

PLAN.
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Plasmaid — 1mg. base / kilo b.i.d. to each monkey

Monkeys to be used: Dose will be in 20cc. water

	<u>Weight Kg.</u>	<u>S. S</u>	
Rh. 733 — 9 1/4 lbs. = 4.19 4.19	2.092	c.c. = 2.1 + 17.9	
Rh. 734 — 8 lbs. = 3.628 mg	1.814	" = 1.8 + 18.2	
Rh. 633 X — 6 1/2 lbs. = 2.948 mg	1.4735	" = 1.5 + 18.5	
Rh. 634 X — 5 3/4 lbs. = 2.608 mg	1.3035	" = 1.3 + 18.7	
		<u>6.7</u>	

Drug used — SN 3115- Plasmaid dihydroiodide
Lot JDH-22
52.8% base

Prepare — Aqueous solution to contain
2 mg. of base per cc.

Amount of drug per 100cc = 378 mg.
379.

$$\frac{200\text{mg base}}{52.8} = 378.7\text{mg}/100\text{cc}$$

6.7cc of stock needed per dose for 4 monkeys
x 8 = for 8 doses
53.6cc

Therefore prepare 100cc of stock = 379mg plasmaid

Drug SN 13058-17 — dihydroiodide — salt.

.53% base

Dose — 12 mg./kilo b.i.d.

Administered in 20 cc of water

Monkeys to be used:

$\frac{\text{Mg. Base}}{12 \text{ mg./kilo}}$ S.S.

Rh. 735 — $6\frac{1}{2}$ lbs. = 2.948 Kg. $\frac{35.38}{12} = 2.948$ C.C.

Rh 736 — 8 lbs = 3.628 " $\frac{43.54}{12} = 3.628$ C.C.

Rh 635X — $6\frac{3}{4}$ lbs = 3.061 " $\frac{36.73}{12} = 3.061$ C.C.

Rh 636X — $6\frac{3}{4}$ lbs = 3.061 " $\frac{36.73}{12} = 3.061$ C.C.

17.3 cc
stock for 4 monkeys
per dose

Prepare — Aqueous solution to contain

10 mg base per cc 1887 mg.

Amount of drug/100cc = 1887 mg.

943.5
2.830.5

$$\frac{1000 \text{ mg base/100cc}}{53} = 1886.8 \text{ mg/100cc}$$

17.3 cc of stock sol. per dose for 4 monkeys
x 8 (doses)

138.4 cc of stock sol. needed.

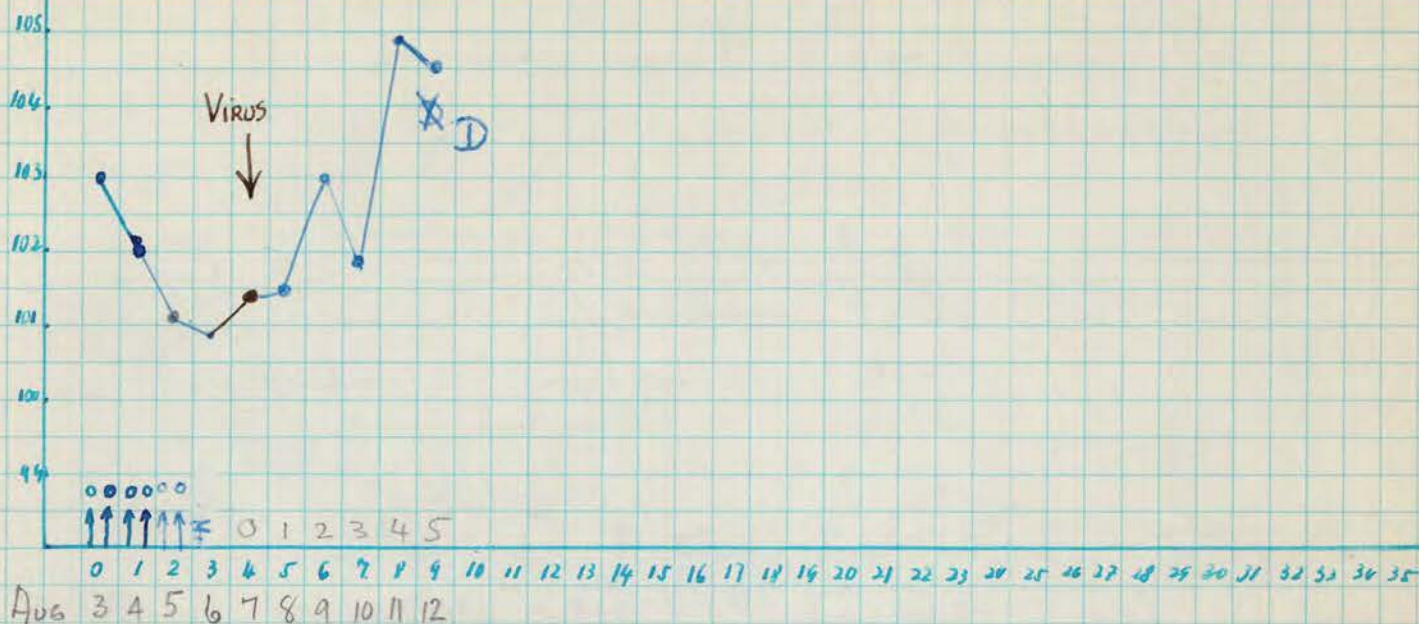
August 3-48

PLASMACID TRIAL -

Rh # 733 =

o = Oral administration
At 8⁰⁰ AM and 4⁰⁰ P.M.

1 mg base / kilo / bid



Aug. 6 - AM - Convergent strabismus, horizontal nystagmus, ataxic. Easily exhausted. Drug discontinued

Aug. 7 - Sits in cage, hunched over. Does not move without being prodded. Nystagmus, ataxic.
Ice of 1:500 "Hoferkamp" strain ^(GENT) Polio Virus into right frontal lobe.

Aug. 8 - condition same

Aug. 9 - Sits up in cage - eyes wide open - pupils dilated - Very strong grip, marked ataxia, incoordination of movements. Climbed back into cage.

Aug. 12 - No change in neurological signs associated with fever

August 13 - AM. Dead, cyanotic, equimorose face and supraventricular chest.
Autopsy - Sarcoid formation.

- Monkey was found dead - still in rigor mortis. The position of the body ~~was~~ and chain did not indicate strangulation - although the appearance of the face - blue, oedema of eye-lids, bitten tongue - suggests that there may have been a terminal ^{tonic} convulsion - which put pressure on the chain around the neck.

