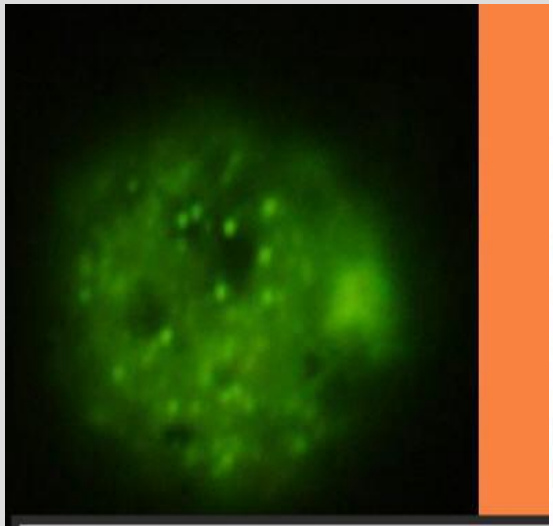
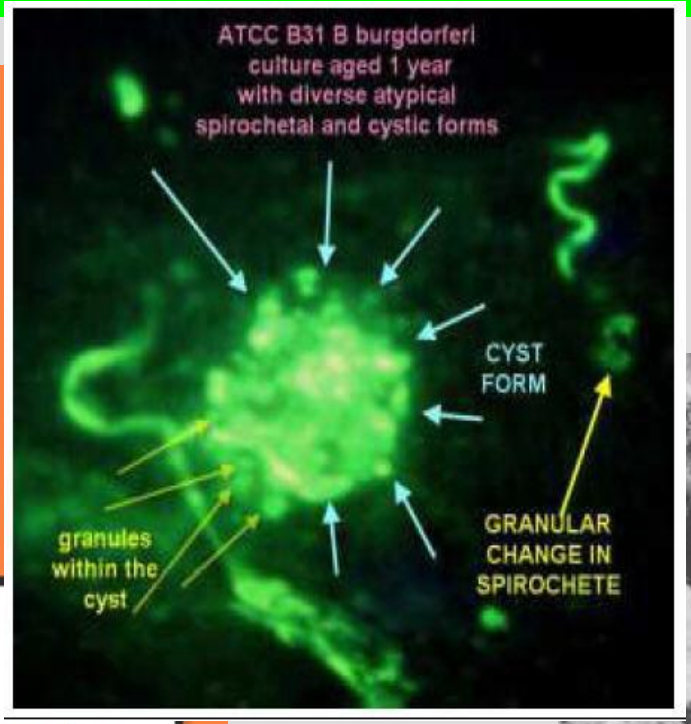
Dementia caused by Borrelia infection of the Central Nervous System

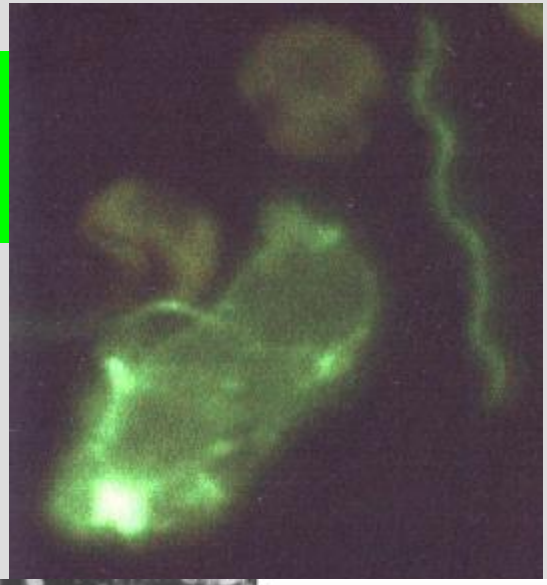
Alan B. MacDonald, M.D.
Staff Pathologist
St Catherine of Siena Medical Center
Smithtown, New York

Columbia University LDA National Scientific Meeting
October 20,2006 , Philadelphia Pennsylvania

Walking on Thin Ice



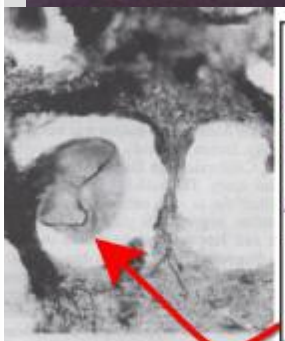




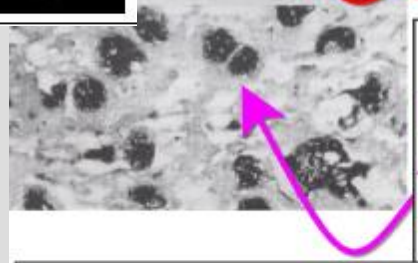
DLB

Diffuse Lewy Body Disease

Cystic Borrelia Form



Cystic Borrelia in Alzheimer Autopsy Brain 1987



Plaques Alzheimer Disease

Concurrent Neocortical Borreliosis and Alzheimer's Disease 1988 Ann. New York Acad Sci, vol 539 p. 468-470

Spirochetal

Hypotheses ^ About Dementia

- Noguchi […hypothesis testing]
  --1913
- MacDonald[..hypothesis….]
  ---------1985
- Miklossy[hypothesis …]
  ----------1992

Brain “Fog” as a Metaphor

Clouded Mentation

Apraxia of Thought

Senility

“Old Timer”

Apraxia…

Loss of ability to carry out purposeful movements, in the absence of paralysis, .. Especially inability to make proper use of an object…

Perseveration

- "Broken Record" Type –

  Perseveration in Dementias

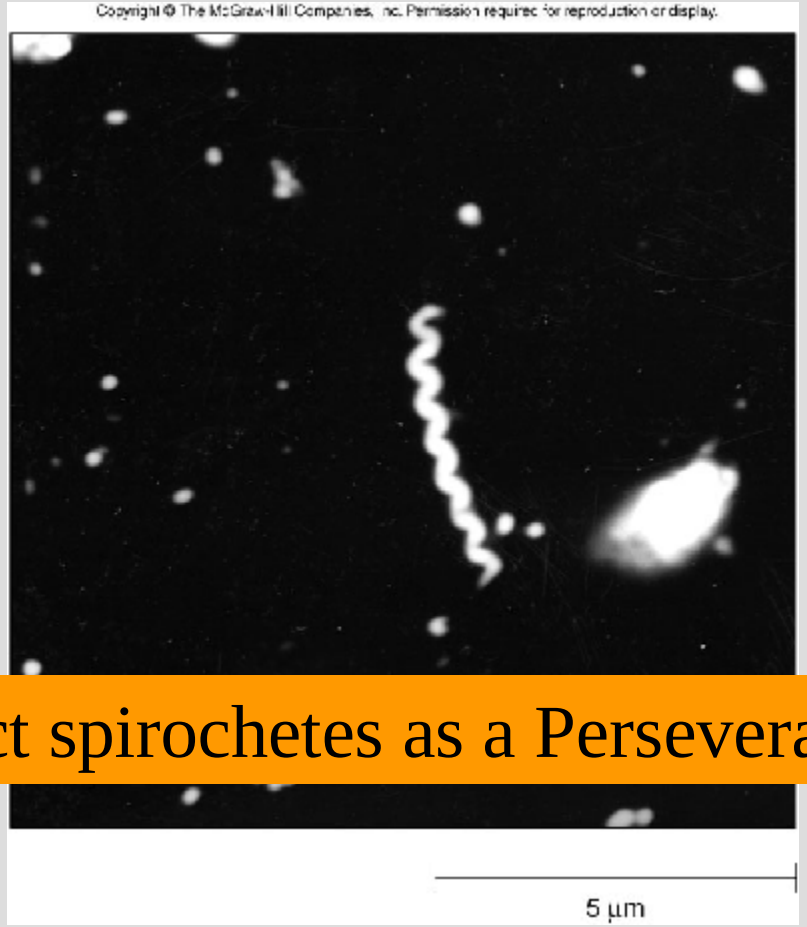
  Repetitions without Cognizance

- ***Scientific Perseverations as a Motif***

  Rigid and unweilding

  "Herr Professor Types"

Problem of the Perfect spirochetes



Perfect spirochetes as a Perseveration “motif”

Anecdotes in Medicine

Un - Scientific

Un - Informative

Un - trustworthy

Where is it Written ??

Did you “Get it Past an Editor”?

Overview

Inside of the Nerve

Infections by Borrelia

Cystic Borrelia

(Rationale for Chronic Disease)

Evidence for ***Neural Invasion***

Trans-synaptic transmission

of Infection

Neural Circuit Infections –

Progressions in Nerve Disease

Time Capsules

*****

1. **Dementia – What makes it Alzheimer's**
2. **Plaques - of Alzheimer's**
3. **Tangles - of Alzheimer's**
4. **GVB - of Alzheimer's**
5. **DNA in the GVB's**
6. **DNA in Plaques**
7. SSPE model – *Tangles from Viral Infection*
8. Borrelia to Tangles – *Pathway inside the Neuron*
9. Trans-Synaptic transmission of Infections
10. Trans-Synaptic Neuroborreliosis
11. Braak Stages- *of Alzheimer's Disease*
12. Redefined Braak Stages -
13. Dr Miklossy – *Landmark observations in Alzheimer's*
14. Dr Noguchi – *Landmark observations in General Paresis*

Time Capsules - Continued

*****

15. ***Negative Reviews*** – *Borrelia and Alzheimer's*

16. **Rebuttals** - *from Miklossy and MacDonald*

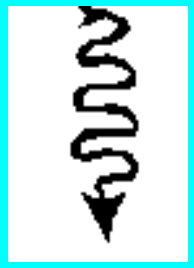
Antibodies – Are they Necessary???

…..Evidence for New Discoveries?

