 8 9 10

↑↑↑↑↑↑↑↑↑↑

DRUG:

DATE FEB:

16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB - 18 - 5 PM Eyelids almost completely shut.

" 19 - 8:30 AM - Same condition.
10:30 AM - Eyelids completely shut. closed
12 AM - Eyes completely closed.

" 20 - AM - Eyes completely closed - thin - Pupils to be lying down.

" 21 - AM - Right eye 1/4 open. track.
Right side - pupil contracted; does not react to light - enophthalmos
Left Pupil - reacts to light - no enophthalmos. dilates wide + constricts alternately i.e. hippus

" 22 - AM - Temp. less than 94 - Prostrate - but no evidence of paralysis except of eyelids. No strabismus. ~~Left~~ Right pupil - still hippus
Right eye - enophthalmos - constricted pupil
Drug not given

1 2 PM. Prostration - sacrificed with

chloroformic anesthesia was started. The washing ^{out} of blood. 1500 cc. of saline were employed. Time: \approx 50 minutes.

Formaldehyde-Saline-A.A.: 2,000 cc. in a 1 1/2 hours. In order to obtain a good fixation on spinal cord, the animal was maintained inclined (head down) at an angle of \approx 20°.

Good fixation in skull and spinal cord.

Ricinus in L.A. all others in Formalin.

Rh. 1249

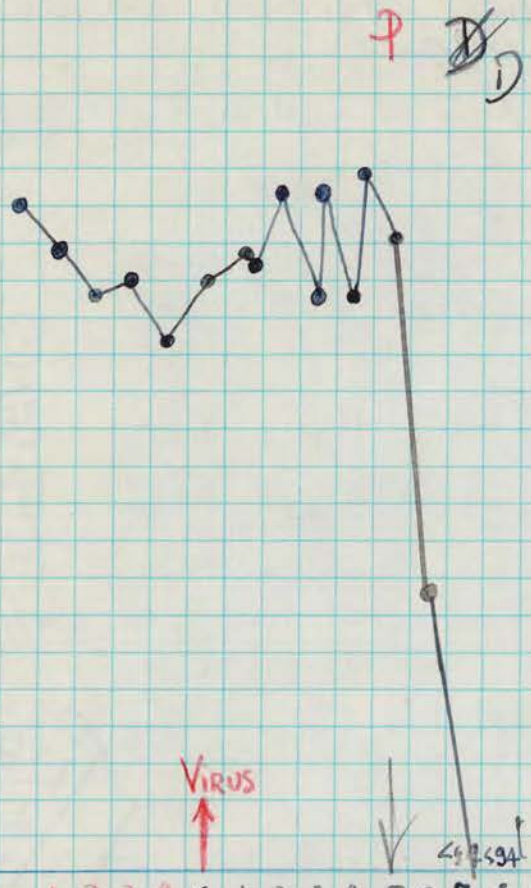
METHYL PLASMOCID

FEB 17 1949

16 mg oral / DAY
8 mg / eye b.i.d
E.T.

Total Dose: 11 1/2 days: 184 mg O.K. / Total

107
106
105
104
103
102
101
100
99
98
97
96
95
94



DRUG
FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10
5 6 7 8 9 10 11 12 13 14 15

FEB 19 - O.K.

- " 20 - AM - O.K. Sits hunched over;
- " 21 - AM Sits hunched over; Eyes O.K. Same weak.
- " 22 - A.M. - Eyes closed by pink edema affecting eyelids and extending about 2 cm on skull over brows. Sits up otherwise and is active.
- " 23 - A.M. Sits hunched over. Less edema on left eye.
- " 24 - AM. Edema eyes almost disappeared. Hunched over. Ptosis not evident.
- " 25 - AM. Hunched over. No ^{very} active. No edema on eyes. No definite ptosis.
- " 26 - AM. Same condition. 103.4.
P.M. - Same condition. 103.4.
G.P.M. - Partial paralysis bowers.

FEBR. 27 - AM. Partial paralysis
both lower. Weakness
on both arms (x)

PM - Sits up. Partial
paralysis lower and
right upper. -

" 28 - Eyes down - Cannot sit
up
Completely flaccid para-
lysis both arms
Horizontal myelogram.

MARCH 1 - Prostrate. Genital edema
+ back and neck paralyzed.
Oedema of eyelids + dependent part of face

" " : Dead 6 PM. -

" 2 : 9:30 Autopsy: No gross pathologi-
cal changes in
viscera.
Spinal somewhat enlarged.
C.N. 5. - L.A.

FEB - 20 AM. Same condition. -

6 PM. Partial paralysis both arms. -

9:30 PM. Partial paralysis all four extremities and lower

u 27 - 7:30 AM - Prostrate, when stimulator can sit up helped by the wall of the cage. -

PM. Prefers to lie down on cage - alert. Can climb but easily fatigued. - Paralysis right lower

28 - AM - Complete paralysis arms - Partial left lower

MARCH 1 - AM - Complete paralysis both arms and all lower. Partial paralysis on right lower back & neck paralyzed.

PM: Prostrate. Does not eat. -

u 2 - AM: Prostrate. " " "

" 2 - PM: Prostrate " " "

" 3 - AM: Prostrate. " " "

" 4 - AM Same condition

u 5 - 3:45 PM Head, no rigor, warm

u Autopsy: March 5/49. At 3:55 PM
no gross pathological changes on view.

C.N.S. - In L.A.

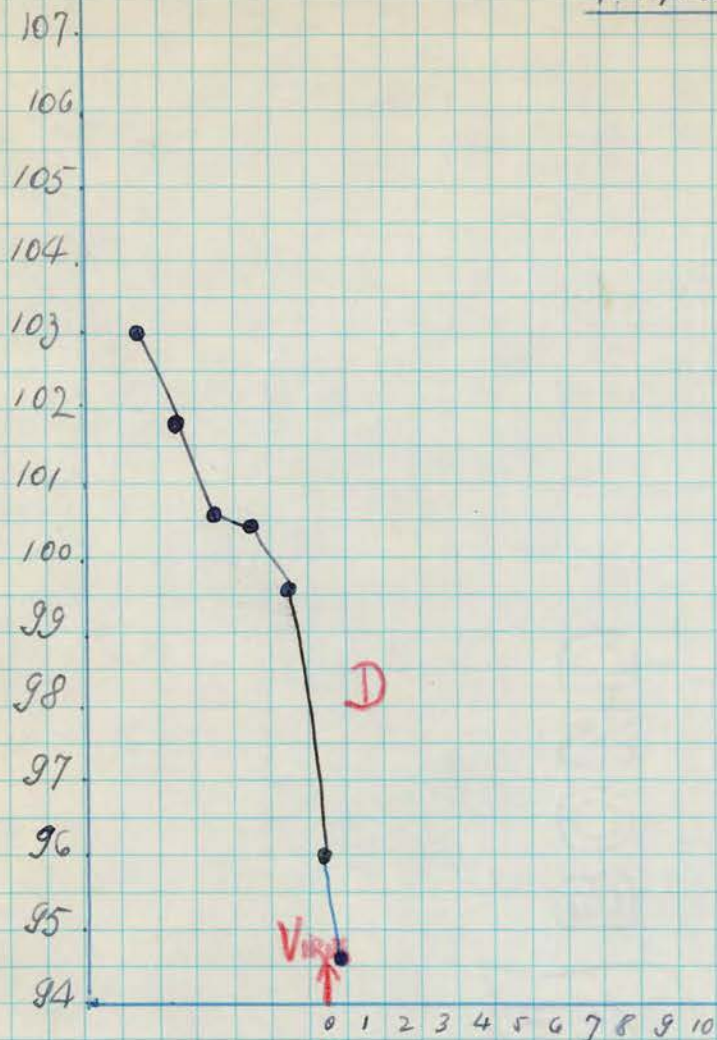
Soft particularly on both enlargement of the spinal cord.