Necropsy - No gross pathological change in the viscera. Perfused with saline and 10% formalin. +1% glacial acetic acid - but perfusion not successful. Tissue in formalin.

Microscopic Pathology

Spinal cord - peculiarly distorted - poor fixation
but very ~~many~~ extensive lesions with
neuronophagia, ~~lesions~~

Medulla - extensive necrosis involving nuclei
cuneatus and gracilis & to lesser
extent vestibular nuclei.
Acute neuronophagia in reticular
substance & elsewhere

Midbrain - Level of inferior colliculi
Complete destruction of region
of trochlear nerve nuclei
Focal infiltrative lesions in
inferior colliculus

Thalamus - negligible lesions

August 3. 48

PLASMACID TRIAL

Rh. # 734



Aug 3 4 5 6 7 8

Aug. 4 - ok.

Aug. 5 - Climbs but seems somewhat ataxic - not too definite or marked.

Aug. 6 - AM - Ataxic, nystagmus, disinclined to move.
DRUG discontinued

Aug. 7 - AM - as before; sits hunched over in cage.

VIRUS - Same as Rh 733

Aug. 8 - same

Aug. 9 - Sits up in cage, eyes open, pupils dilated, ~~very~~ slight nystagmus, very strong grip - marked ataxia and incoordination of movements. Climbs

Sits up in cage but cannot climb - movements incoordinated and awkward - very strong grip in arms & legs. Spastic. Tends to close eyelids - as if somnolent

August 11 - Diarrhea - thin.

August 12 - Diarrhea -

August 13 - AM. Flaccid paralysis of both arms. Cannot get up. No paraspinal paralysis. No oculomotor paralysis. Nystagmus. Paralysis of neck muscles. Head "drop"

August 14 -

Complete quadriplegia. Aphonia. Back and neck muscles paralyzed. Abdominal respiration. Involuntary paralysis. No paraspinal. No oculomotor paralysis. Monkey in terminal stage

- K. Perfused: 1000 c.c. saline. After, 1 cc. morphine 10%

in saline, 1 percent acetic acid
S.N.S. stained in formalin
Rm T.B.C.

No gross pathological change in viscera.

Perfusion good

Microscopic Pathology

Almost all neurones destroyed in spinal cord
& in many levels reaction is now minimal.

Acute & older lesions in medulla

with destruction of — nucleus gracilis & cuneatus
vestibular nuclei

Midbrain — oculomotor nuclei destroyed.

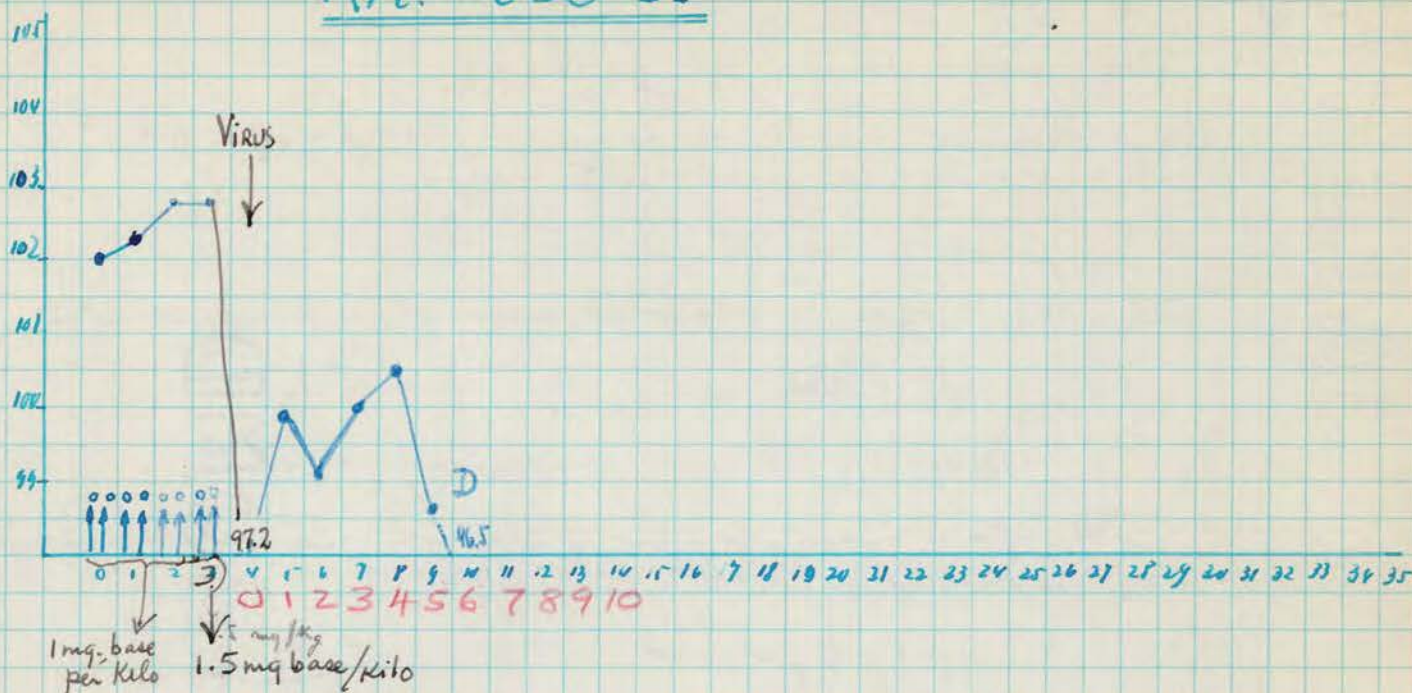
Focal neuronophagia in sup. colliculi
Mesenceph. nucleus of V, Substantia
nigra

Thalamus — negligible

August 3-48

PLASMACID TRIAL -

Rh. #633 X



Aug. 6 - A.M. - not too active; but no definite signs like the others. Drug increased to 1.5mg base/kilo (2.25cc stock sol. + 17.75cc H₂O)

AUG. 7 - A.M. - Marked signs this A.M. - Pupils dilated, head moving uncontrollably, nystagmus, ataxic, "staring look", sits hunched over. Prolapse of rectum (diarrhea) - pushed back.

VIRUS - same as Rh 733

Aug. 8 - Lies down in cage - moves with difficulty. Eyes dilated - wandering gaze.