{IDSA version of Truth ??}

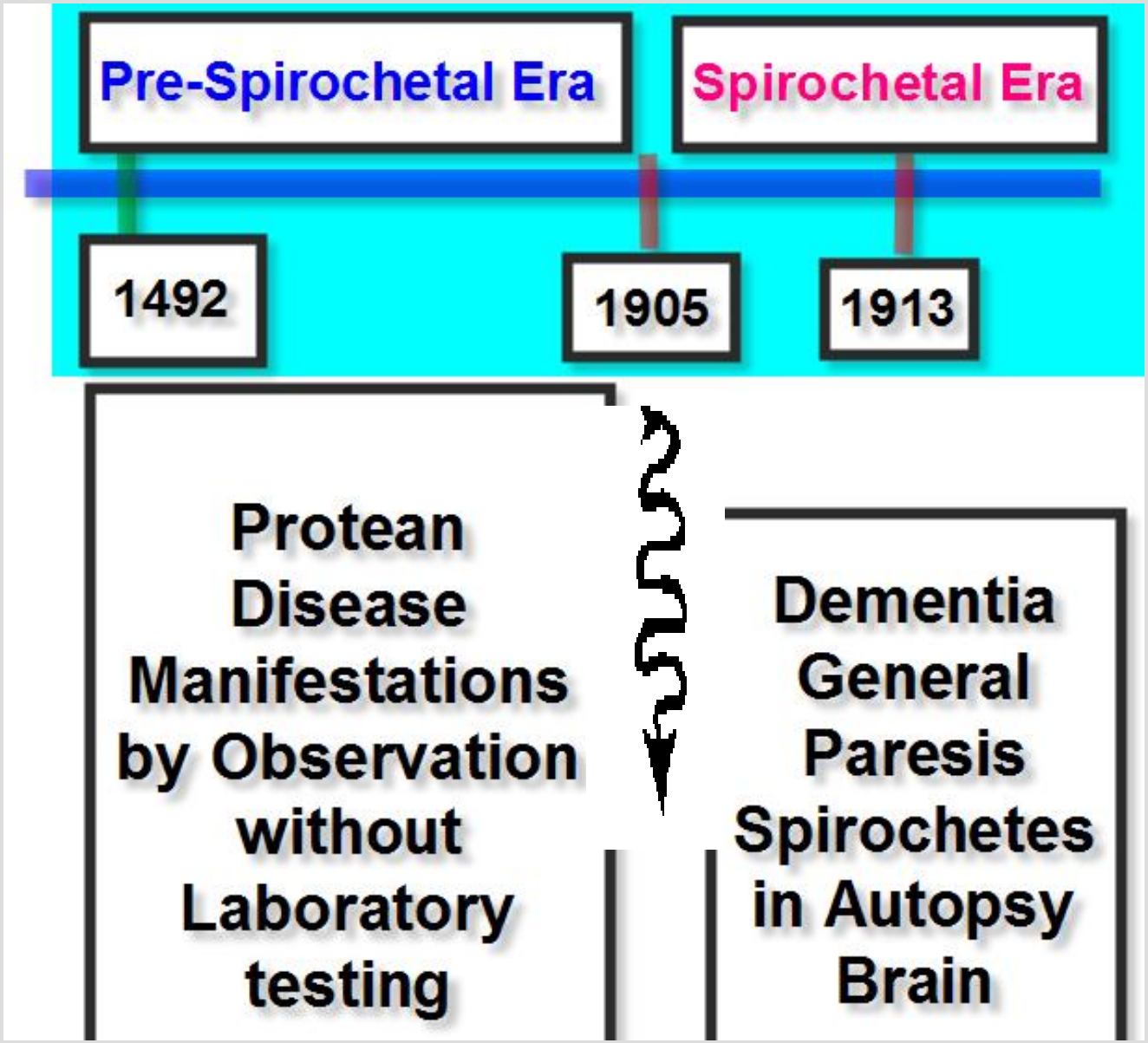
Pre spirochetal times

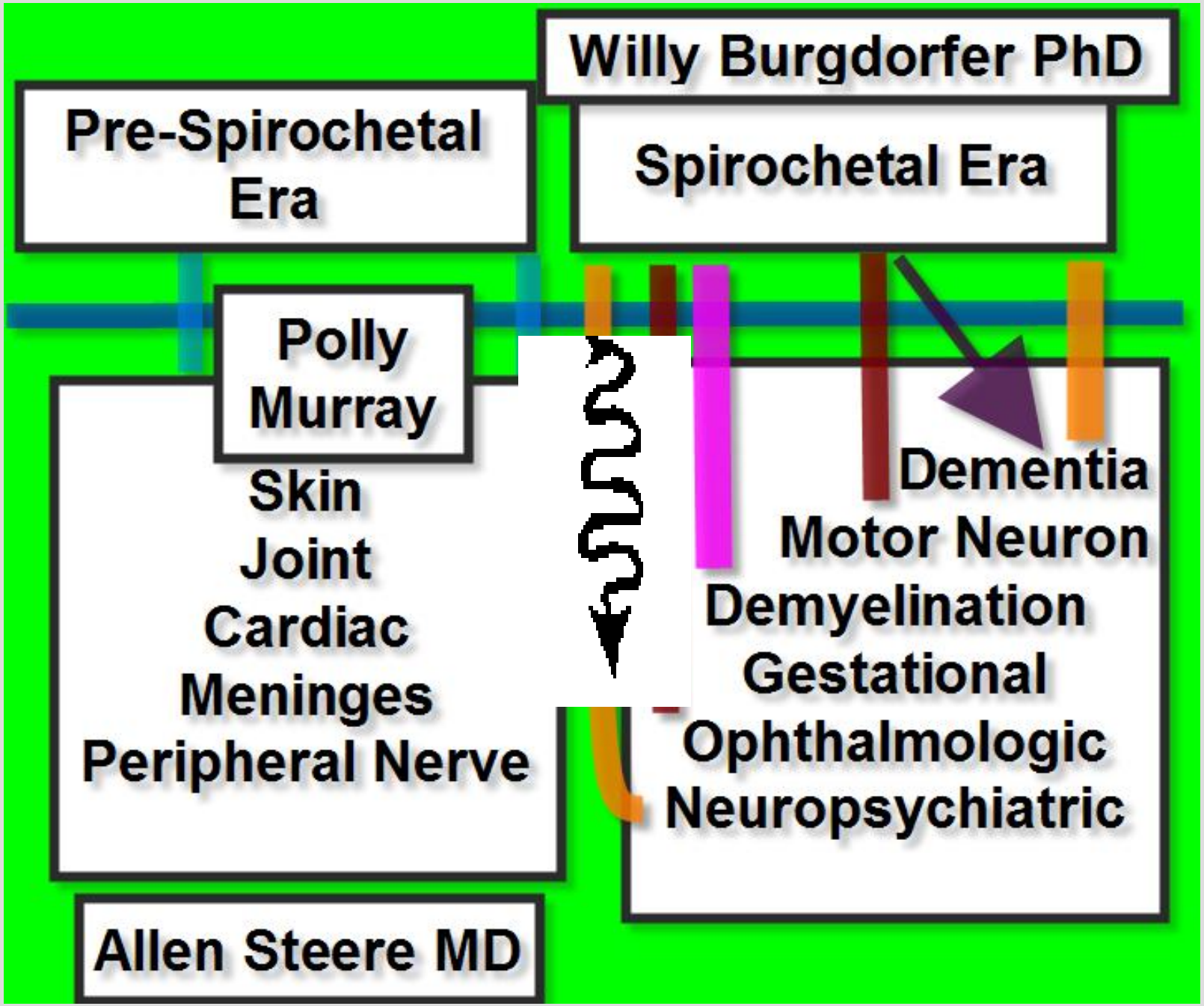
Knowledge Acquired before the Etiologic Agent



was in the Textbook

Post spirochetal times


Pre-Spirochetal Era
Spirochetal Era
1492
1905
1913
Protean Disease Manifestations by Observation without Laboratory testing
Dementia General Paresis Spirochetes in Autopsy Brain


Willy Burgdorfer PhD
Pre-Spirochetal Era
Spirochetal Era
Polly Murray
Skin
Joint
Cardiac
Meninges
Peripheral Nerve
Dementia
Motor Neuron
Demyelination
Gestational
Ophthalmologic
Neuropsychiatric
Allen Steere MD

Borrelia and Dementia – Previous Lecture

Topics from Miklossy 2004 LDA Lecture

And MacDonald 2005 Ilads Lecture

Cultures Alzheimer Brain tissue --------POSITIVE

Alzheimer Brain tissue – ----------**Positive for Borrelia**

Spinal Fluid –---------- **Positive for Borrelia Antibodies**

DNA Hybridization – **Positive signals in Specific Brain regions**

New Topics in 2006 - Bridges to Pathogenesis of

Alzheimer's Neuroborreliosis

Tangles of Alzheimer's Disease – ***Infection Connections***

Plaques of Alzheimer's disease –*DNA Probes Borrelia Specific*

Mutations in Alzheimer's Disease- ***Transfection Mechanisms***

Spinal Fluid Testing in Alzheimer's Disease –

Borrelia DNA detection methods

Braak Stages of Alzheimer's Disease-

TransSynaptic spread of Infection in Neural Networks

Dementia – What makes it Alzheimer's

Under the microscope: ***The Big Three***

Many **Plaques** --- (Silver +, Amyloid , Tau protein +)

Many **Tangles** --- (Silver +, _____, Tau protein +)

GVB Granules ---- (Silver +, _____, _____)

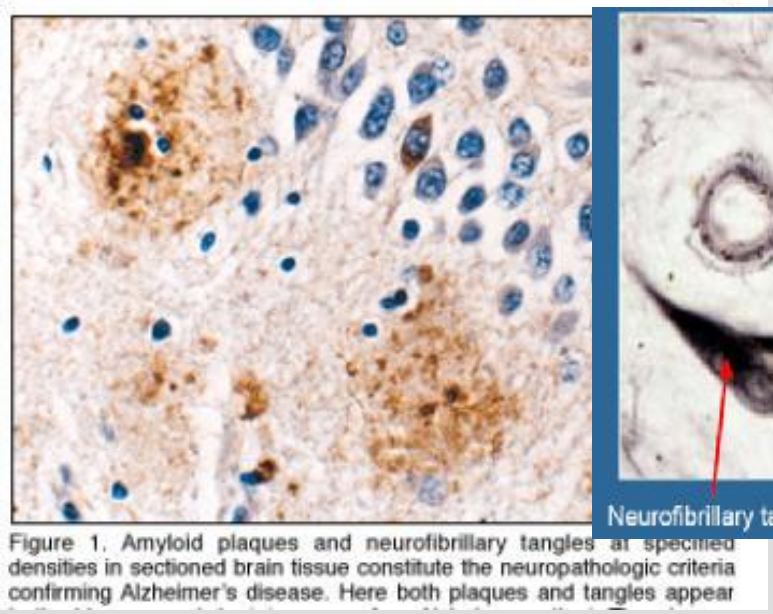
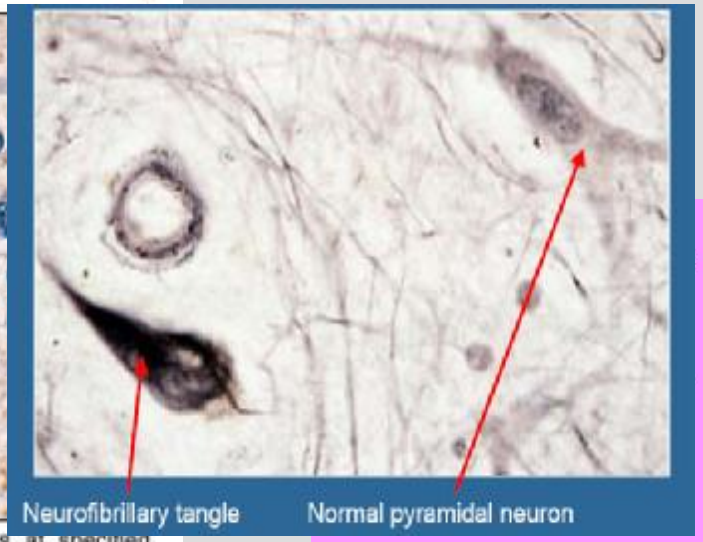
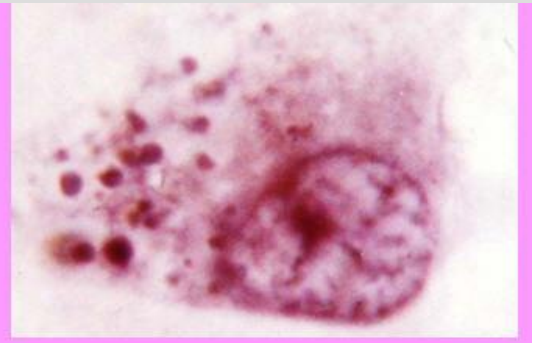
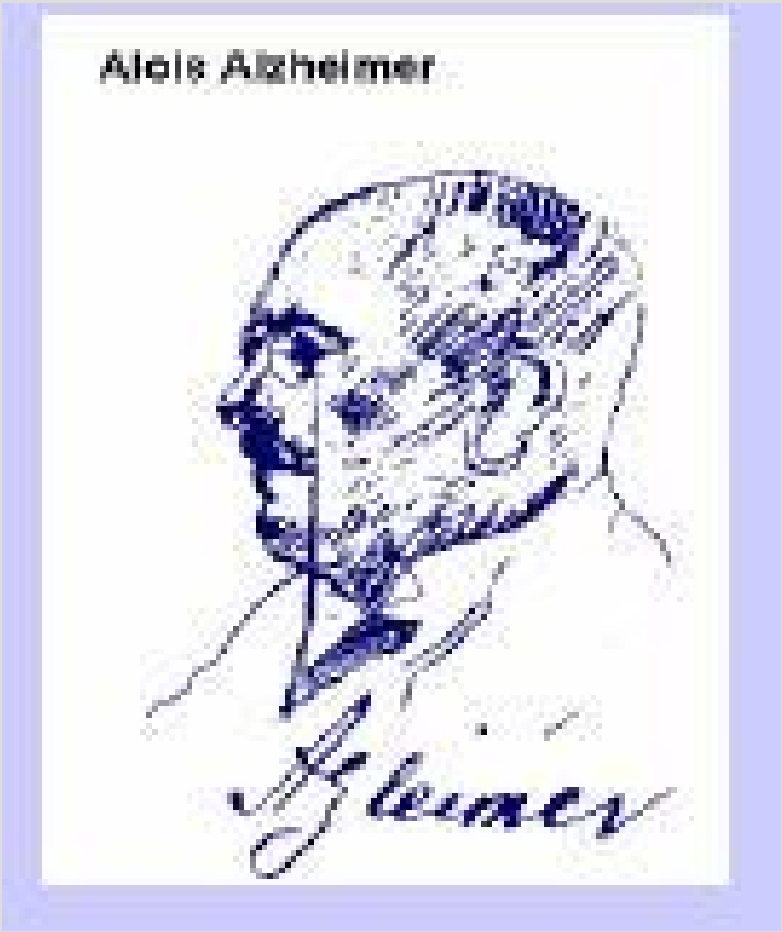


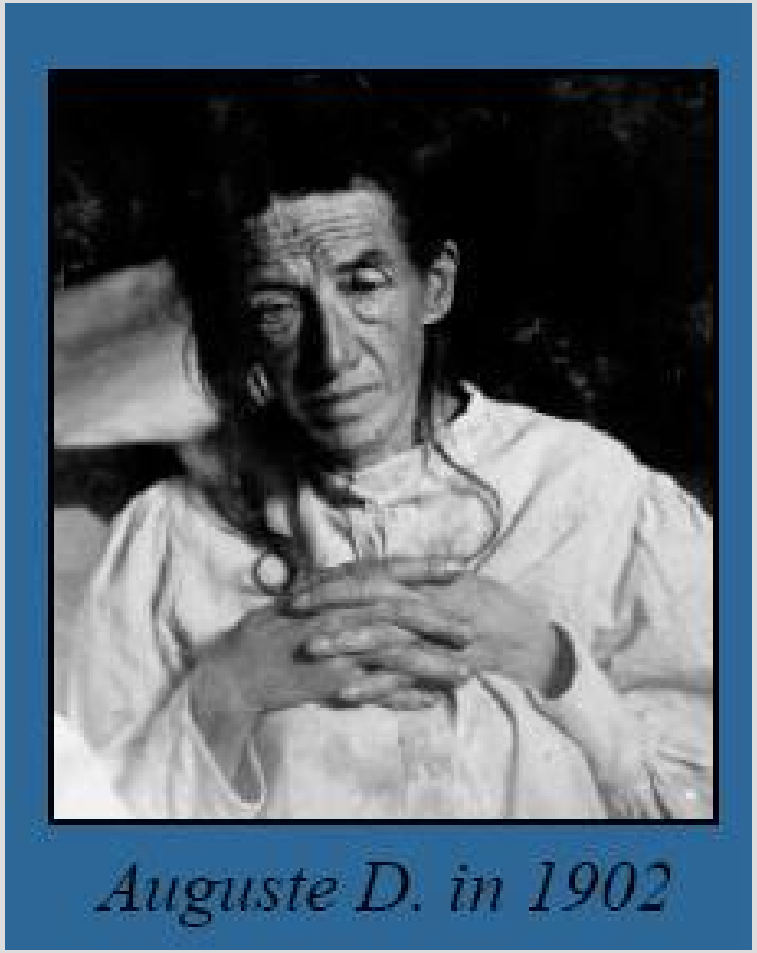
Figure 1. Amyloid plaques and neurofibrillary tangles at specified densities in sectioned brain tissue constitute the neuropathologic criteria confirming Alzheimer's disease. Here both plaques and tangles appear