Rh. 1252

FEB 17 1949

Methyl Plasmonid

16 mg Base/K 2/day
8 mg Base* b.i.d. I.T.
Total 4 1/2 days: 72 mg B/K.



DRUG

{ 1 2 3 4 5
↑↑↑↑↑↑ -

DATE: FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB - 19 - O.K.

" 20 - AM - Mild prostration thin ? ? - OK

" 21 - AM - Thin, weak,
4:30 PM - Prostrate 94.6
Drug not given

" 22 - 8:30 AM - Dead
autopsy - no gross pathological
changes on viscera
C.N.S. in X.A.

Rh. 1253

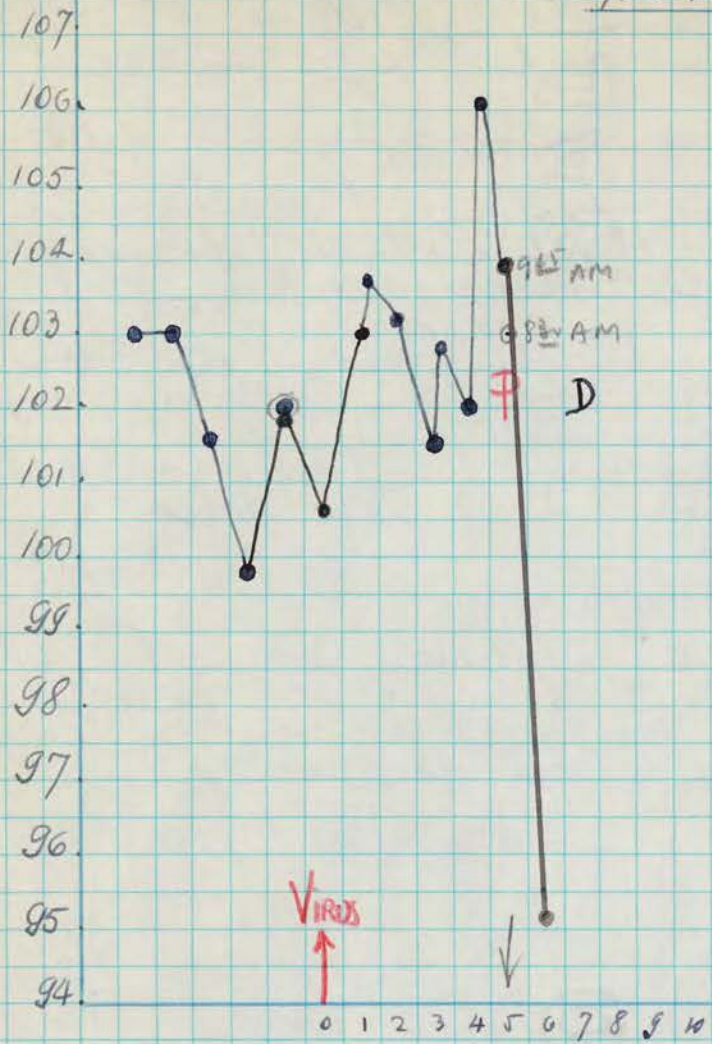
FEB 17 1949

Methyl Plasmoid

10 mg Base / 4 / day
8 mg Base ¹⁰ b.i.d. E.T

Total: 11 days = 176 mg B.K

Histology - severe and extensive
Polio



DRUG

1 2 3 4 5 6 7 8 9 10 11
 { M M M M M M M M M M M M

DATE-FEB. 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB - 19 - AM -

- " 20 - AM - Ptoxis, 3/4 open
- " 21 - AM - Proptosis of nucleus, at 2 cm reduced
PM - Ptoxis, same - ptomotor -
- " 22 - Ptoxis same; ptomotor - active.
- " 23 - General good condition but some general weakness. Ptomotor appears active and alert.
- " 24 - Same as yesterday
- " 25 - AM - No ptoxis - otherwise the same.
PM - Excited - 106.1 -
- " 26 - Same condition -

FEB - 26 - 6 PM: Complete flaccid
paralysis both upper
partial paralysis lower
facial paralysis left side?

" 27 - AM - Facial paralysis left
side -
Complete flaccid paralysis
both arms + partial paralysis
lower and back + neck. -

PM: Prostrate - Flaccid para-
lysis all four extremities
left complete facial paralysis
nystagmus and - in frontal
strabismus of left eye.

" 28 - 7³⁰ Dead, cold, rigor mortis.

= 9¹⁵ Autopsy: Spleen somewhat
enlarged (Z.A.)
no other gross pathological
changes on viscera.

C.N.S.: Pius in Z.A.