Aug. 9. Lies down in cage. Pupils dilated - no nystagmus. Uncoordinated, purposeless movements of head. Cannot climb or sit up - rolls from side to side on floor. Tone and power good in arms & legs.

August 11 - Wandering - thin

August 13 - A.M. - Monkey prostrate; corneae dry - upper lid doesn't close. No paralysis of extremities. P.M. - Dead. Autopsy - L.A. (Brain and spinal cord)

Found dead at 4:15 P.M. Necropsy - 1 1/2 hrs. later put in refrigerator

Viscera - no pathological change, except the colon which showed several very thin

hemorrhagic zones. Pieces of colon put in Zenkers

Microscopic Pathology

The most remarkable findings here are:

- 1) the extensive acute lesions in the spinal cord, involving almost all neurones — despite the absence of paralysis just prior to death.
 - 2) Extensive (older) necrotic lesions (infiltrated with glia and Gitter cells) in the medulla in the region of the — abducens nucleus, the vestibular nuclei and cuneate nucleus.
- Nuclei of Cerebellum — older + more recent lesions

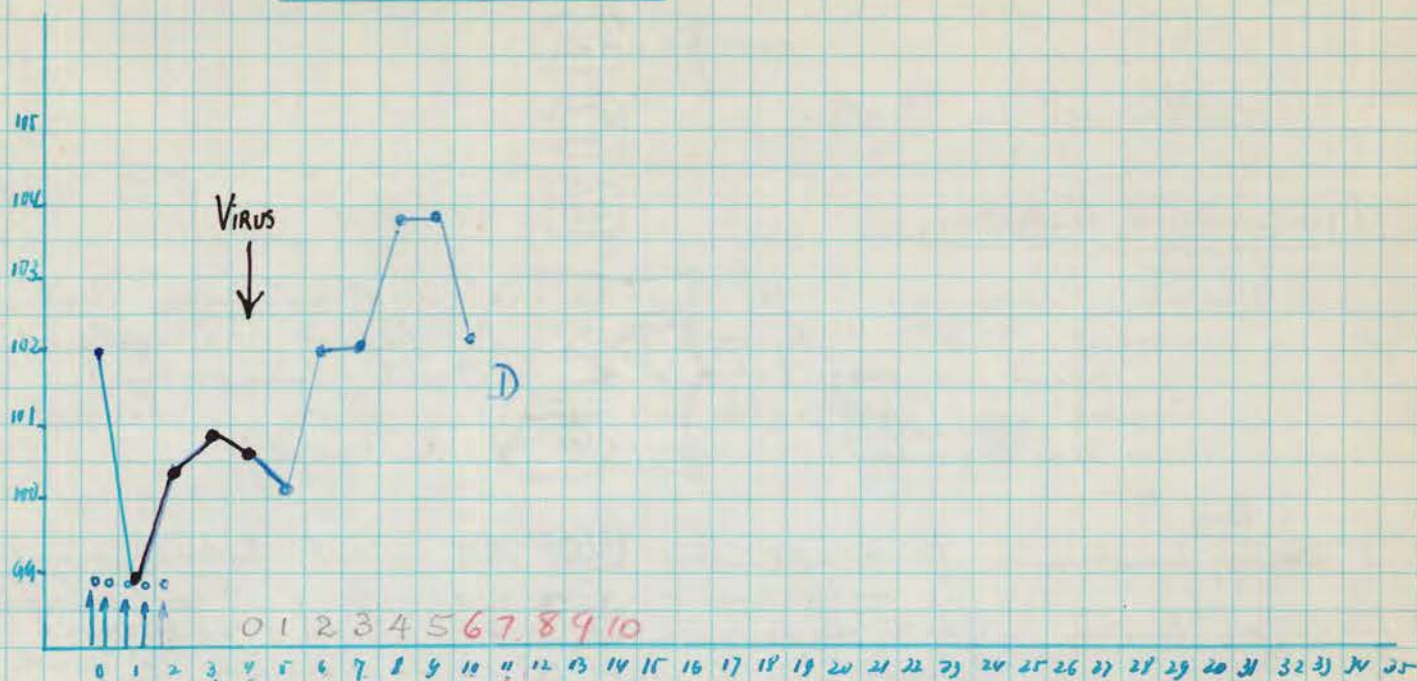
Midbrain — section missed the oculomotor region
Lesions (focal) in substantia nigra.

Thalamus — ~~essential~~ negligible focal lesions.

August 3-48

PLASMACID TRIAL -

Rh #634 X



Aug. 3 - mild diarrhea - prior to beginning drug

Aug. 4. - A.M. Within less than 24 hours after the first dose and before the third one was given this morning, the monkey was found hunched in the corner of the cage. The head is "floppy" there is a peculiar wide-open staring of the eyes with dilated pupils. There is marked nystagmus. Does not appear to be blind. Does not climb or run spontaneously. Upon being prodded the movements are ataxic, jerky and incoordinated. There is no paralysis of the extremities or of the facial and eye, and jaw muscles.

Drug given just the same.

Aug. 5 - Condition same

Morning dose given. Drug then discontinued

Aug. 6 - Condition same

Aug. 7 - Sits hunched over in cage, ataxic on movement, nystagmus not noticeable, but pupils dilated

VIRUS - same as Rh 733

Aug. 8 - Same

Aug. 9 - Sits hunched over in cage - grip strong - Pupils dilated - vertical nystagmus. Spastic, ataxic - does not climb.

August 11 -

Aug. 13 - no paralysis; signs same

August 14 AM dead, warm - Put in refrigerator until
autopsy at 9:30 AM

Viscera - no gross pathology

Sections in Z.A.

Microscopic Pathology

General Impression - the most severe and extensive destructive lesions that I have ever seen before. Despite absence of paralysis day before death, the ant. horn cells in spinal cord are, with very few exceptions in lowest lumbar segment, ^{+ one thoracic} completely destroyed.

Spinal Cord

Lower lumbar - Some ant. horn cells still intact - but not normal. Extensive neuronophagia + cuffing, & interst. infiltr.

Middle + Upper lumbar - All nerve cells in ant., lateral and post. horns in process of neuronophagia - with polymorphs.
(3 sections)

Thoracic - 2 poor sections but extensive lesions; 1 other - many lesions but some ant. horn cells spared.