Granules vary in size ---little to big

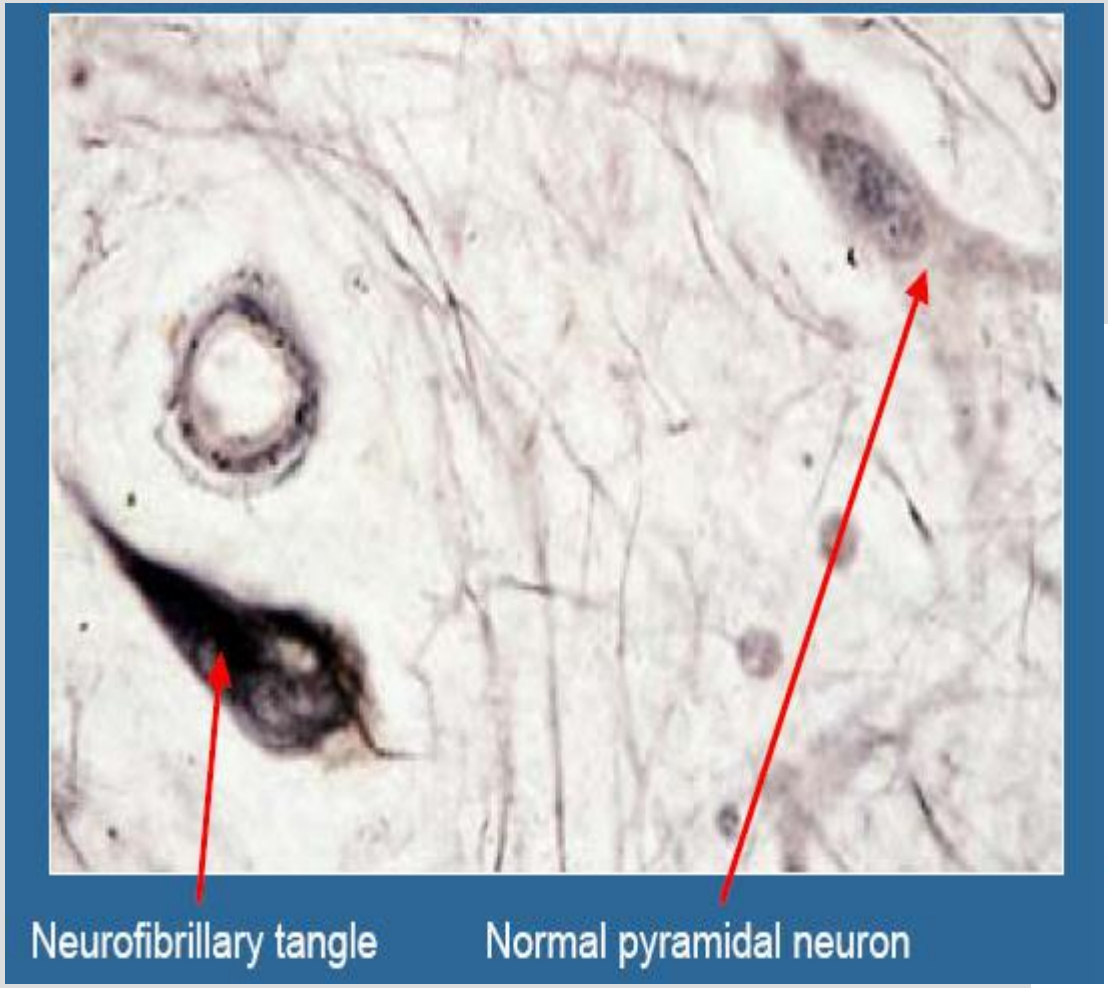


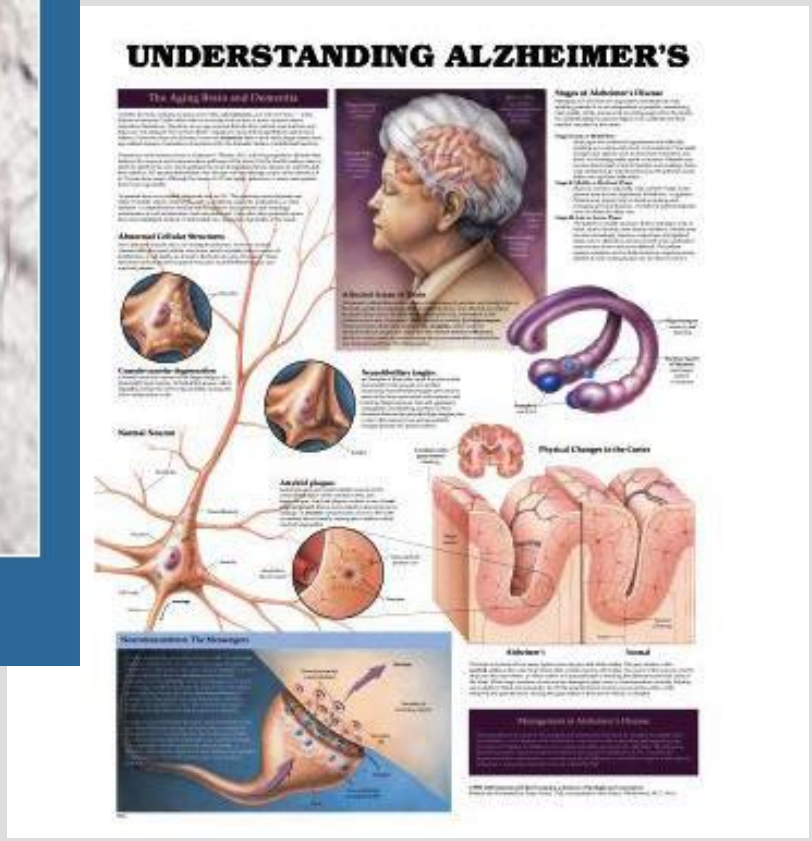


Auguste D. in 1902

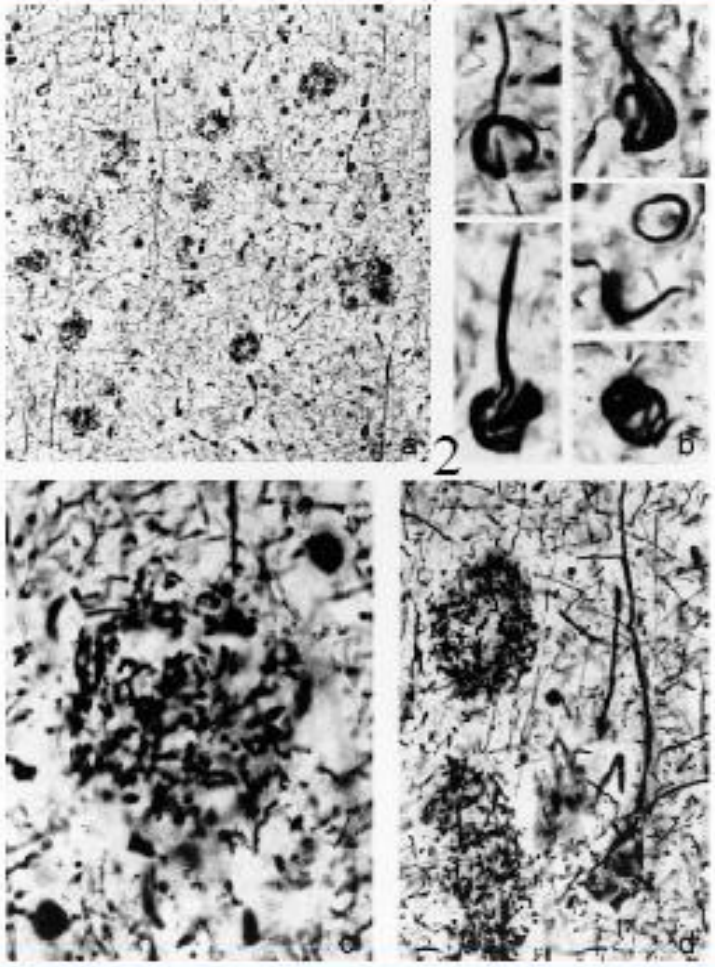
An Anecdotal Case Report – Just one !!

Dementia – What makes it Alzheimer's



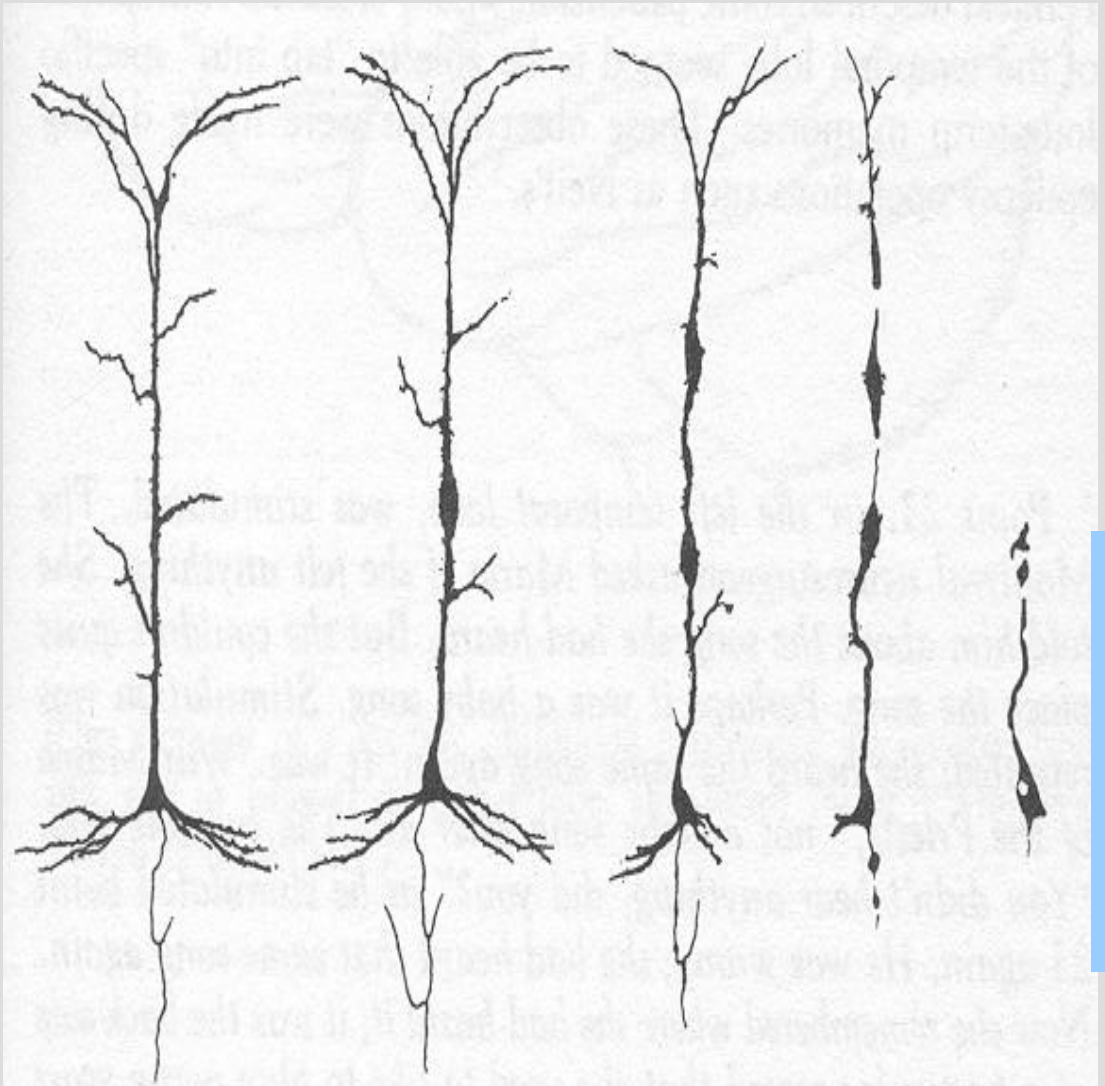


Über eine eigenartige Erkrankung der Hirnrinde A. Alzheimer (1907)



Allg. Zeitschrift Psychiatr. *64*: 146-148

Dementia – What makes it Alzheimer's



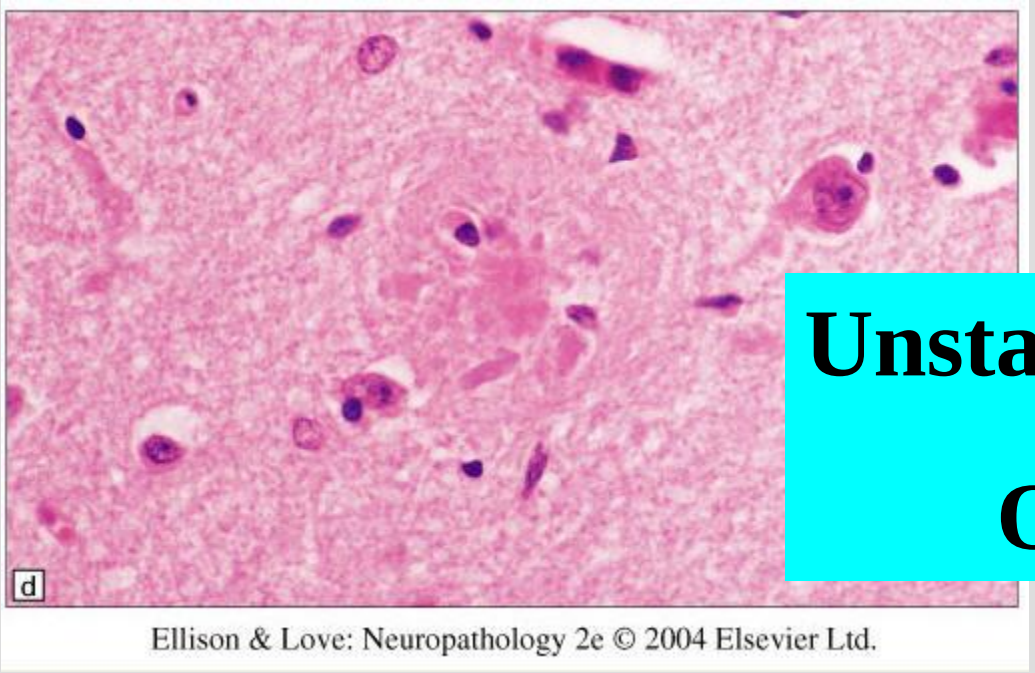
Sequence of dendritic tree changes in senile dementia (from Scheibel and Scheibel 1977).

Synapses Are Lost

Nerve Structure Lost

Chemistry Corrupted

Sparkle - Dimmed



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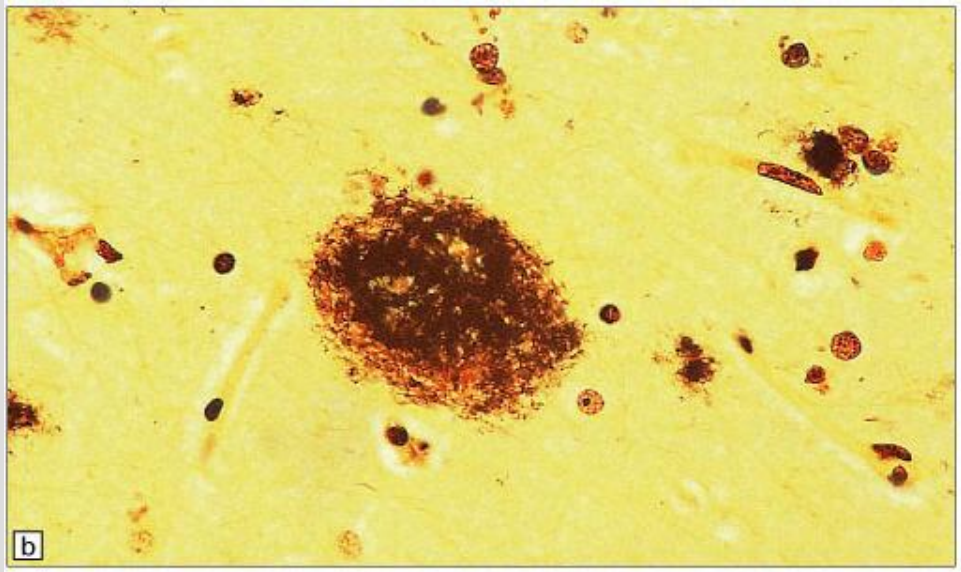
Unstained Plaques are Overlooked