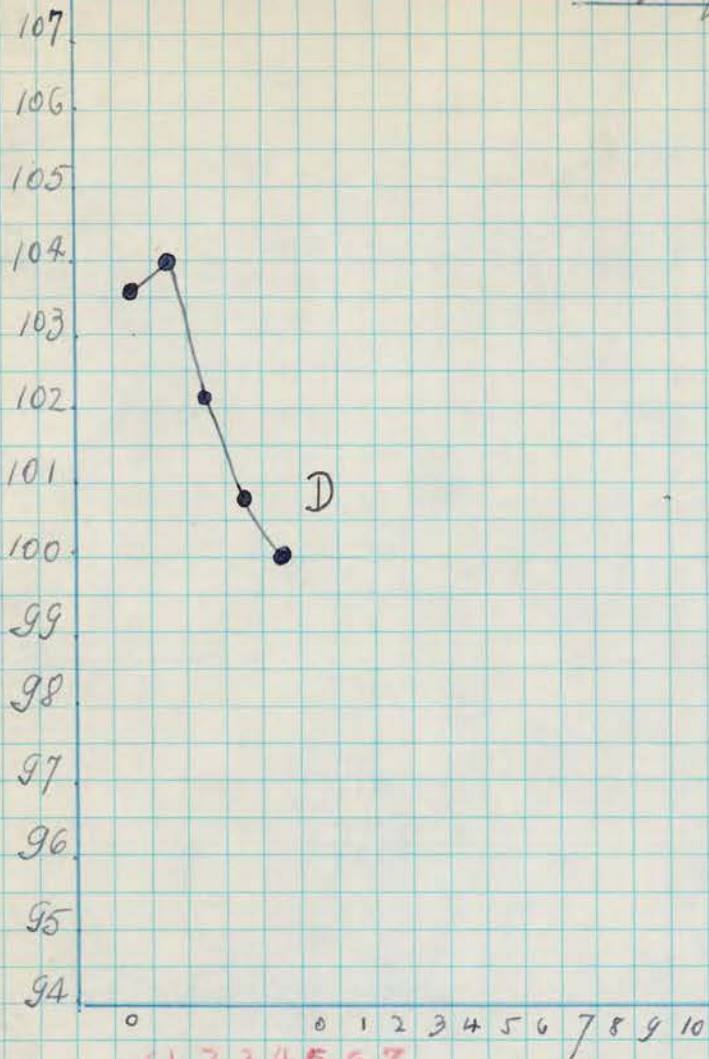
Rh. 1254

Methyl Plasmonol

FEB 17 1949

10 mg Oral / K.H. / day
8 mg Oral / K.H. / b.i.d.
~~F.H.~~

Total: 4 days = 64 mg. B.K.



1 2 3 4 5 6 7
↑↑↑↑↑↑↑

DRUG:

DATE: FEB. 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB - 18 - Edema eyelids -

19 AM Edema eyelids + mild ptosis ^{sup.} eyelids.
12 AM Bilateral ptosis - almost 3/4 closed -

" 20 AM - Ptosis ~~and edema~~, same as before, but prefers ^{sup.} lying down on the floor of the cage - weakens (generalized)

" 21 - 8¹⁰ Dead - Rigor mortis -
Autopsy: No gross pathological changes or necrosis -

CNS in L.A.

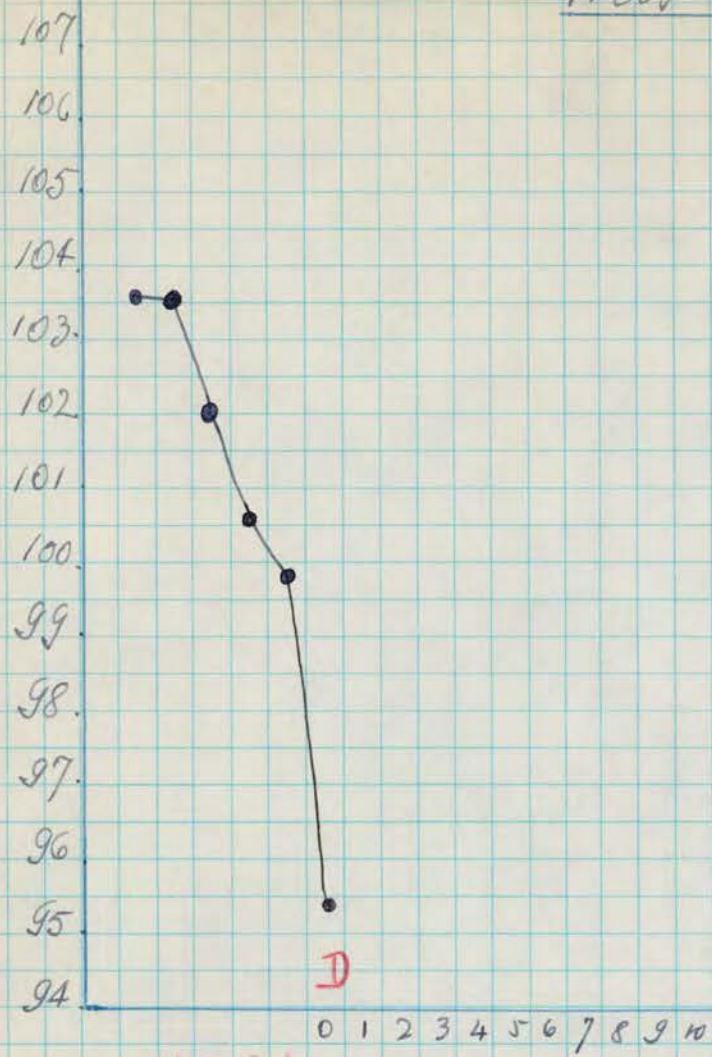
Rh. 1255

Methyl Phenol

FEB 17 1949

16 mg Base/Kg/d
8 mg Base/Kg/b.i.d
E.T.

Cosal: 4 days - 64 mg. B.K.



DRUG:

1 2 3 4
↑↑↑↑↑

DATE: FEB:

16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB 18 - 4 PM - Ptosis in vidus.
5:30 PM - Eyelids almost complete shut. - 3/4 closed

" 19 - AM - Same condition.

" 20 - AM - Ptosis the same. Thin, glassy - not weakness. Looks sick

" 21 - AM - Thin - weak - Ptosis 3/4 closed. Looks sicker than yesterday.

8:30 : NOT DRUG

Prostrate - at time of inoculations - virus not given.

1:30 PM - While getting ready for perfusion - died under observation. No evidence of bacterial infection.

Perfused as usual - Cervical, thoracic, medulla + midbrain well fixed. Lumbar cord - not fixed - rest of brain not fixed.

Viscera appear grossly normal.

Thin slices of perfused formalfixed C65
put into Zenker-acetic.

FEB 28 :

Almost complete park
lysis left upper and lower
partial paralysis right upper
eye on the floor -
can't get up.

MARCH 1 -

Prostrate - Complete
flaccid quadriplegia.

" 2 -

Back + neck also paralyzed.
Prostrate.

6:30 P.M.: Acid, warm, no rigor
Autopsy 7 P.M.: no gross pathology -
great changes in nervous

CNS: L.A.

and almost complete
paralysis. left upper
limb partial paralysis right
upper and lower
limbs on the floor. Can
sit up.

MARCH 1 8:30 AM - Dead, rigor mortis.
= 9:15 autopsy: No gross pathological
changes in viscera.
Spleen somewhat enlarged.
CNS - 7A.