Cervical - 3 sections - almost all ant. horn cells gone extens. focal neuronophagia, cuffing, interst. infiltration

1 section - Only part of the ^{same} ant. horn cells affected. left - but most destroyed

Medulla - only one level at caudal end of 4th ventricle
Scattered lesions only in floor of 4th ventricle + reticular substance

Midbrain - Extensive necrosis with glial infiltration in region of oculo-motor nuclei - "swiss-cheese" appearance & glial infiltration looks like older lesion (probably due to plasmaeol)
Many nerve cells still intact
Also focal neuronophagia in substantia nigra.
Sup. colliculi - ok.

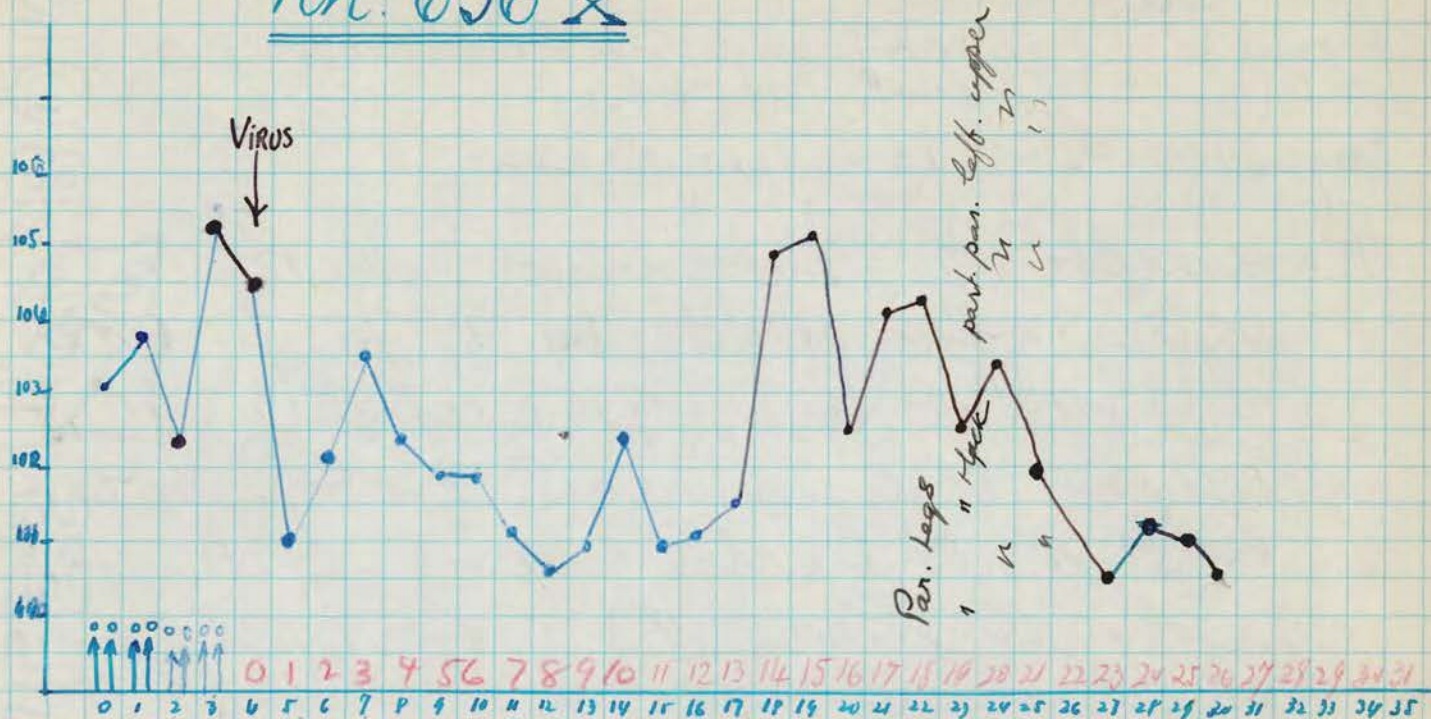
Thalamus and Hypothalamus - only negligible focal lesions

August 3-48

SN-13058-17

12 mg/K hr / b.i.d.

Rh. 636 X



Aug. 6 - O.K.

" 7 - O.K. Virus given as for Rh 733

Aug. 8 - O.K.

" 9 - O.K.

Aug. 16 - appears entirely normal

August 17 A.M. O.K.

P.M. O.K. 101.8

August 18 A.M. O.K.

August 19 A.M. O.K.

August 20 A.M. O.K.

August 21 A.M. No symptoms

P.M. O.K.

August 22 A.M. O.K.

P.M. O.K.

August 23 A.M. O.K.

August 24 A.M. O.K.

P.M. Tremor. Pilomotor. No paralysis

August 25 A.M. - Tremor. Pilomotor. Tremor on both upper. Cannot climb. Partial paralysis left lower. No facial, neither back nor neck.

P.M. - Complete paralysis both lower.