Plaques

First Requirement for Alzheimer's



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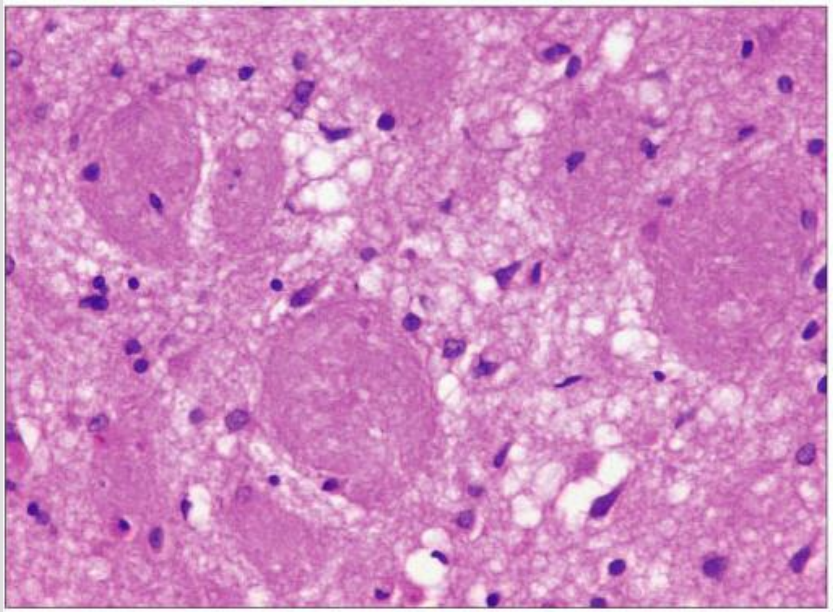
Plaques



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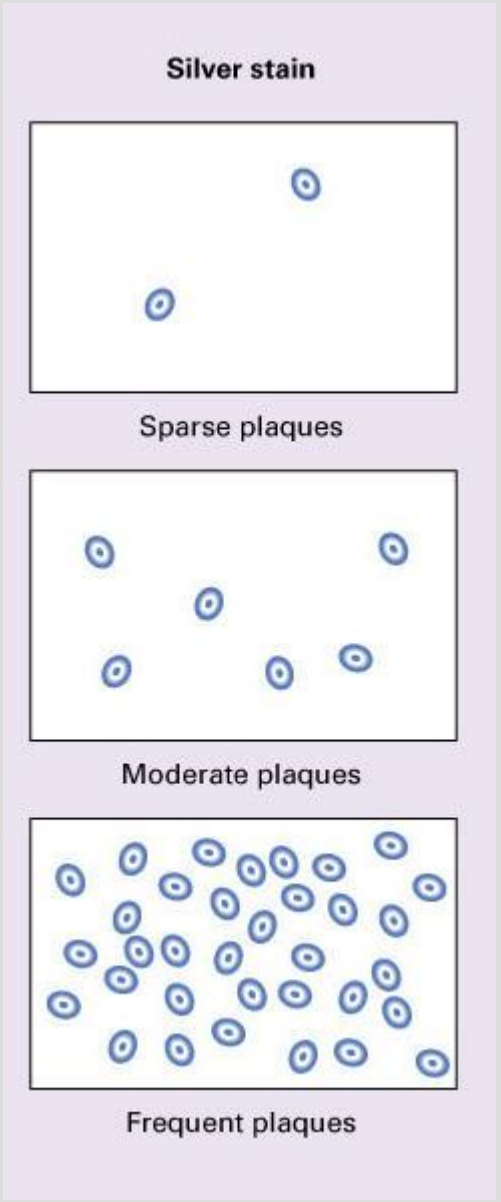
“Amyloid Free”

Plaques of the

Cotton Wool type



Density

Of

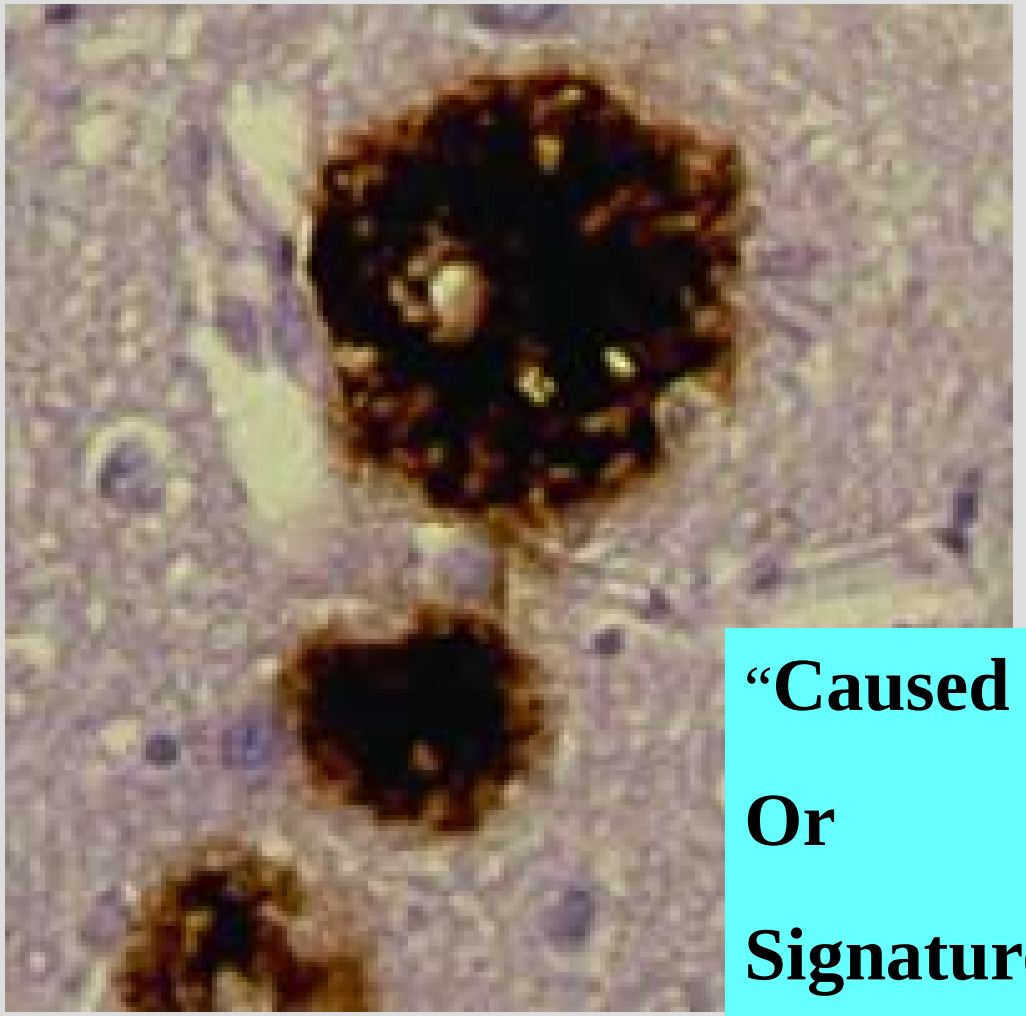
Plaques

And

Loss of

Brain

Weight



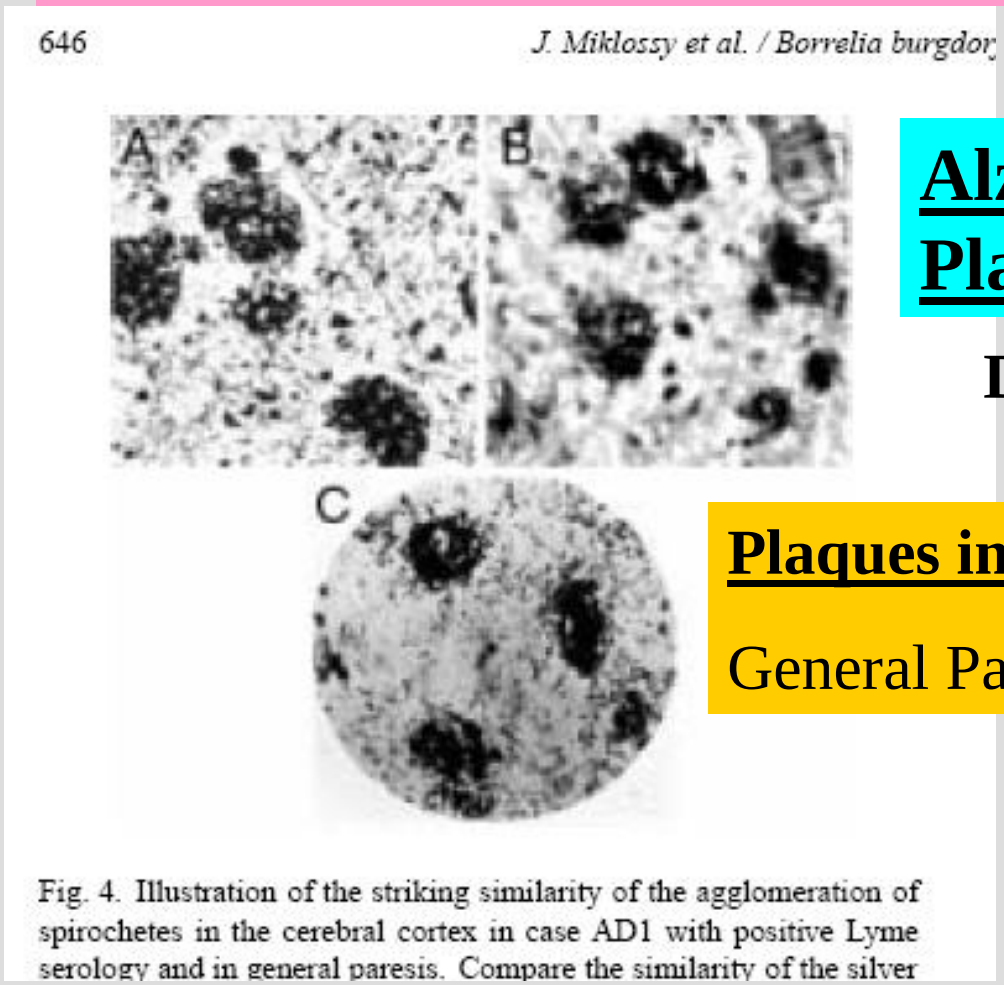
Plaques

“Caused By Amyloid” ???

Or

Signatures of a Microbial Pathogen??