Rh. 1259

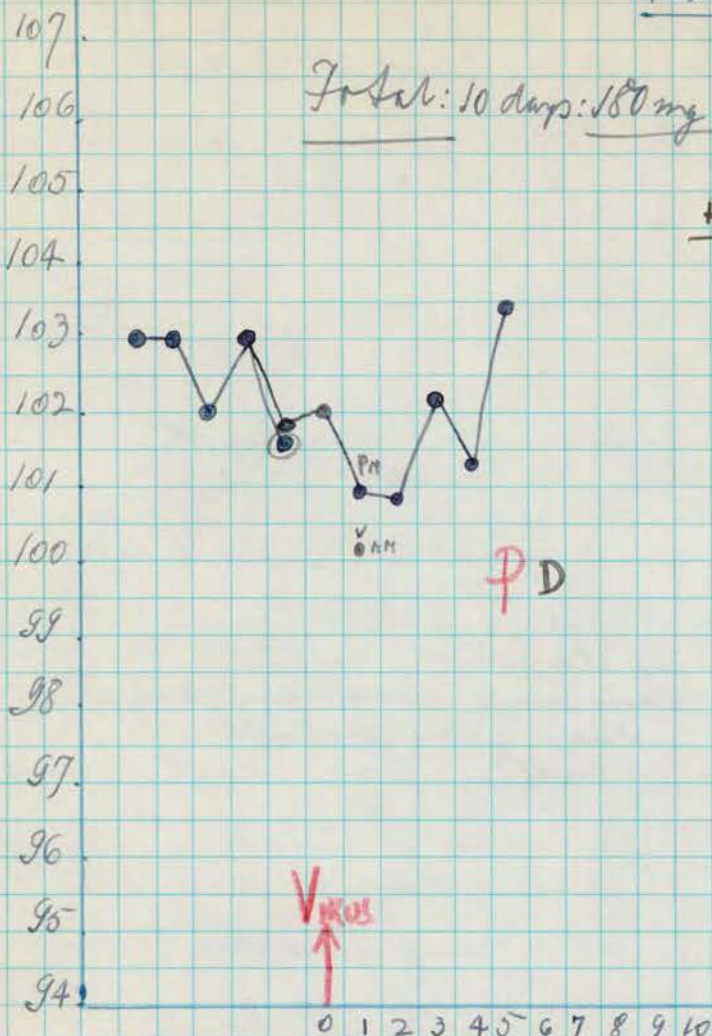
Perfaguine

FEB 17 1949

Total: 10 days: 180 mg B.K.

18 mg Base/K w/ day
9 mg Base/K w/ b.c.i.d
F.D.T.

Histology - Polio - Severe



DRUG
 DATE: FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3

- FEB 19 - O.K.
- " 20 - O.K.
- " 21 - O.K.
- " 22 - O.K.
- " 23 - O.K.
- " 24 - O.K.
- " 25 - Hunched over.
- " 26 - Noon: Flaccid paralysis on both arms and head.

6¹⁵ PM: Partial paralysis all four extremities. Marked vertical nystagmus. Incontinence, the nystagmus is vertical. Partial paralysis all four extremities - prostrate.
 9³⁰ - Completely prostrate. Complete flaccid quadriplegia + back and neck - no nystagmus.

FEB - 27 9:AM - Dead, rigor mortis, cold.

10 AM Autopsy: Spleen enlarged.

No other gross patho-
logical changes.

C.N.S. Pieces in Z.A.

Histology

Thalamus + Hypothalamus - Few infiltr. foci in hypoth.

None in thalam.

Midbrain - thru sup. colliculi -

Scatt. infiltr. foci in Sup.
Colliculi + Subst. nigra

Diff. cell. infiltration in
oculomotor nuclei

~~Many~~ Some neurones necrotic
~ due to polio probably?

Others poor - dead animal

" - thru inf. colliculi -

Scatt. lesions - trochlear nucleus
few aff cells - post mortem?

Medulla - Scattered - neuronal & infiltrative foci

Spinal Cord -

Cervical -

All anterior horn
cells affected by polio process
+ neuroplasia

Thoracic -

Same

Lumbar -

one side completely
affected

other side many ANC
intact

Spleen -

Full of what appears to be
disintegrated red blood cells

Rh. 1260

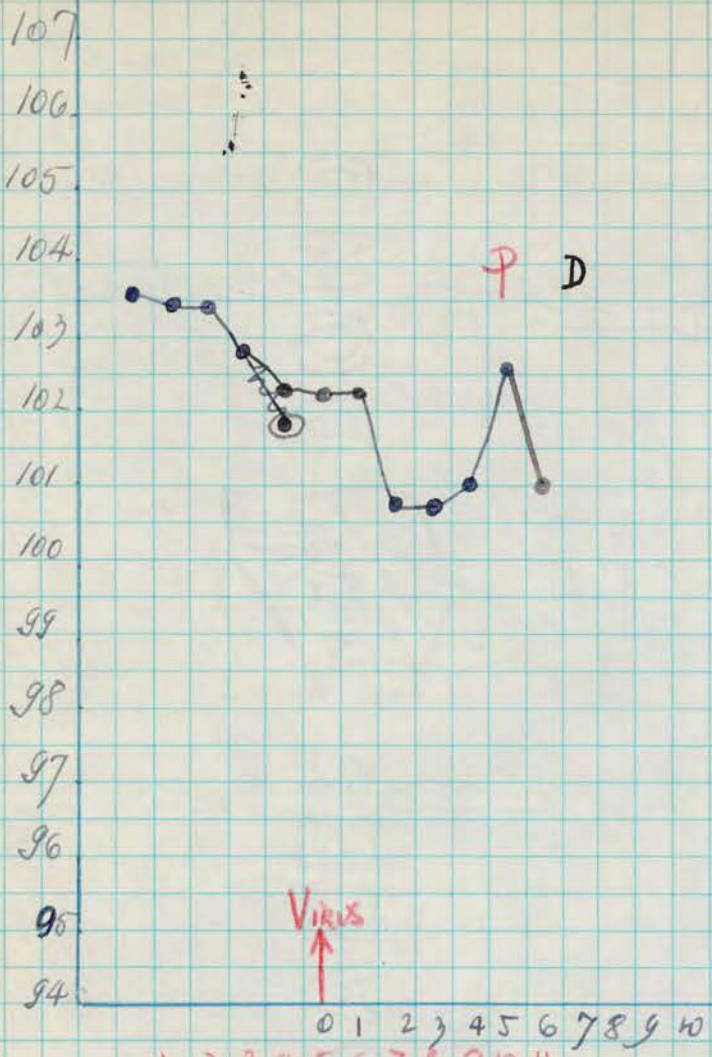
FEB 17 1949

Pen Salvarsan

18 mg base / K 2/day
9 mg base / K 2 / bid
F.I.

Total: 11 days: 198 mg BK.

Histology - Severe and extensive polio



DRUG:

{ 1 2 3 4 5 6 7 8 9 10 11
↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑

DATE: FEB

16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3

FEB 19 - O.K.

" 20 - O.K.

" 21 - O.K.

" 22 - O.K.

" 23 - O.K.

" 24 - hunched over.

" 25 - Hunched over. Not very active.

" 26 - Same condition.

6 PM: This monkey, 1 hour and a half after received his 20th dose of Pen Salvarsan appeared with tremendous "psycho"-motor excitement but rolling on the floor, with partial paralysis on all four extremities and horizontal myasthenus very marked. Cried much even when not spindled, sometimes presented uncoordinated movements, limited by the paralysis. The

FEB. 26 horizontal myasthenia continued
at least for 45 minutes -

9:30 Lying on the floor. Partial
flaccid paralysis on all four
limbs + back and head.
The paralysis was more marked
on his arms.