August 26 - A.M. - Partial paralysis left upper.
Back also paralyzed -

August 27 - A.M. - Same condition

August 28 - A.M. - Same condition - Right upper very
weak. No neck. -

August 30 - A.M. - Same condition. -

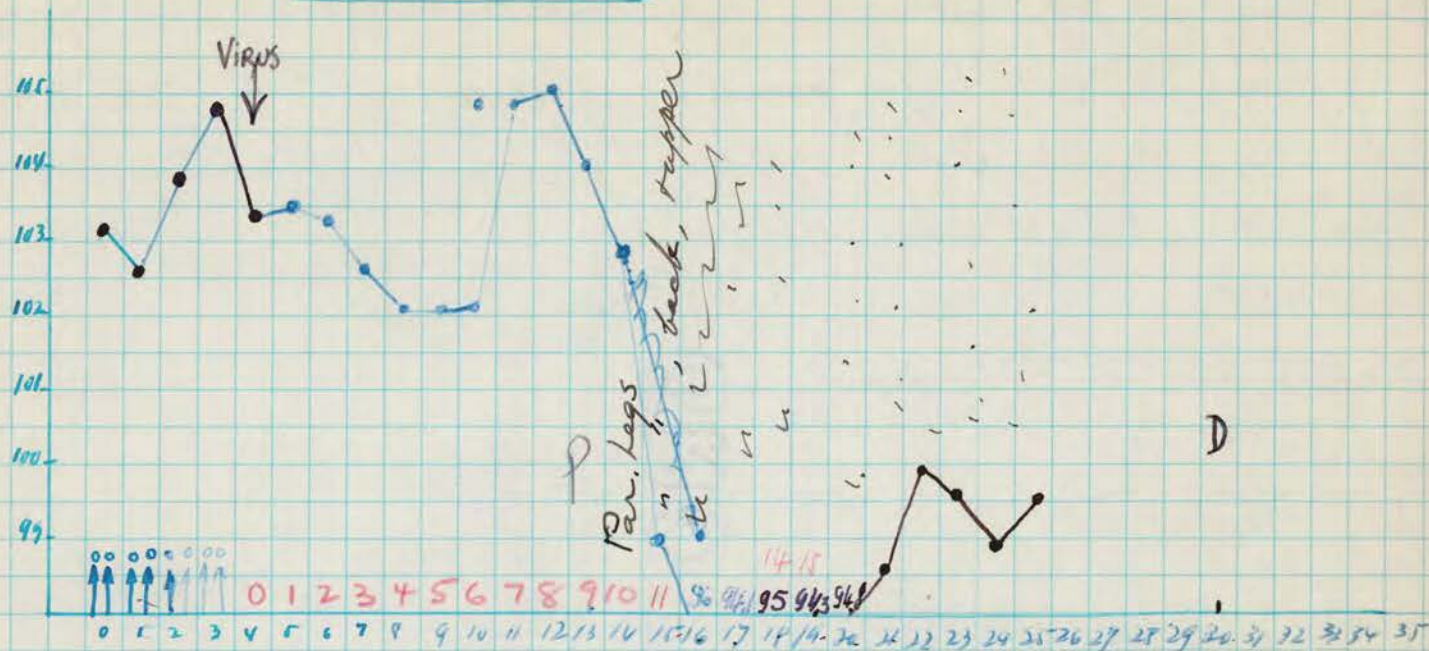
November 13 - Perfused with
saline followed by 10% formal.
saline with 1% acetic acid.
Sections of spinal cord, medulla
and mid-brain into Z. A. for
study changes of corneal
polio. -

August 3-1948

S.N. 13058

TRIAL

Rh. #736



August 5 - Anxious to climb - digger?

" 6 - OK

" 7 - Hair somewhat erect - but otherwise no ^{signs} symptoms

Virus - same as Rh 733

Aug. 8 - Hair ruffled; otherwise OK

" 9 - " " " "

Aug. 15 - No signs of any kind

Aug. 16 - A.M. - excited; tremors

P.M. - definite weakness + some dragging of lower extremities

August 17 - A.M. Paralysis of lower extremities - weakness on both upper. No neck paralysed - No cranial nerves - lies down on the cage.

August 18 - A.M. lies down on cage - Quadriplegia - Back paralysed - No neck - No cranial nerves.

August 19 - A.M. Same condition.

August 20 - A.M. Same condition.

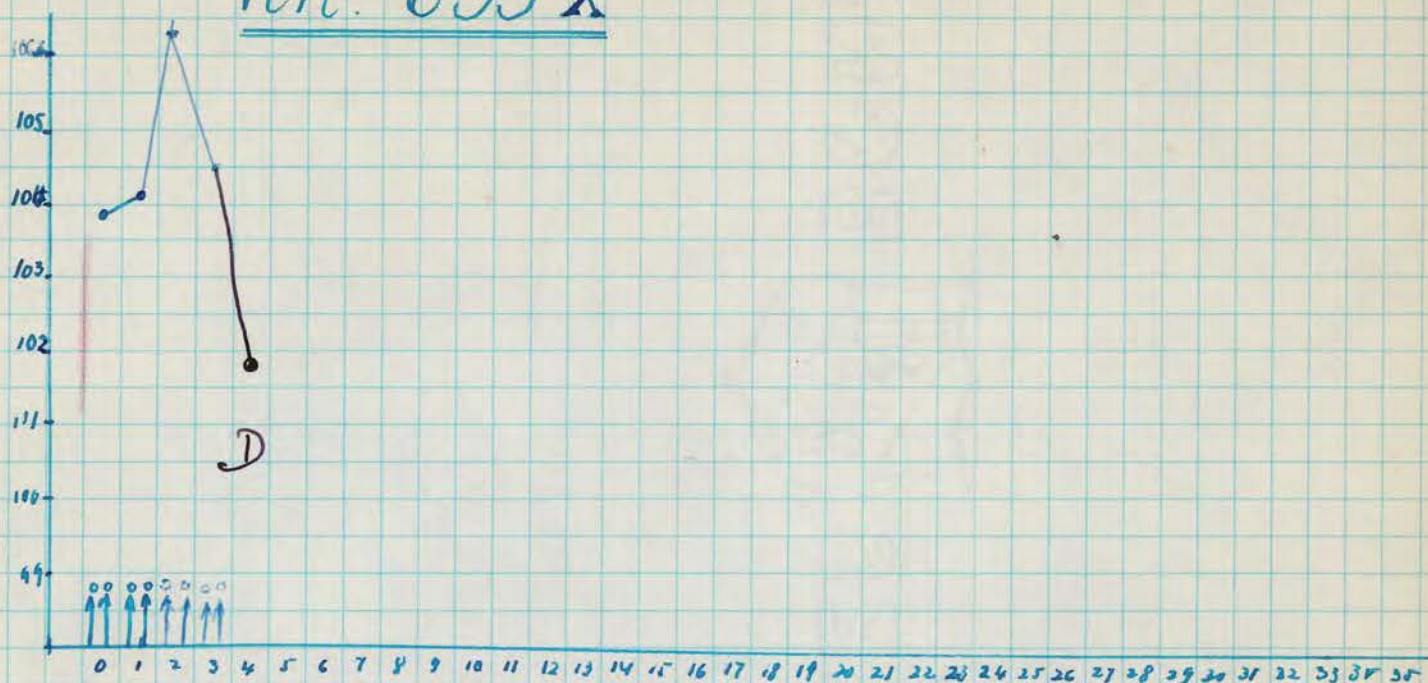
August 21 - A.M. Same condition.
P.M. Same condition.

August 22 AM Same condition. -
August 23 A.M. Same condition. -
August 24 AM Same condition. -
August 25 A.M. Very thin. Same neurologic conditions. -
August 26 A.M. Same condition. -
August 27 A.M. Same condition. -
August 28 A.M. Same condition. -
September 2 P.M. Dead -
- No autopsy -

August 3. 48

S. N. 13058-17. TRIAL

Rh. 635x



Aug. 6 - O.K.

Aug. 7 - Found lying in cage - eyes sunken - cyanotic - very weak
No CNS signs. Died 11:30 AM.