A Tale of Two Plaques



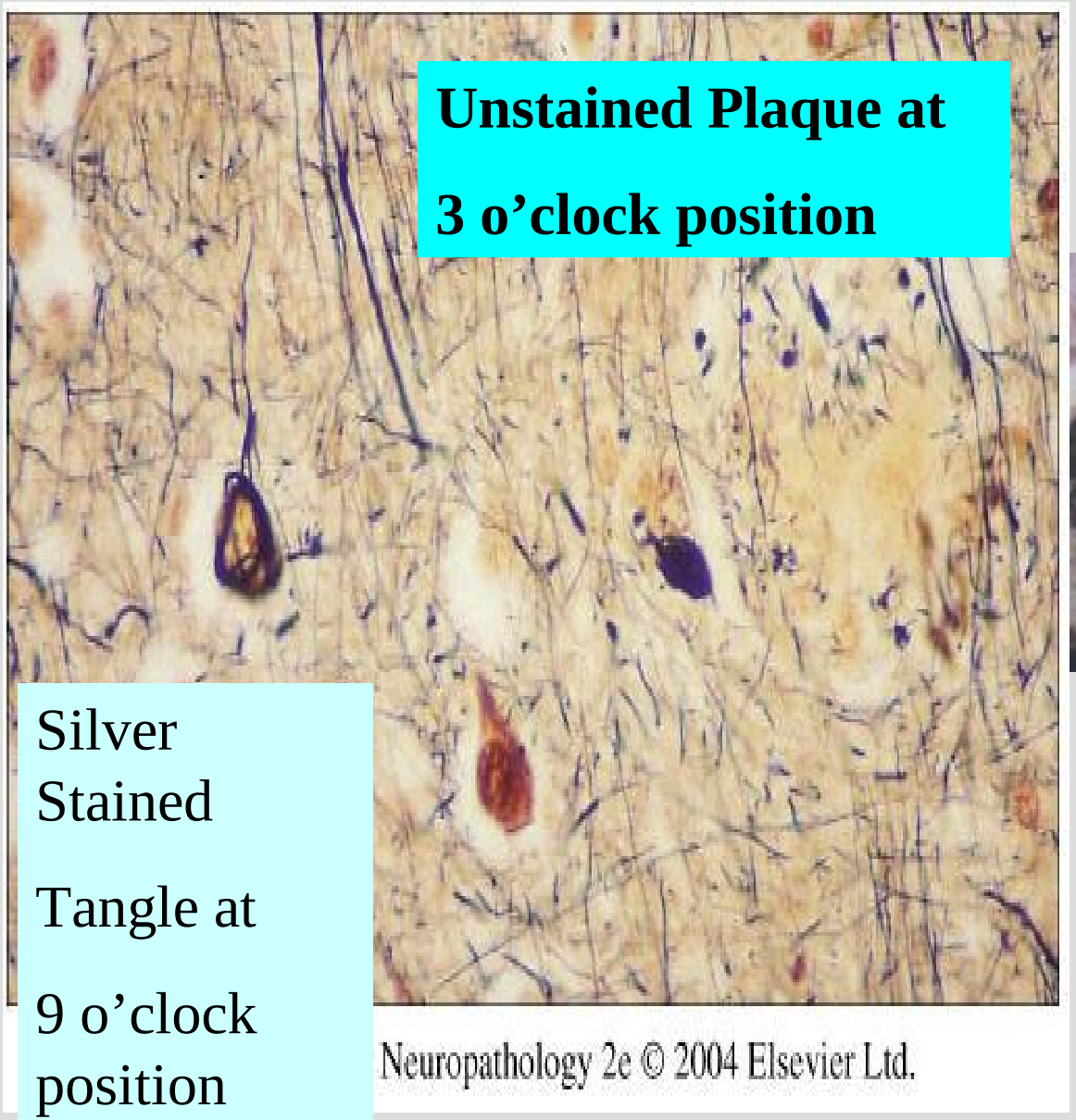
Alzheimer's Disease - Plaques

Dr Judith Miklossy

Plaques in Tertiary Neurosyphilis

General Paresis Brain at Autopsy 1929

Tangles
Second Requirement



Silver Stained

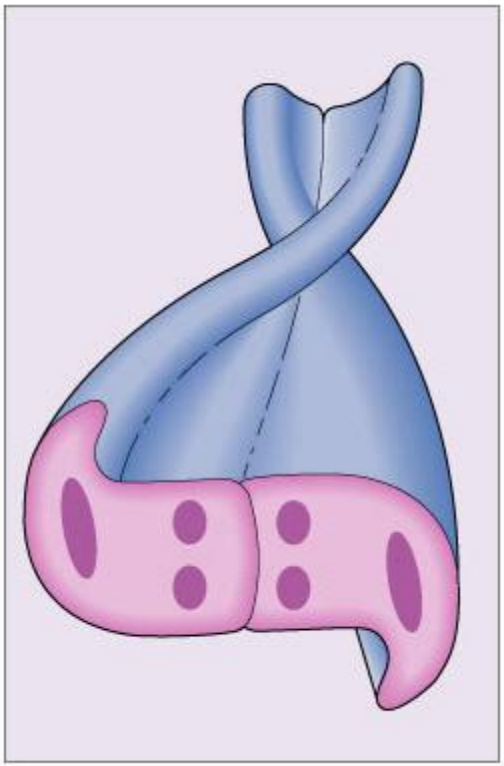
Tangle at

9 o'clock position

Silver Stained Plaques

And Silver stained

Tangles



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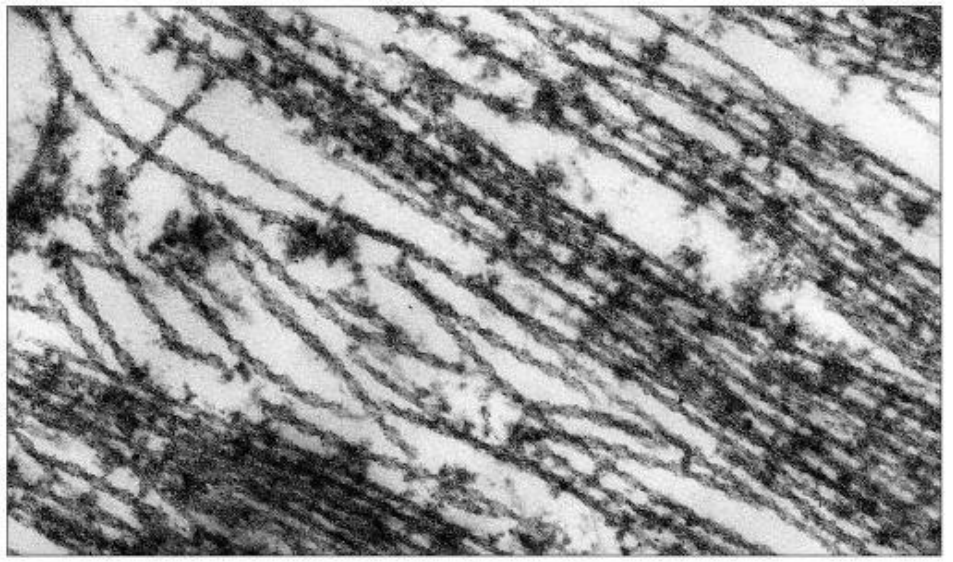
Tangles



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Dr Kidd

Discovers that

Tangles are Not “corpses” of

Previous Microtubules

GVB Third Requirement for Alzheimer's

GVB are

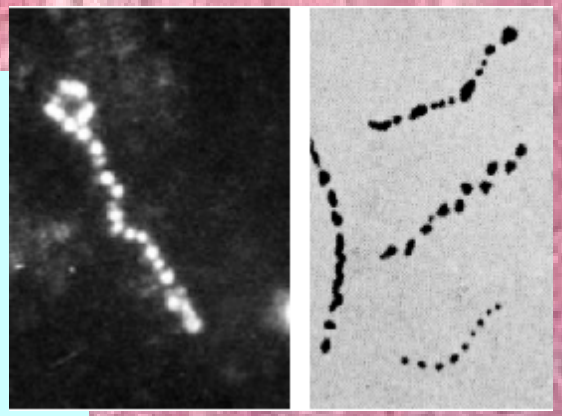
"Dots" inside of

"Bubbles"

Which are

Inside of

Diseased Nerve cells



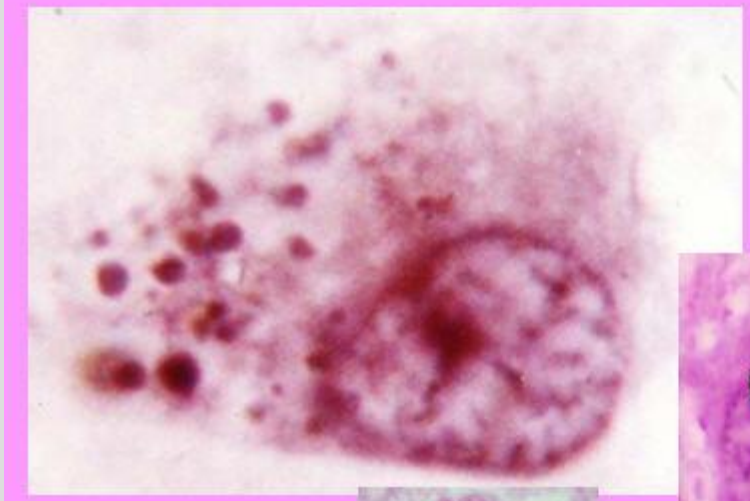
Hypothesis: GVB in Alzheimer's

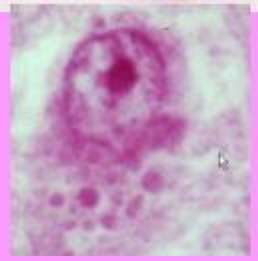
Are the "signature" of

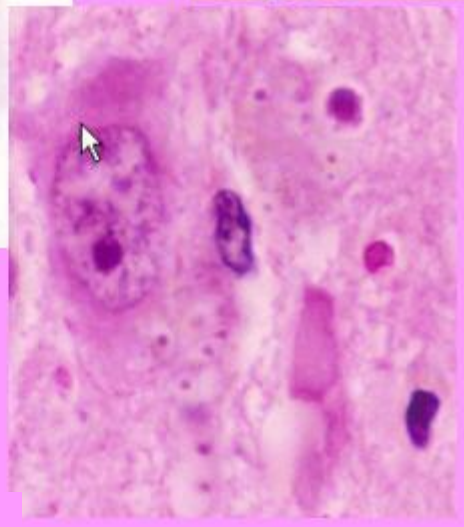
Granular Spirochetes inside

Nerve cells

GVB

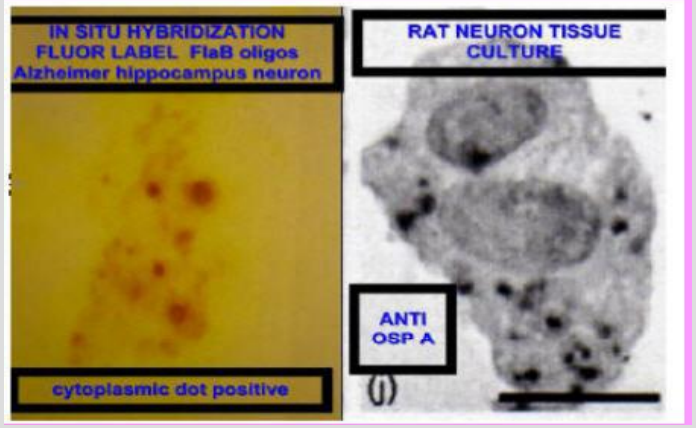




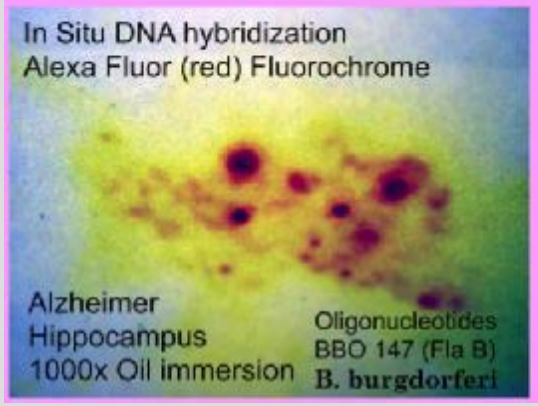


Miklossy
Rat nerve cell
H5332 monoclonal +

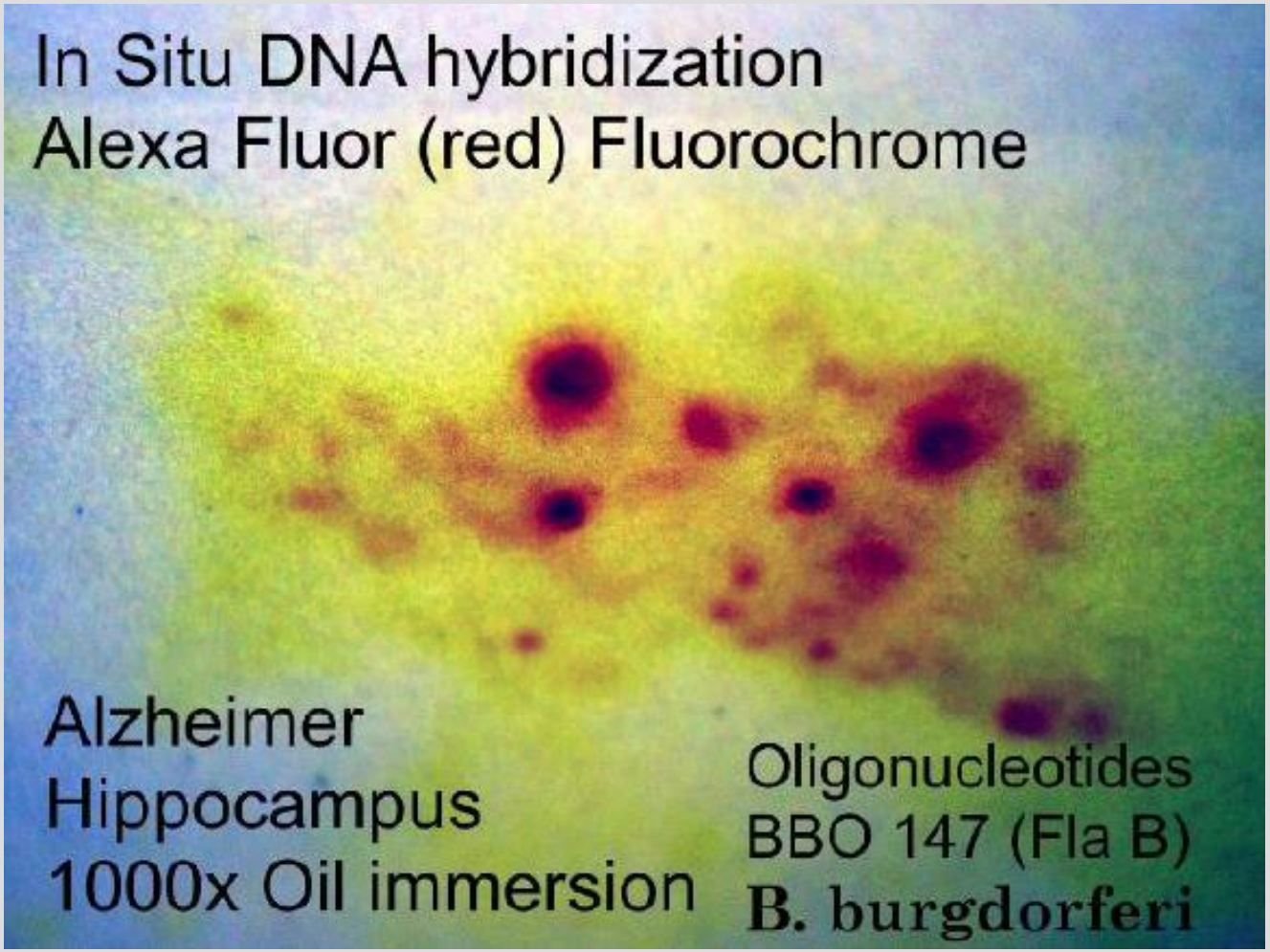
In Situ Dna and Rat Tissue culture



MacDonald
human Alzheimer In situ DNA



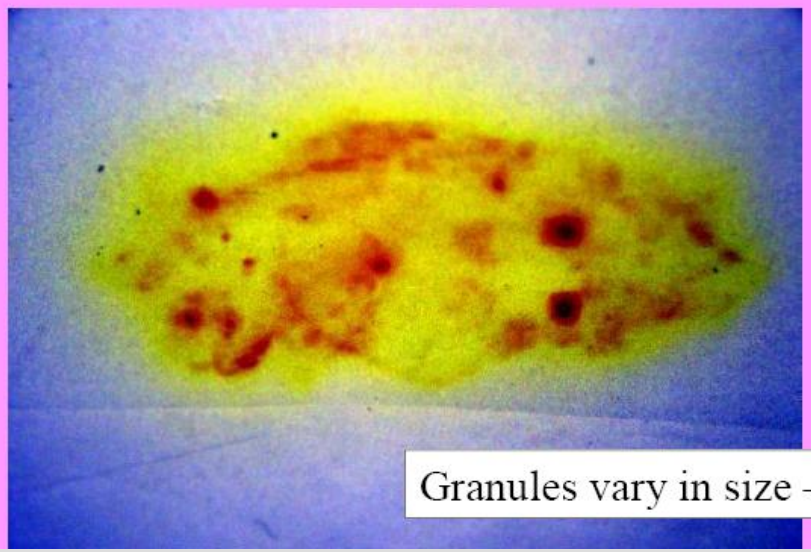
DNA in GVB


In Situ DNA hybridization
Alexa Fluor (red) Fluorochrome
Alzheimer
Hippocampus
1000x Oil immersion
Oligonucleotides
BBO 147 (Fla B)
B. burgdorferi