" 27 2 PM Paralysis more advanced
but still incomplete.

" 28 - 8:00 - Dead, in gas, cold

= 10 AM Autopsy: Lungs did not collapse
completely. No other
gross pathologic changes.
P. like in L. A.
C.N.S.: Pieces in L. A.

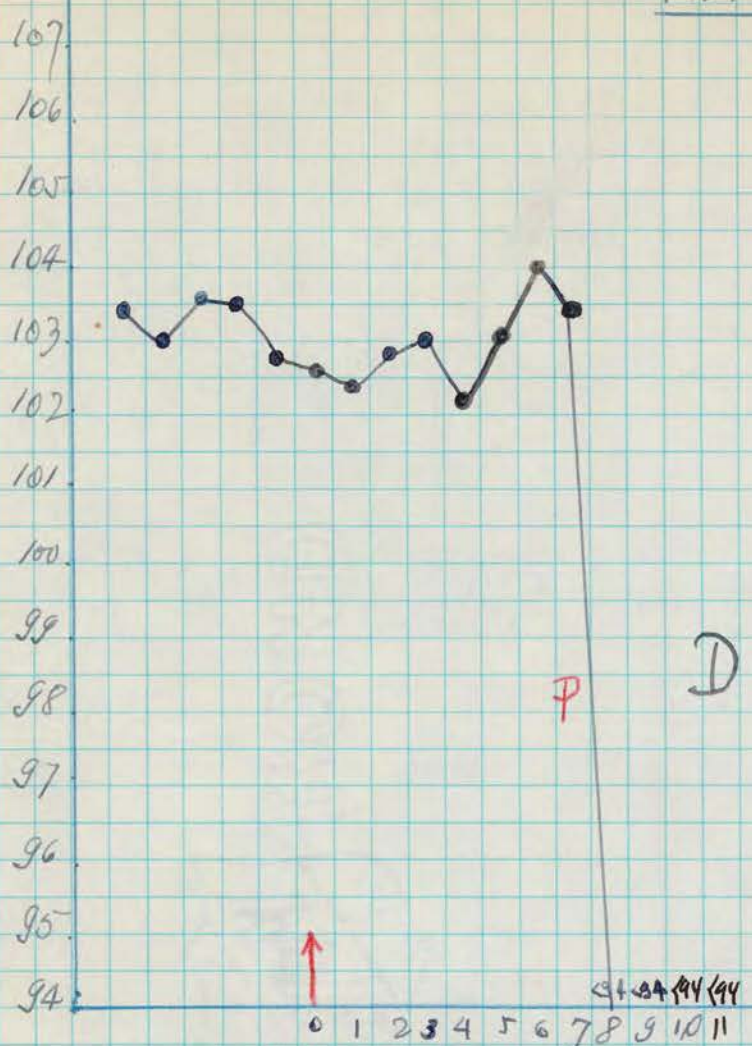
Rh. 1261

Penicillin

FEB 17 1949

18 mg Base / K b/day
9 mg Base / K b / b.i.d
E.I.I.

Total: 12 days = 216 mg. B.K.



DRUG
 DATE: FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

FEB 19 - O.K.
 " 20 - O.K.
 " 21 - O.K.
 " 22 - O.K.
 " 23 - O.K.
 " 24 - O.K.
 " 25 - Somewhat hunched over.
 " 26 AM Hunched over.
 6 PM Same condition.
 9:30 PM - Same condition.
 " 27 - AM - ~~Partial paralysis left lower~~
~~Pilonator.~~
 PM - ~~Outstanding involvement~~
~~of the left foot.~~
 DM - No paralysis. -

FEB 28 - tumor excised

- P.M. Partial paralysis
- MARCH 1 - AM: Complete paralysis both arms. Partial para-lysis right lower limb.
- " 2 - AM: his down. Complete paralysis both arm. Partial R. lower limb + back.
- " 3 - AM - his down: Complete paralysis on arm. Partial paralysis on both lower limbs. back and neck paralyzed.

" 5 - 12 45 A.M. (Dead - warm)
↓
Autopsy: No gross pathology -
Hospital changes
in midbrain.

C.N.S. → L.A.
↓
Soft.

Rh. 1262

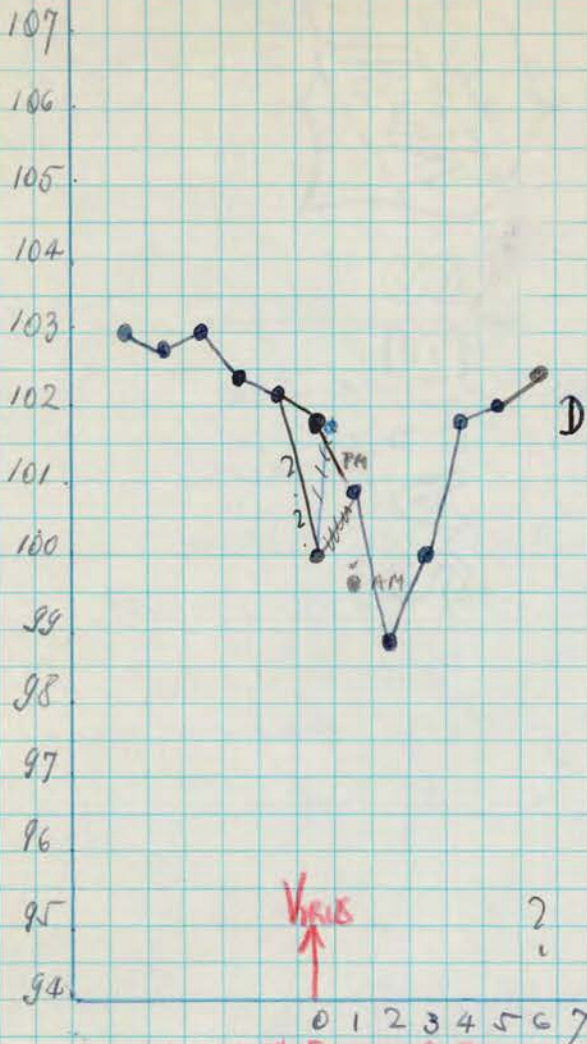
FEB 17 1949

Penicillin

18 mg Base/K, 4/day
9 mg Base/K 2/bil. d
E.I.

Total: 11 days = 198 mg. O.K.

Polio lesions in medulla
(early)



DRUG: { 1 2 3 4 5 6 7 8 9 10 11
 ↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑

DATE FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4

FEB 19 - O.K.

" 20 - O.K.

" 21 - O.K. hunched over

" 22 - hunched over

" 23 - Same condition

" 24 - hunched over

" 25 - Hunched over. Thin.