IMMEDIATE AUTOPSY

No gross tuberculosis, but right lower lobe and left lobe have acute pneumonic processes. Fluid found in abdomen after perfusion with saline + formal-acetic lesion around recto-sigmoid suggesting possible perforation with thermometer. Larynx + trachea - clean - too small to permit passage of catheter used.

Spinal cord + medulla - bloodless and apparently well fixed by perfusion
Rest of brain - mostly soft + pink
Saved in formalin.

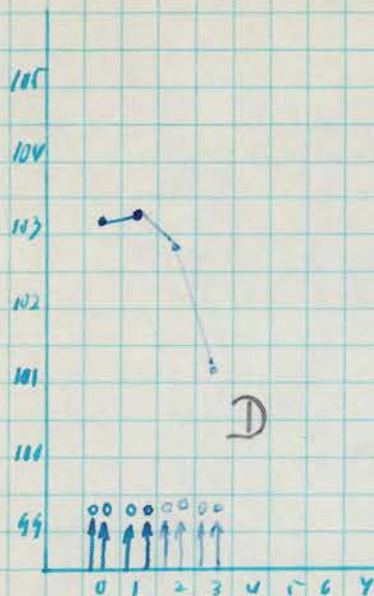
MICROSCOPIC EXAMINATION - Well-fixed and stained

Post mortem change evident Cells in excellent condition - no evidence of neuronal degeneration in spinal cord, medulla or midbrain. But not good enough to judge chromatolysis.

S. N. 13.058-17 TRIAL -

August 3. 48

Rh # 735



August 5. dissection

August 6. ~~dissection~~ - ~~examination~~ - ~~examination~~

Aug. 7 - Found dead at 8 A.M. - still in rigor-mortis

Necropsy - extensive tuberculosis of lungs, spleen and liver. Ziehl-Neelsen - numerous acid fast organisms.

Perfused 1500cc saline - then 10% formalin and 1% glacial acetic

Brain and cord in formalin

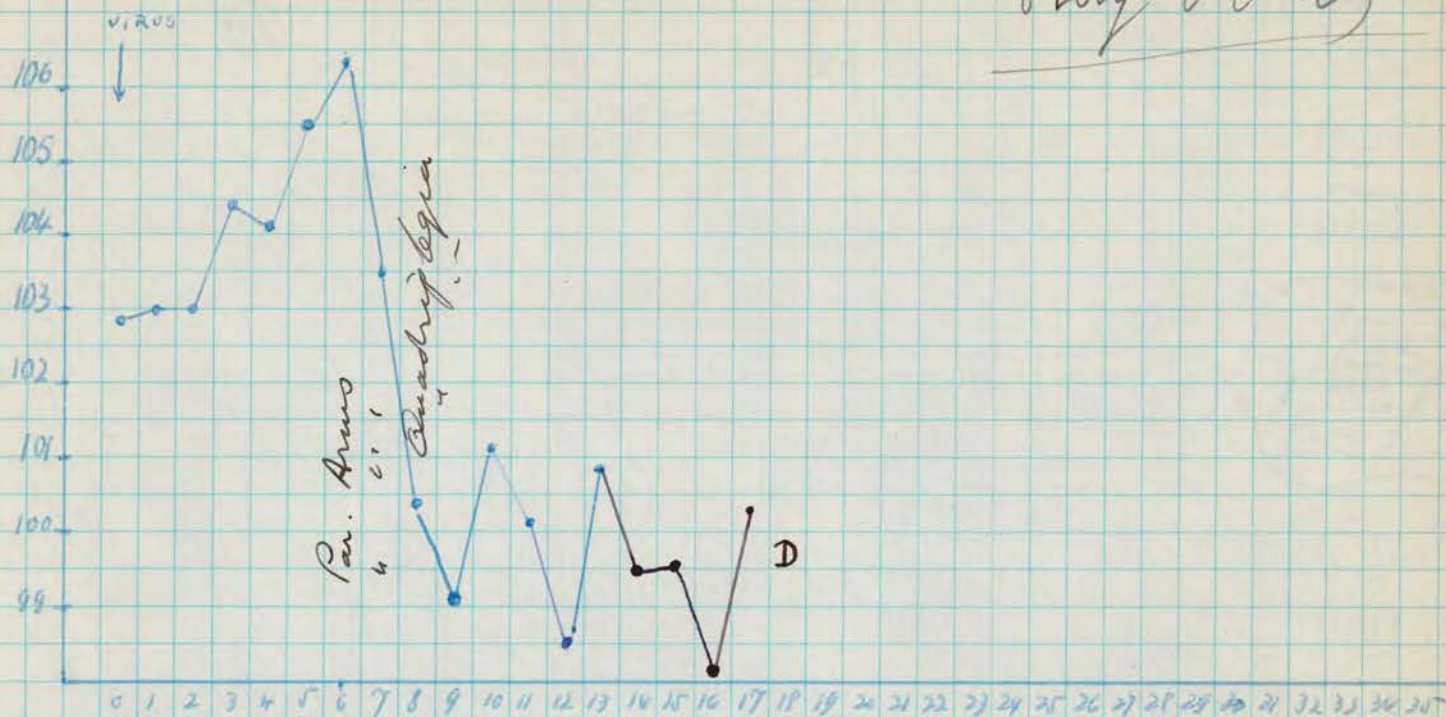
Microscopic Examination of Spinal Cord, Medulla & Midbrain show no changes which cannot be accounted for on basis of post mortem change in large neurons.

August 7th

PLASMALOID 221 J.N. 13058-17. — CONTROL

Rh # 663.X —

only Virus



August 7- VIRUS 1 cc. of "Hofekamp" strain, 1/500, intra-cerebrally through right frontal lobe.

August 13 A.M. Tremor and paralysis of left upper - Does not climb - lower extremities and back muscles OK
P.M. Both upper, paralysis.

August 14 - Both arms paralysis. No cranial nerves.

August 15 - Complete quadriplegia. Back and neck muscles also No cranial nerves paralysed. Tail good.

Aug. 16 - Prostrate

August 17 - A.M. Completely prostrate. Abdominal respiration. Paralysis of intercostals muscles. No cranial nerves paralysed.

August 18 A.M. Same condition but cyanosis and aphonia.

August 19 A.M. Same condition

August 20 A.M. Same condition

P.M. Same condition

August 21 A.M. Same condition

August 22 A.M. Same condition.