DNA

in GVB

Human Alzheimer
In situ DNA hybridization for
Borrelia burgdorferi DNA

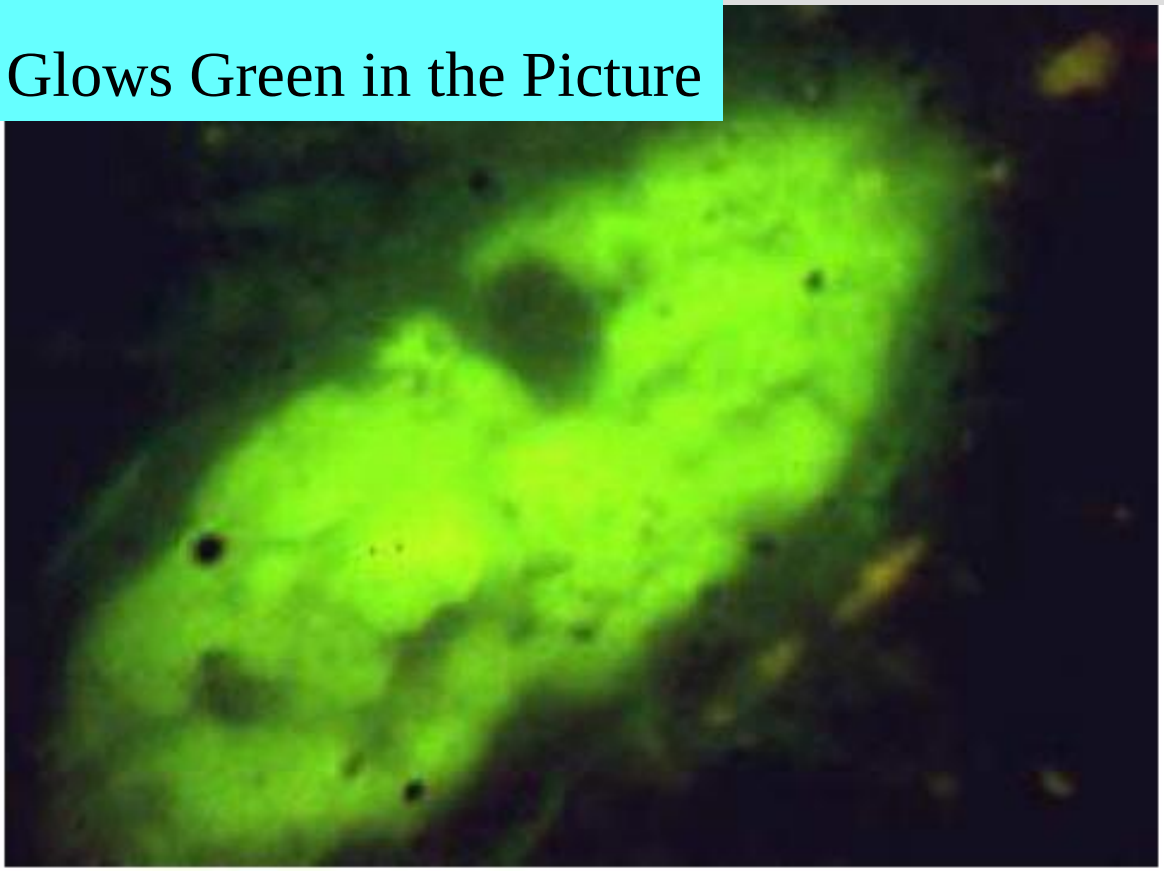


Granules vary in size – from little to big

DNA in Plaques

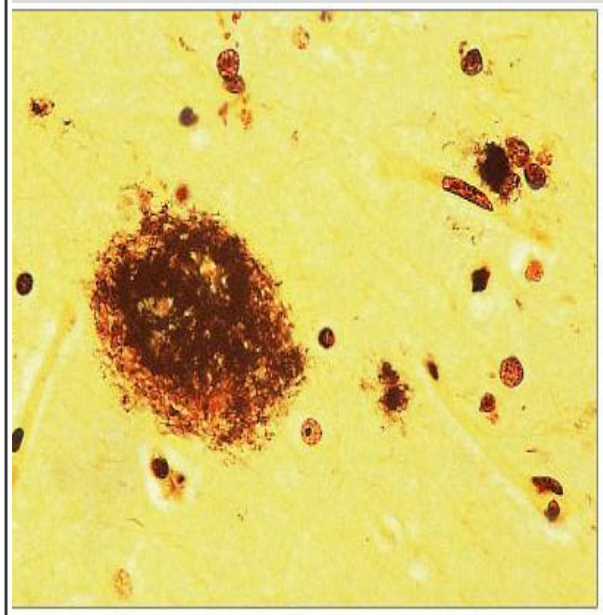
Only Borrelia DNA

Glows Green in the Picture



Borrelia burgdorferi **Flagellin DNA , In situ hybridization, Large Plaque**

1000x original magnification



DNA

Only Borrelia DNA

Glows Green

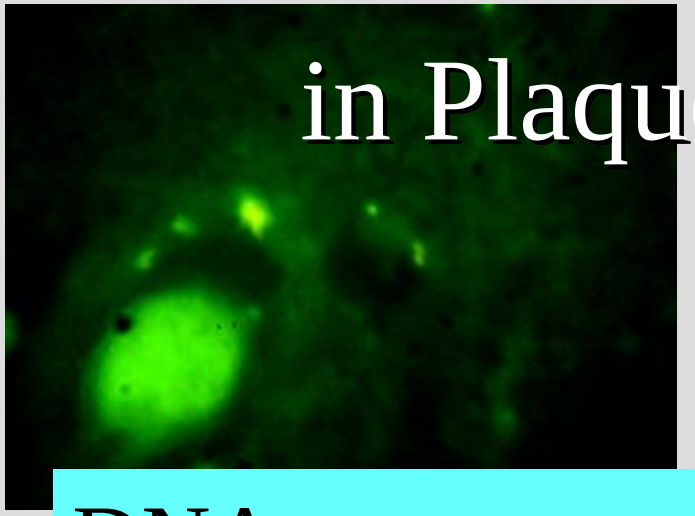
In the picture

Plaques

Borrelia burgdorferi **flagellin DNA in situ DNA hybridization, Alzheimer hippocampus 1000x magnification.**

DNA

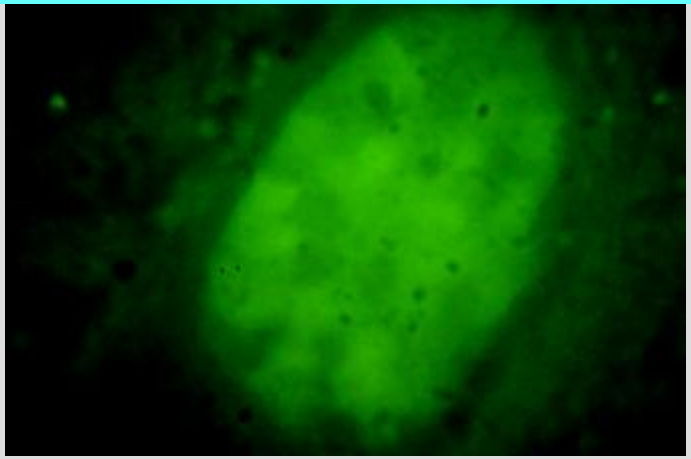
in Plaques



MacDonald 1987
Cyst form H9724 +
Alzheimer Brain

A “water balloon” containing Granules

DNA Hybridization



Monoclonal Antibody for

The Flagellin protein of Borrelia

Developed by Dr Alan Barbour

Perfect Model for Tangles

Based on Inside of the Nerve Infection

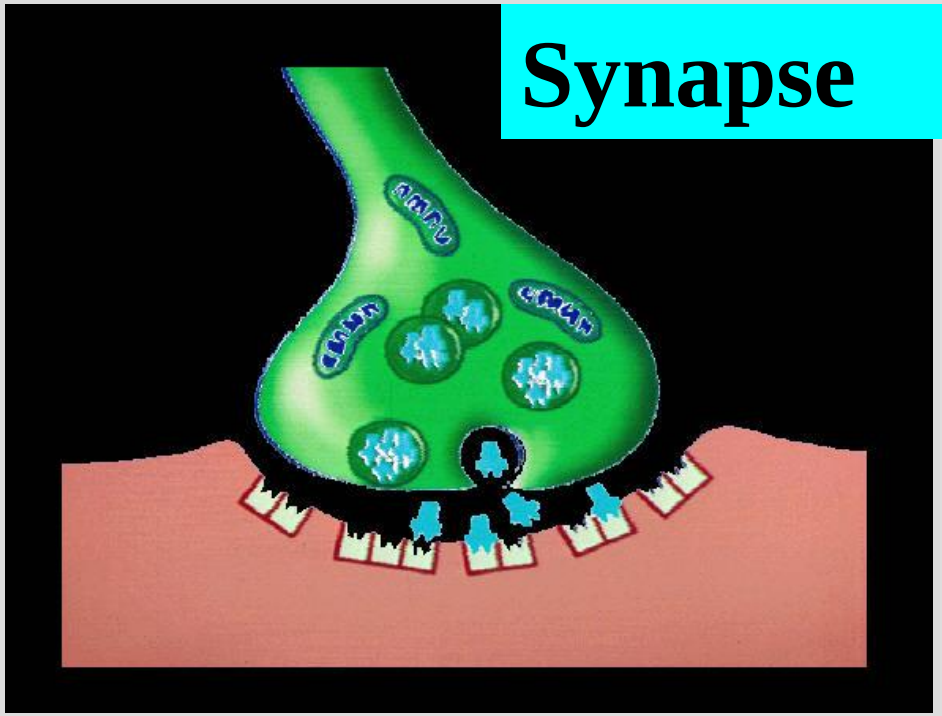
In Children

SSPE

Model

The distribution of Alzheimer's neurofibrillary tangles and gliosis in chronic subacute sclerosing panencephalitis

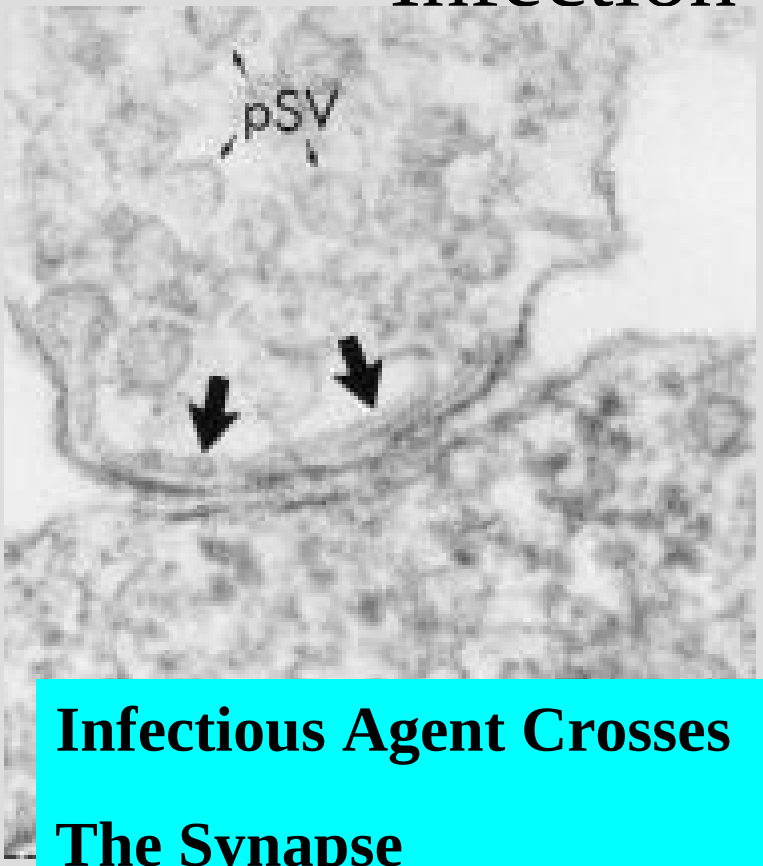
Journal	Acta Neuropathologica
Publisher	Springer Berlin / Heidelberg
ISSN	0001-6322 (Print) 1432-0533 (Online)
Subject	Medicine
Issue	Volume 80, Number 3 / July, 1990