" 26 AM Same

9:30 PM: ~~partial paralysis both arms.~~
~~Weakness on both lower.~~

" 27. ~~ATT. ~~partial paralysis~~~~
~~on both upper.~~
~~partial paralysis on both~~
~~lower and both.~~
PM - ~~not paralysis~~

" 28 - AM: dead, rigor, cold.

940 Autopsy: Spleen somewhat enlarged. No other gross pathological changes on viscera.

C.N.S. in L.A.

Histology - Foci of acute neurophagia in 4 of 5 levels of medulla. 18 levels of spinal cord show no polio neuronal lesions - one infiltrative focus in cervical cord.

Spleen - evidence of blood destruction & phagocytosis of RBC.

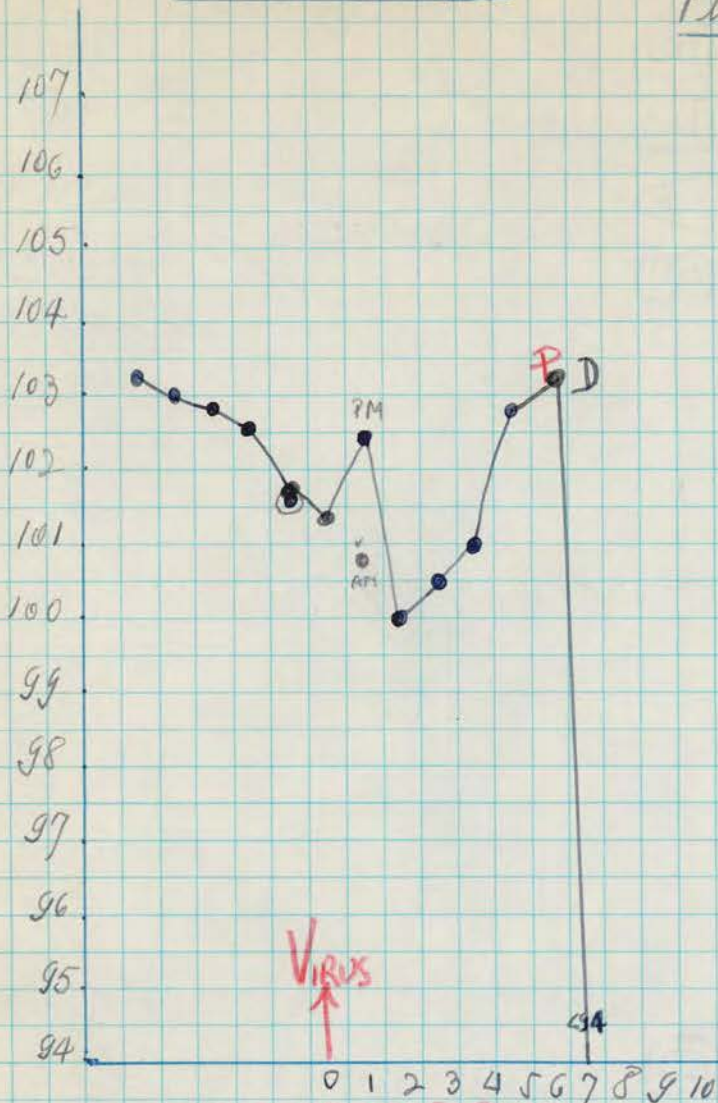
Rh. 1263

Penicillin

FEB 17 1949

18 mg Base /K w/ day
9 mg Base /K w/ b.o.d.
E.T.I

Basal: 11 days: 198 mg B.K.



DRUG
 { 1 2 3 4 5 6 7 8 9 10 11
 { M M M M M M M M M M M M }

DATE FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28

FEB. 19 - O.K.

" 20 - O.K.

" 21 - O.K.

" 22 - O.K.

" 23 - O.K.

" 24 - Hunched over -

" 25 - Same condition -

" 26 - Same -

" 27 - AM: ~~Partial paralysis right lower~~
 NOON: ~~Partial paralysis~~ Complete para-
 lysis ⁱⁿ arms, partial lower
 back.

Can sit up - Can stand up
 on both lowers

" 28 - AM: Complete paralysis both arms.

3:30 PM - Dead, still warm, no rigor yet.

4 Feb - 28 - 3⁴⁵ PM

Autopsy: No gross
pathological changes
on viscera but spleen
enlarged. - (Z.A.)

C.N.S. - Virus in L.A.

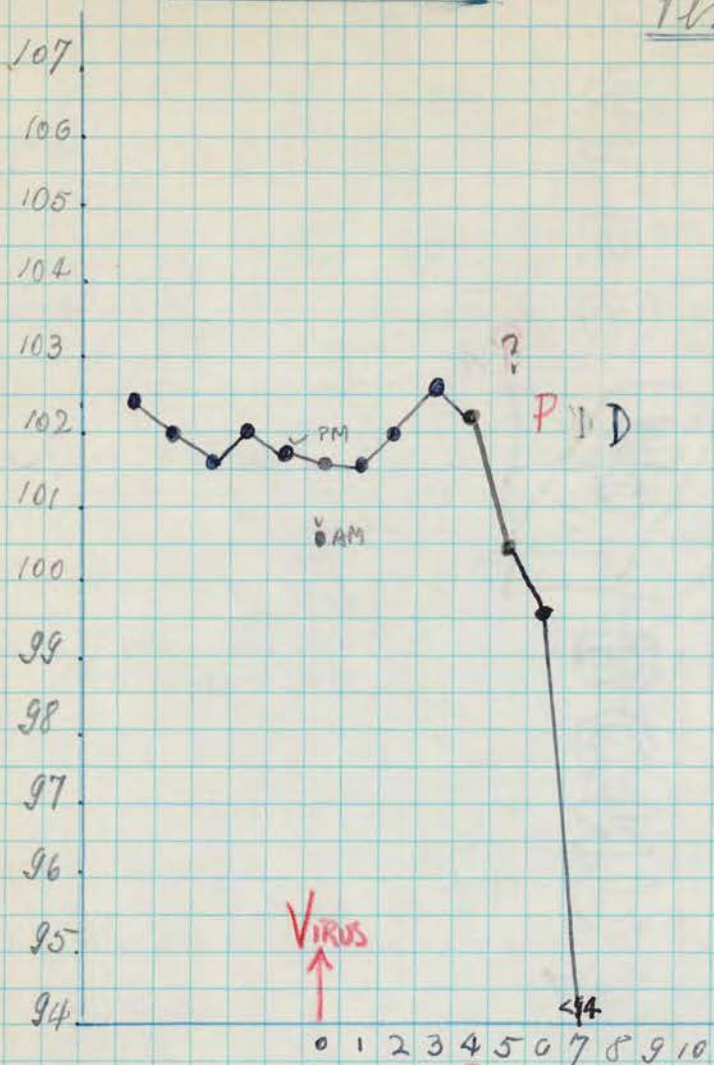
Rh. 1264

Rhinopneumonia

FEB 17 1949

18 mg Benz/K 2/day
9 mg Benz/K 2/b.i.d.
F. II.