August 23 - A.M. - Same condition. -

August 24 - A.M. - Same condition - Very thin. -

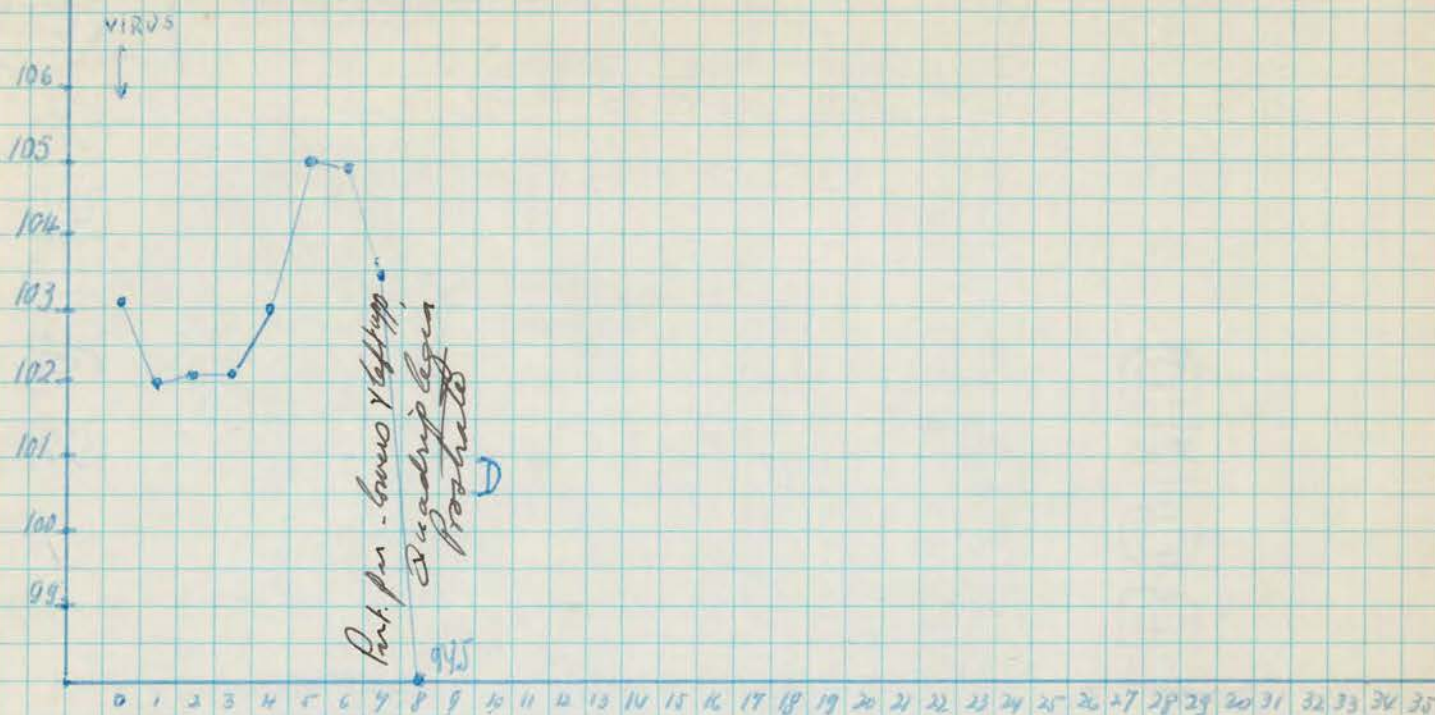
August 25 - A.M. - Dead. -

- No autopsy -

— PIASMAICID ANT S.N. 13058-17 — CONTROL

August 7.

Rh # 664 x. —



August 7 - VIRUS - Same as Rh # 663 x.

August 14 - Does not climb. Partial paralysis of lower extremities and left upper.
Head: tumor and weakness of neck muscles.
No cranial nerves.

August 15 - Quadruplegia - Back and neck also.

Aug. 16 - Prostrate

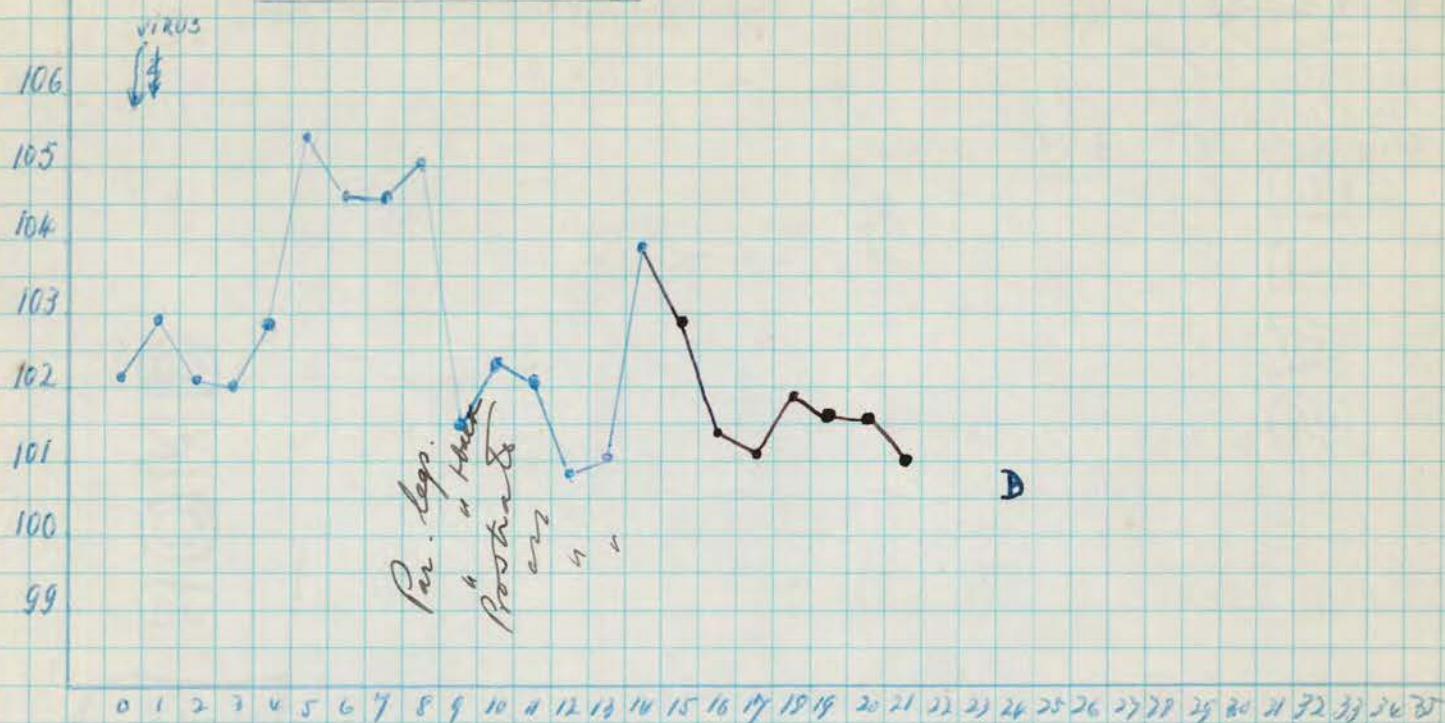
August 17 - A.M. 7³⁰: Dead, rigor mortis -
No autopsy -

August 7-

— PLASMACID cont. J.W. 13058-17 — CONTROL —

Rh # 665 X

Virus Only



August 7- VIRUS - Same as Rh 663 X -

August 14 - Excited.