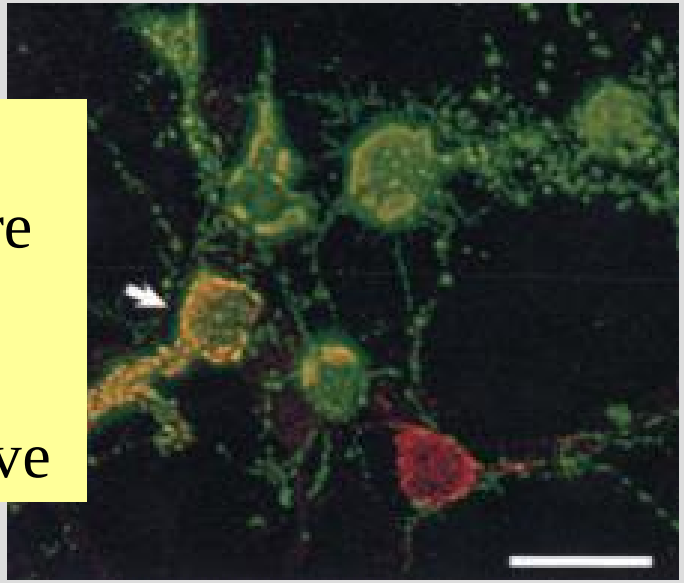
Synapse

SSPE Model

Tangles from Infection

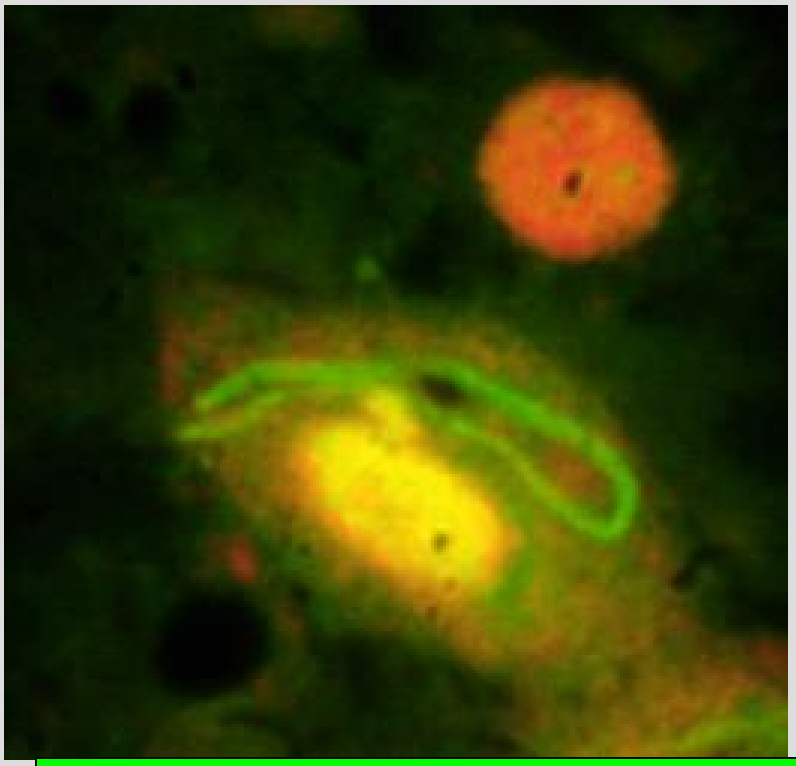


Infectious Agent Crosses The Synapse



Golden particles are Viruses Inside Nerve

Borrelia to Tangles

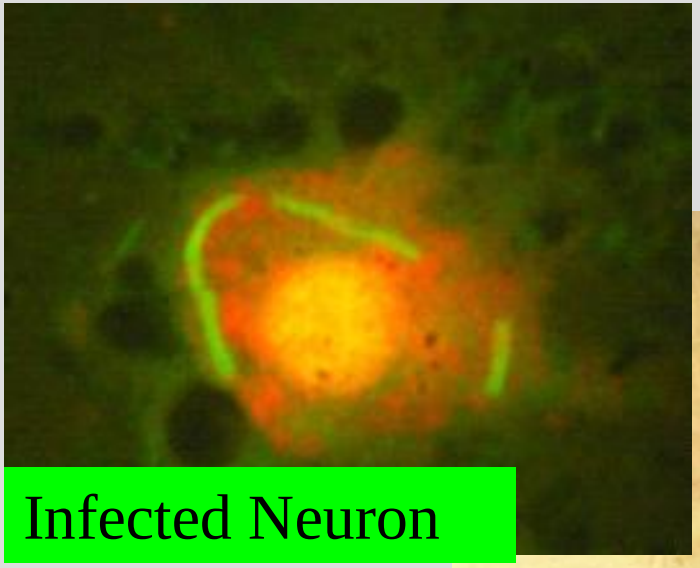


Borrelia spirochetes inside Hippocampal neurons in Alzheimer's disease

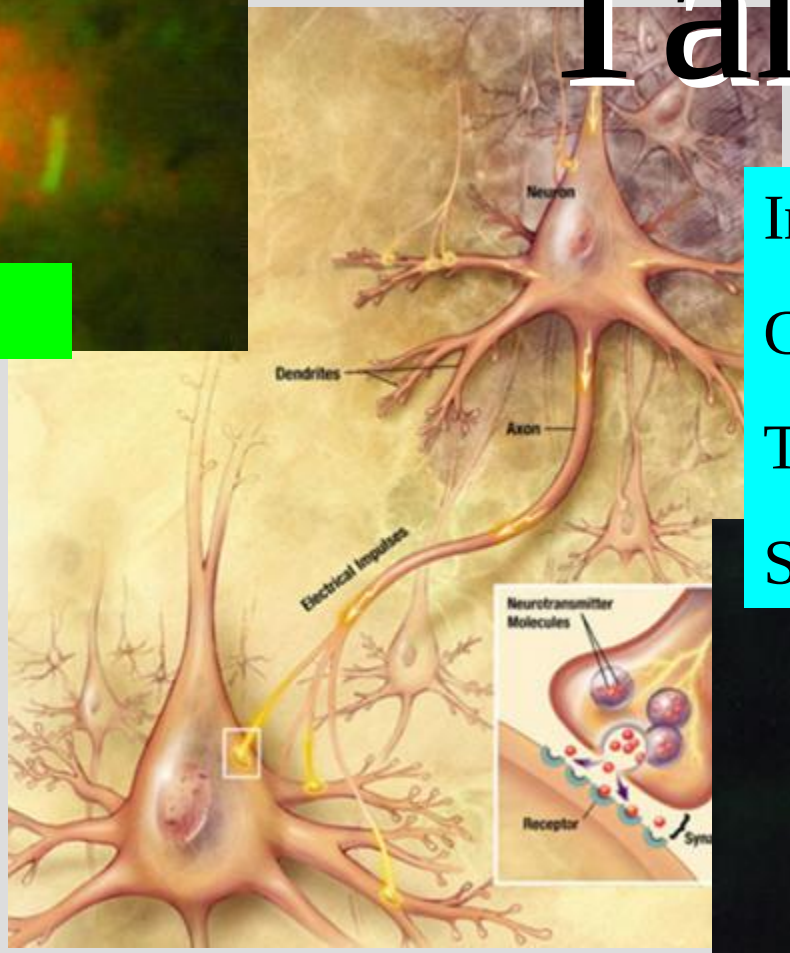
Infectious Agent Inside of the Nerve cell

Inside of the cell Infection

Borrelia to Tangles



Infected Neuron



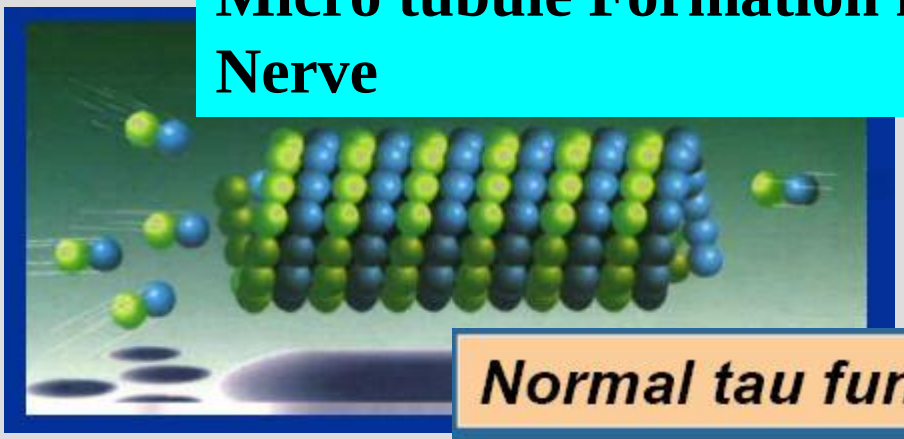
Infection

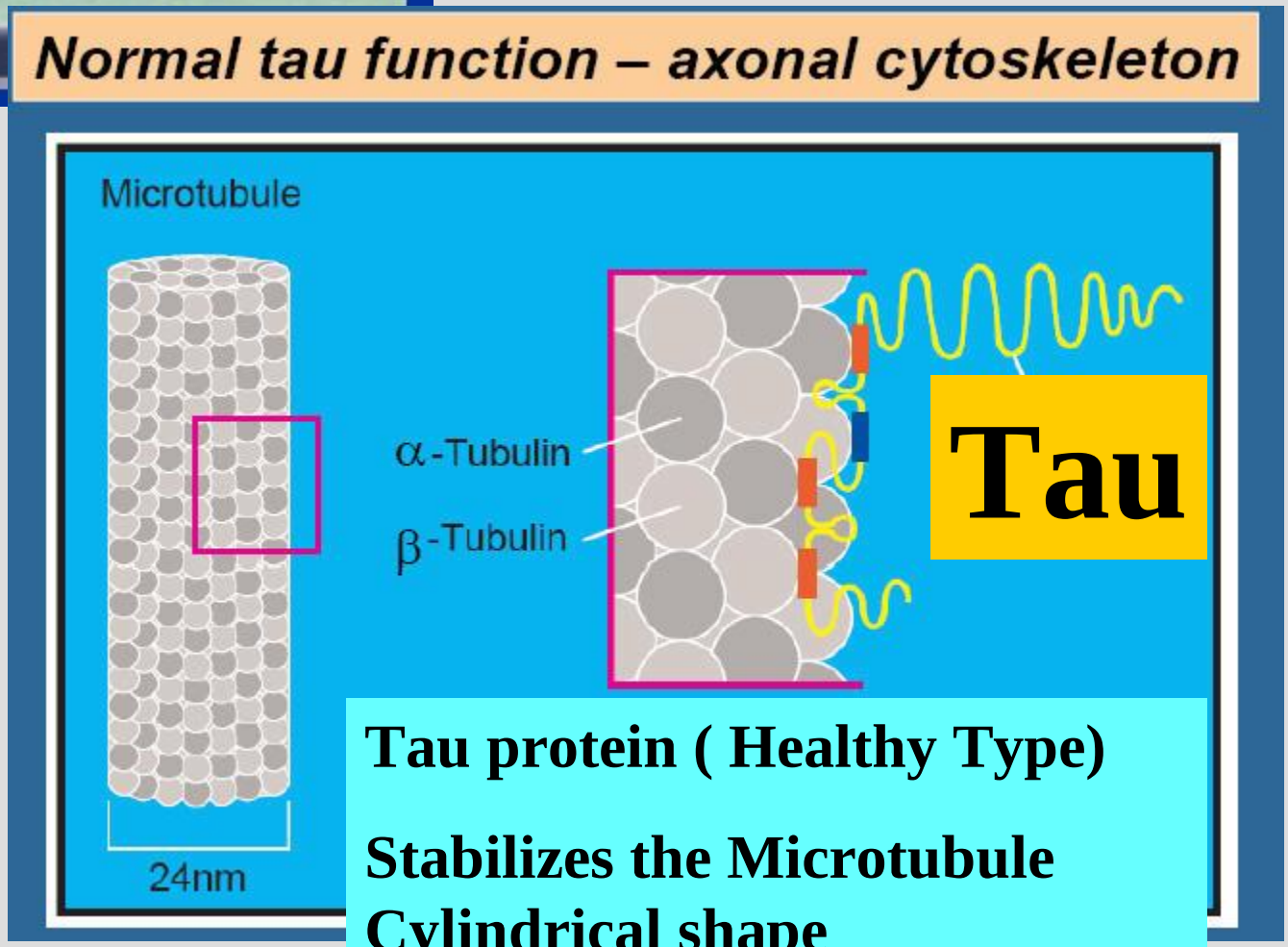
Crosses

The

Synapse

Micro tubule Formation inside the Nerve

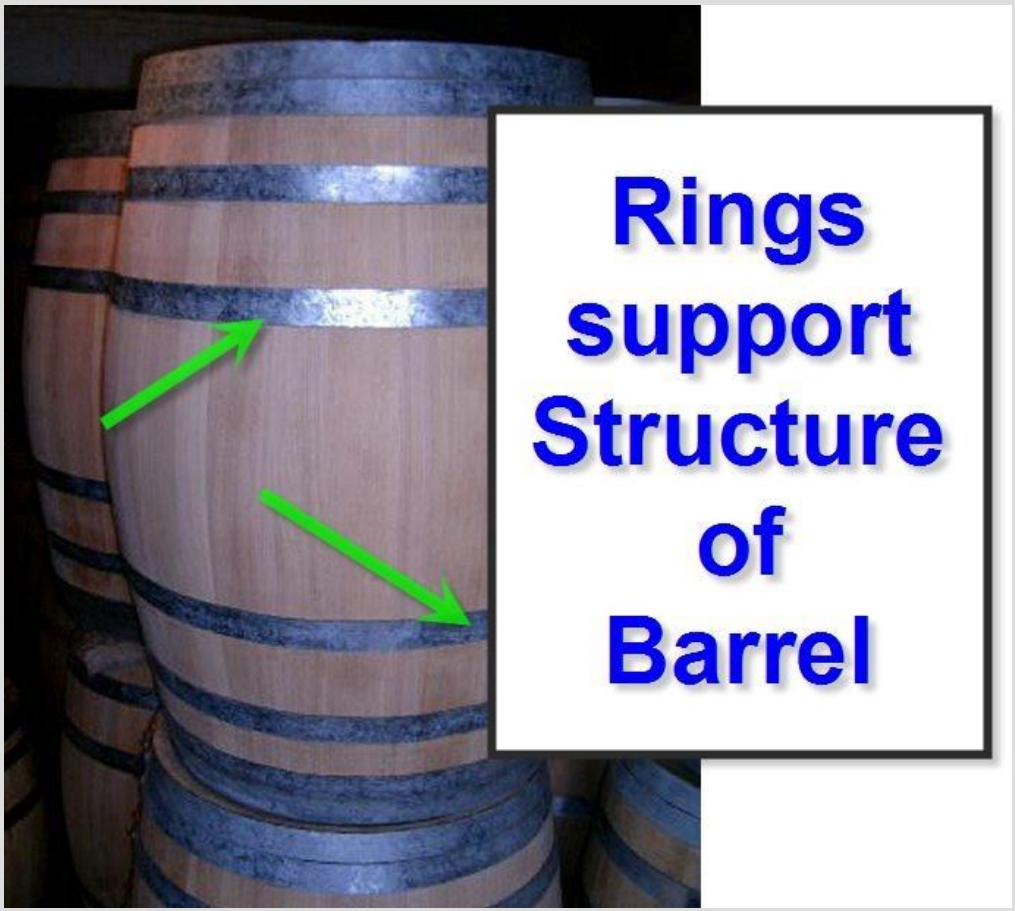




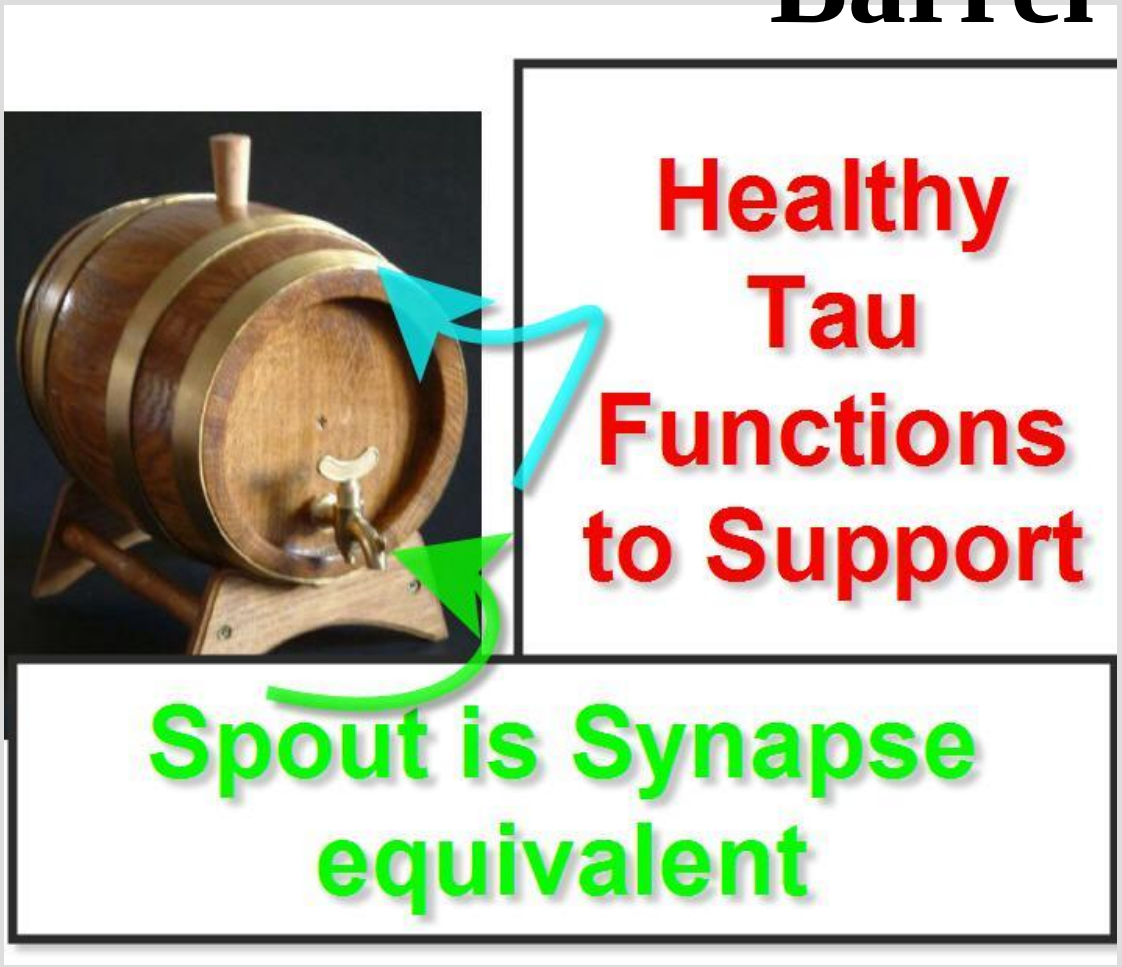
Tau protein (Healthy Type)

Stabilizes the Microtubule Cylindrical shape

Tau support
and the Model of the Barrel



Tau and Rings of the Barrel



Healthy Nerve

Needs

.