Total: 11 days: 198 mg B.K.



DRUG
 { 1 2 3 4 5 6 7 8 9 10 11
 ↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑

DATE FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4

FEB. 17 - AM - This monkey presented (before to start the administration of the drug) a lesion in skin on his anterior neck, right side. From the lesion come a fluid serum-like, with some yellow corpuscles, about 2 mm size.

FEB. 18 - The edges of the lesion are today more definite. Not yellow corpuscles had been seen in the morning.

FEB. 19 - The lesion same condition. But somewhat swollen on the face, left side, inferior part.

" 20 - Same condition about lesion on neck, but red eyelids (superior, both eyes) and external corners of the eyes.

" 21 - The swollen region is today almost unms.

Liceash - Skin brown looks better.

FEB - 22 - O.K.

" 23 - O.K.

" 24 - O.K.

" 25 - O.K. Good cicatrization.

" 26 - Numbled over.

6 PM. Same condition, but weakness on both upper?

" 27 - PM - ~~partial paralysis~~
both lower
weakness on both upper (2)
Weak: partial p. all lower

PM - severe tremor
easily fatigued.
~~weakness~~ weakness on
all four extremities -
cat, alert.

10³¹ lies on floor. Almost
complete paralysis both
lower and right upper.

" 28 - Prostrate. Complete flaccid
quadriplegia.

MARCH. 1³⁰ AM. Dead, no rigor, cold.

Autopsy: 9¹⁵ viscera w gross
pathological changes.

CNS - L.A

uu

uu uu

Rh. 1265

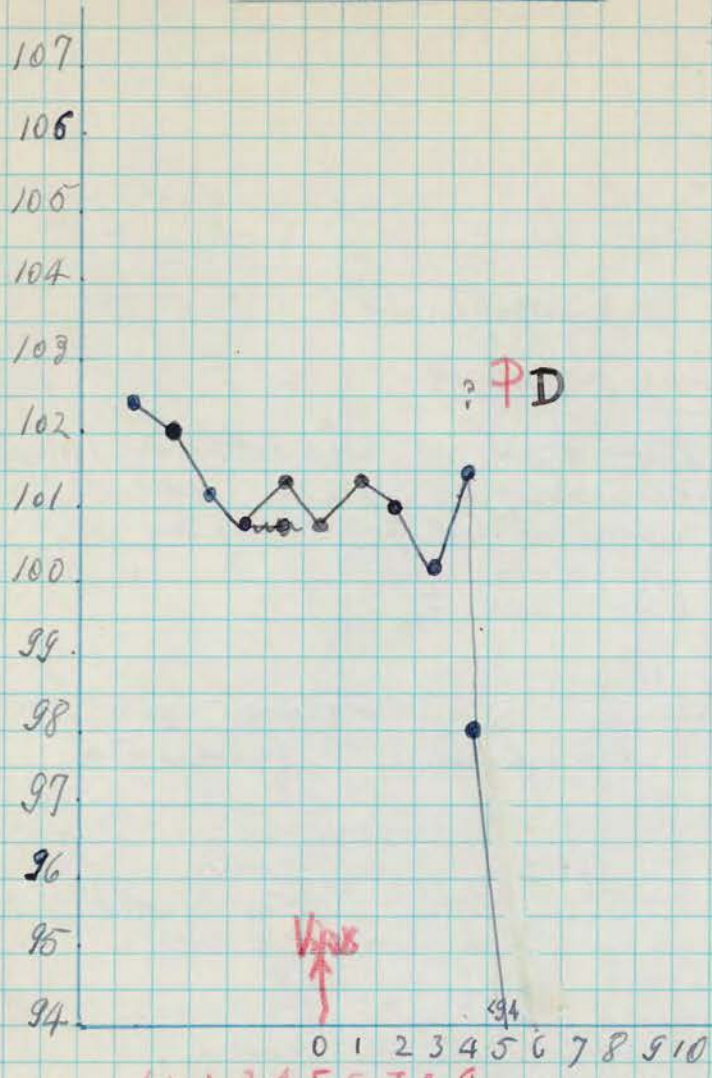
Pentagamine

FEB 19 1949

18 mg Base / K 2/day
9 mg Base / K 2/day

Histology - Polio - Severe

Total: 8 1/2 days = 153 mg B.K.



DRUG

DATE:

16 17 18 19 20 21 22 23 24 25 26 27 28

FEB - 19 - O.K.

" 20 - O.K.

" 21 - O.K.

" 22 - O.K.

" 23 - O.K.

" 24 - Not very active - Nunched over.

" 25 - Same condition - 9:30 AM

11:30 - Found lying on floor.
 Very difficult to decide whether the monkey is exhibiting partial paralysis of extremities or generalized weakness - temp. taken twice was 98.6 + 98.0 - Cannot climb but can sit up. Appears alert like a "polio" monkey in early stages but legs are very weak. Arms ok. If this monkey were in control - he would be called polio
 Tried to eat.

P.M. - Same condition - DRUG NOT GIVEN

FEB - 2 @ 8 AM Completely prostrate
Flaccid paralysis both
arms and head. Partial pa-
ralysis lower. Complete paralysis
on back.

6 PM - Complete flaccid quad-
riplegia.

9:20 Same condition.

" 27 - AM. Head, right, cold.

10:15 AM Autopsy: No gross pathological
changes but spleen
somewhat enlarged.

C.N.S.: Prices in L. A.

Histology - Scattered ^{proles} lesions in thalamus-hypothal. (latter)
Midbrain (? of trochlear) + medulla.

Spinal cord - with except. of ^{several} few levels
at which some AHC
are still intact
all the others are
completely destroyed -
+ neuronophagia.

Spleen - full of what appears to
be fragmented red cells.

KN. 1266

FEB 17 1949

Polio

18 mg Base / 2 / day
10 mg Base / 2 / 10. Ltd
E.T.