August 15 - Paralysis lower extremities. Upper strong.

Aug. 16 - Back muscles also involved now - but head & upper extremities OK. Alert - eats

August 17 AM - Lies down on cage. Complete paralysis of both lower extremities. Partial paralysis of left upper. Back also paralysed. No neck paralysed. No cranial nerves.

August 18 A.M. - Same condition.

August 19. A.M. - Same condition.

August 20 A.M. - Marked weakness.

August 21 A.M. - Same condition. - Don't get food.

August 22 A.M. - Same condition.

August 23 A.M. - Same condition.

August 24. A.M. - Same condition.

Lower paralysis
Neck paralysis

August 25 - A.M. - Same condition. -

August 26 - A.M. - Same condition.

August 27 - A.M. - Same condition

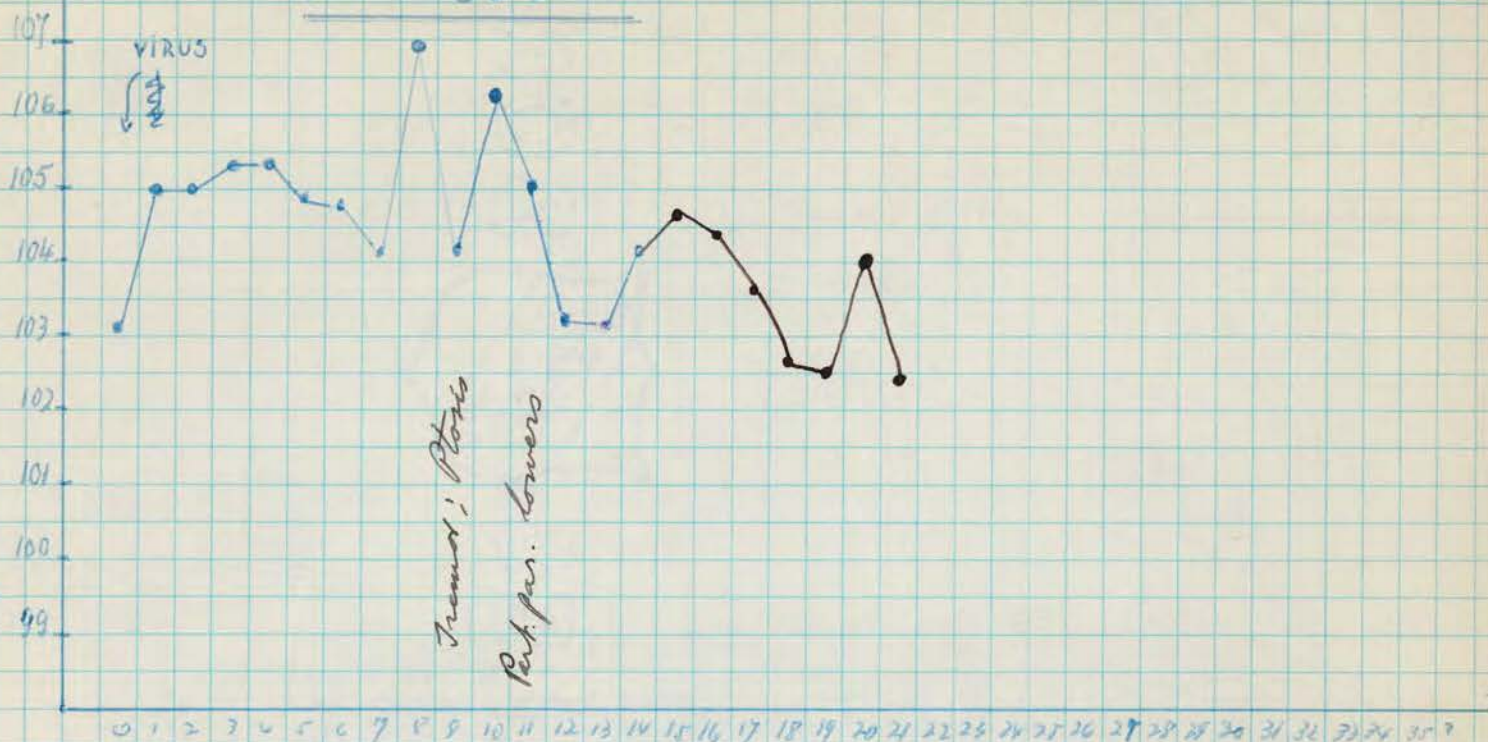
August 28 - A.M. - Same condition

August 31 - A.M. - Dead.

- No autopsy -

August 7. -

Rh # 666 x -



August 7 - VIRUS - Same as Rh 663 x -

August 8 - Very excited

" 9 - Very excited

" 11 - Excited

" 12 - Disoriented. Excited.

August 15 - Can't climb - No paralysis

Aug. 16 - gross tremor; holds head to left side
Some ptosis of upper eyelids. No
paralysis.

August 17 - Same condition -

August 18 - A.M. Marked weakness on both upper -

P.M. - Partial par. of lower extremities + tremors as above

August 19 - A.M. Partial paralysis lower extremities and weak
neck both upper - Cannot climb -

P.M. Same condition.

August 20 - A.M. Same condition.

August 21 - A.M. Same condition.

August 22 - A.M. Same condition.

August 23 - A.M. Back also paralyzed.

August 24 - A.M. Same condition.

August 25 - A.M. - Same condition.

August 26 - A.M. - Same condition. -

August 27 - A.M. - Same condition. -

August 28 - A.M. - Same condition. -

September 28 - A.M. - Dead.

No autopsy.