Dose: 8 1/2 days = 15 3/4 mg

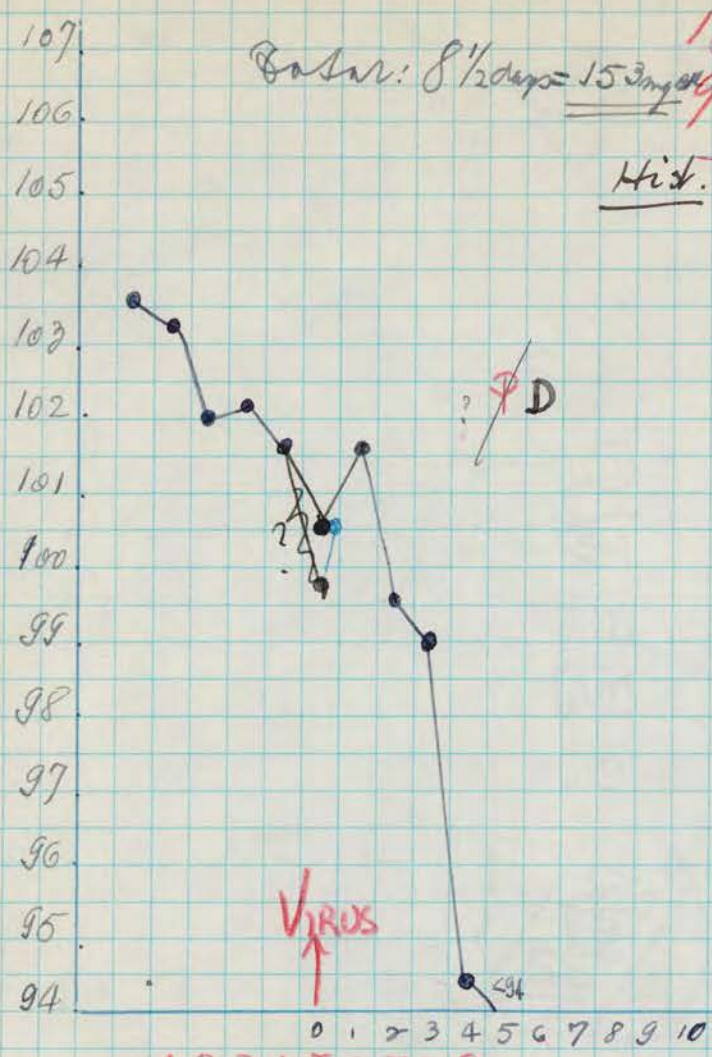
Hit. Polio - Severe in Midbrain
(Oculomotor)

And Medulla

Early & focal in
spinal cord.

Prostration - not due
to destruction of Ant.
horn cells in spinal
cord as in polio.

Dead with polio on
6th day.



DRUG

1 2 3 4 5 6 7 8 9
↑↑↑↑↑↑↑↑↑↑↑↑↑↑↑

DATE:

1 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB - 19 - O.K.

" 20 - O.K.

21 - O.K. - hunched

22 - Same condition.

23 - Same.

24 - hunched over. Some time lies on the floor.

25 - Very thin and weak - 9:30 AM.

11:30 lying down - almost same as 12:45
Arms stronger - Legs weaker - Sits up when prodded - Temp 93.8

PM Same condition DRUG NOT GIVEN

26 - AM - Prostrate.

6 - Prostrate.

9:30 Same - Very slow respiration.

FEB - 27 1^{1/2} AM - Dead, rigor, cold.

= 11 AM: Autopsy: Viscera: No gross
pathological changes

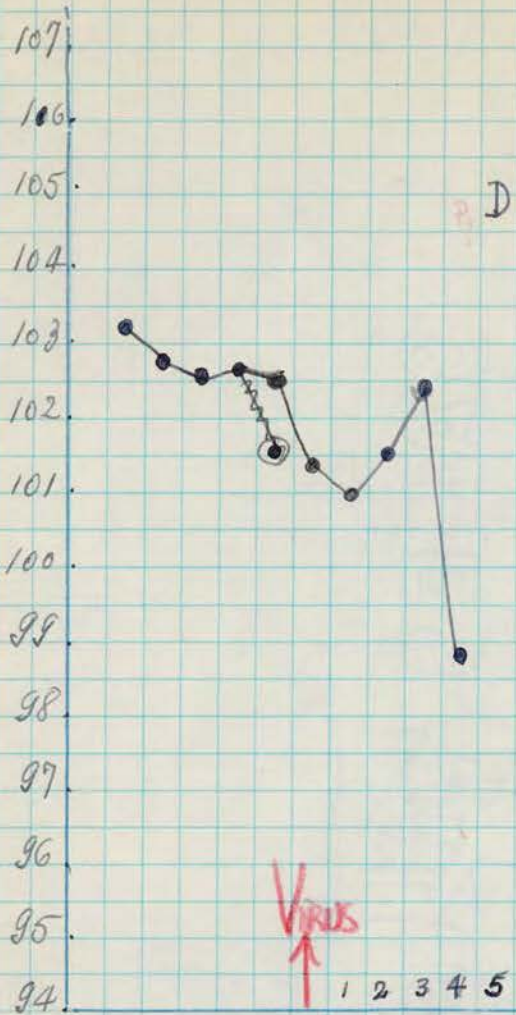
CNS: Pieces in L.A. -

Rh. 1267

FEB 17 1948

Pentaprisin
18 mg. Base / K 2 / day
9 mg Base / K 2 / 2 i. d.
E.I.

~~Basal: 8 1/2 days = 159 mg B.K.~~



Dead with polio on 5th day.

Prostration not due to polio involvement of ant. horn. cells.

DRUG
 DATE: FEB: 16 17 18 19 20 21 22 23 24 25 26 27 28 1 2 3 4 5 6 7 8 9 10

FEB 19 - O.K.

" 20 - O.K.

" 21 - O.K.

" 22 - O.K.

" 23 - O.K.

" 24 - Hunched over

" 25 - Very thin - Hunched over -

11:30 - Generalized weakness - cannot climb - but head and all extremities appear very weak

PM - Same condition - DRUGS NOT GIVEN -

" 26 - 8:5 AM. Dead - Rigor mortis cold

9:30 Autopsy: No gross pathological changes in viscera

CNS in L.A.

Focal lesion in medulla

Pentagaine Group

| <u>Monkey No.</u> | <u>Clinical</u> | <u>Histology</u> | <u>Record as</u> |
|-------------------|---|--|--------------------------------|
| 1256 | Partial 6, Ext. Par. 7 Prostrate 8, D9 | | P ₆ D ₉ |
| 1257 | Part. par. -6; Ext. par -7; D8 | | P ₆ D ₈ |
| 1258 | Very Weak 4; D5 | Lesions in Sp. Cord but not enough for par. | D ₅ \bar{c} polio |
| 1259 | Ext. flacc. Par. 5 Dead 6 | Severe Polio | P ₅ D ₆ |
| 1260 | Paral. 5 Ext. " 6; D7 | | P ₅ D ₇ |
| 1261 | Partial par. 7 Extensive par. 8, D11 | | P ₇ D ₁₁ |
| 1262 | | Dead 6 Early polio in medulla | D ₆ \bar{c} polio |
| 1263 | Paral. 6, Dead 7 | | P ₆ D ₇ |
| 1264 | Paral. 6, D8 | | P ₆ D ₈ |
| 1265 | Par. 4 D6 | <u>Severe polio</u> | P ₄ D ₆ |
| 1266 | <u>Prostrate 4</u> D ₆ | Polio but prostr. not due to destr. of ANC | D ₆ \bar{c} polio |
| 1267 | Very wk. 4, D5 | as 1266 | D ₅ \bar{c} polio |

4 days - 1/12 4
 5 " - 4/12 20
 6 " - 6/12 36
 7 " - 1/12 7
67/12 =