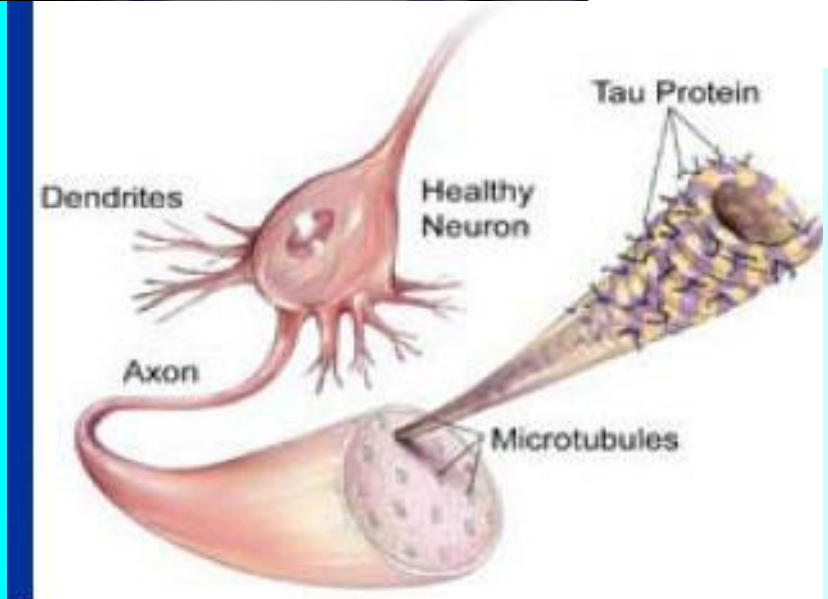
Healthy

.

Tau Protein to

Stabilize the

Microtubules

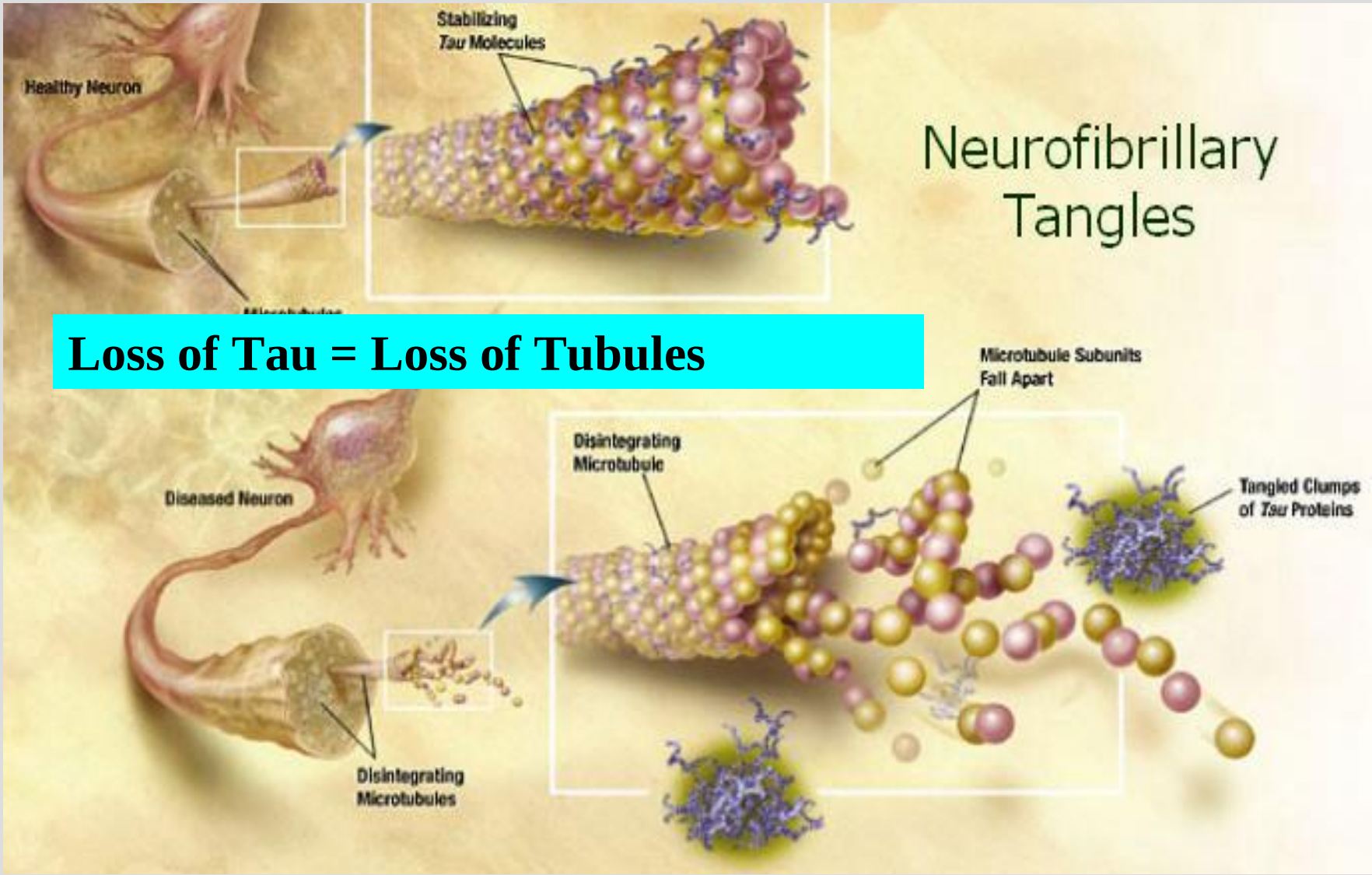


Many Healthy Tau structural supporting proteins—

A Ring of supports around

The tubule

Borrelia to Tangles



Borrelia inside the Nerve – and pathway to Tangle Formations

1. Infection inside of the Neuron

2. Biochemical Derangements

3. “Toxic” Products – (Phos) added to Tau

4. Loss of “healthy” Tau Supports

5. Tangles (Unhealthy Tau proteins)_----------Replace Microtubules -----Death of cell

Infections Crossing Synapses

Herpes Zoster

"Shingles"

Dormant Virus from Childhood Chicken Pox

Stays hidden inside of Nerves for 50-80 years

and ***Reactivates to "March " down Nerve pathways***

Other Trans-synaptic Infections

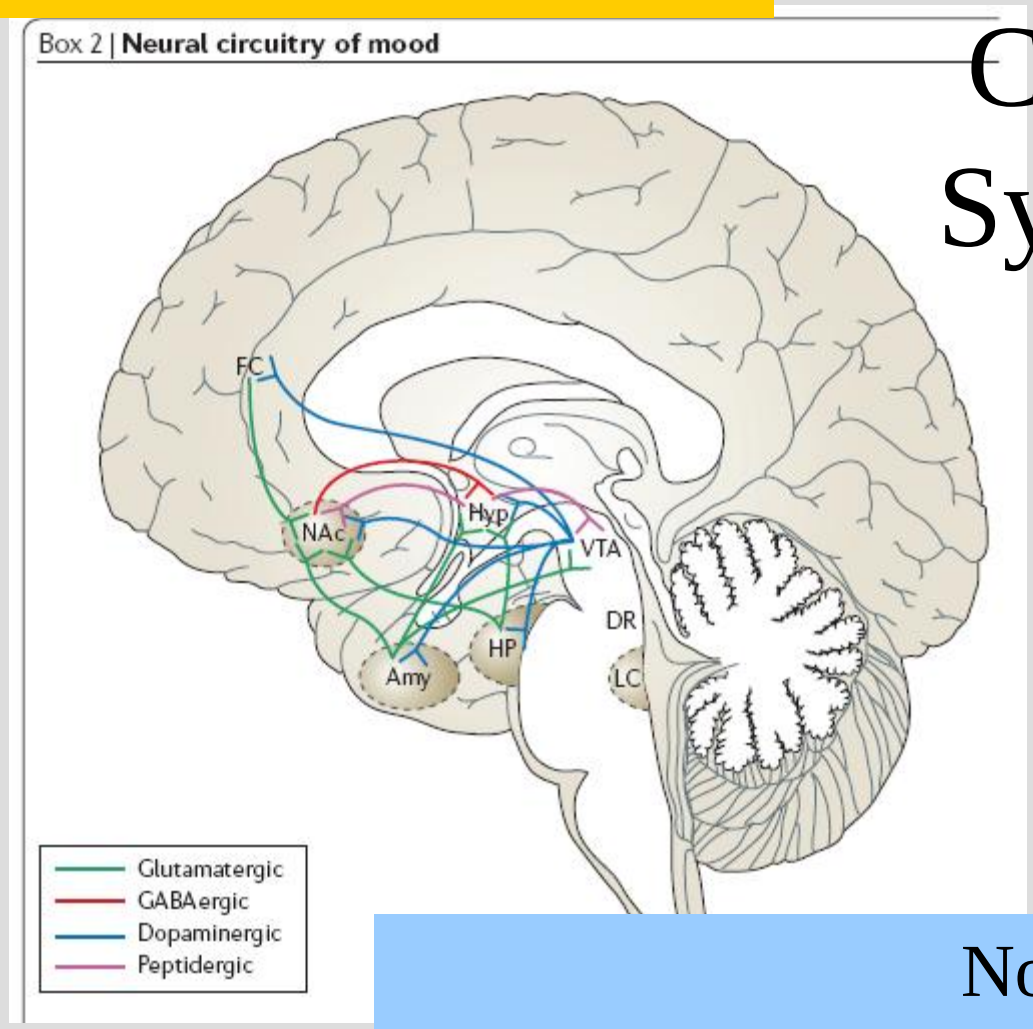
Infections Crossing Synapses

Rabies

Lethal March of Virus inside Nerve Networks

Pseudo Rabies Virus

Infections Crossing Synapses



Non lethal Virus

Used to “Map” Neural Networks

Trans-Synaptic Neuroborreliosis

YMEHY 3712
4 October 2006; Disk Used
ARTICLE IN PRESS
No. of Pages 4
Medical Hypotheses (2006) x, xxx–xxx

1

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medical hypotheses

http://intl.elsevierhealth.com/journals/mehy

2 **Alzheimer's neuroborreliosis with *trans*-synaptic**
3 **spread of infection and neurofibrillary tangles**
4 **derived from intraneuronal spirochetes**

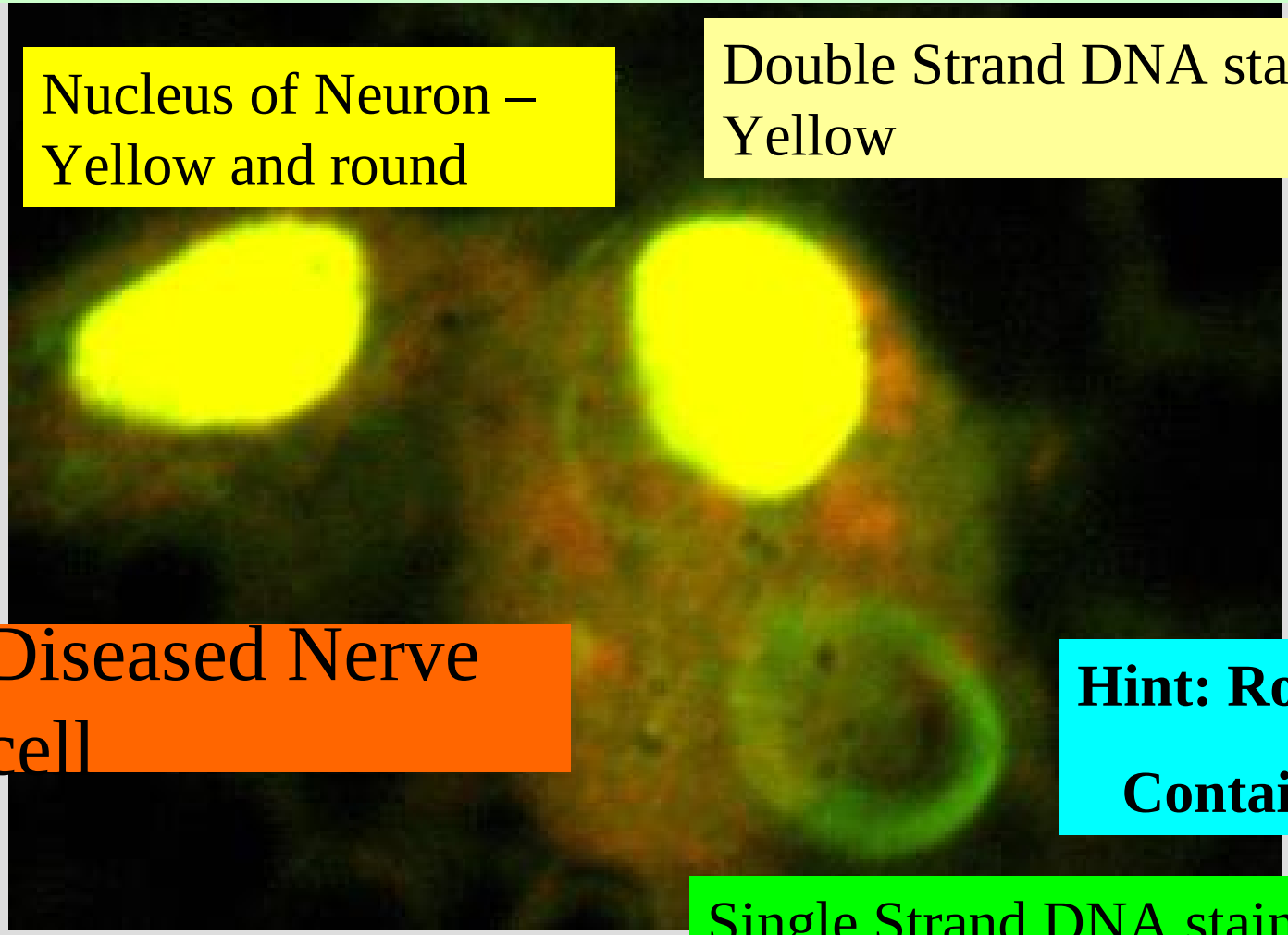
5 **Alan B. MacDonald ***

6 *Department of Pathology, St Catherine of Siena Medical Center, 50 Rte 25 A, Smithtown, NY 11787,*
7 *United States*

8 Received 22 August 2006; accepted 22 August 2006

Alzheimer's Disease – A Neuron with a Round "Green thing"

Describe what you see, Please



Nucleus of Neuron – Yellow and round

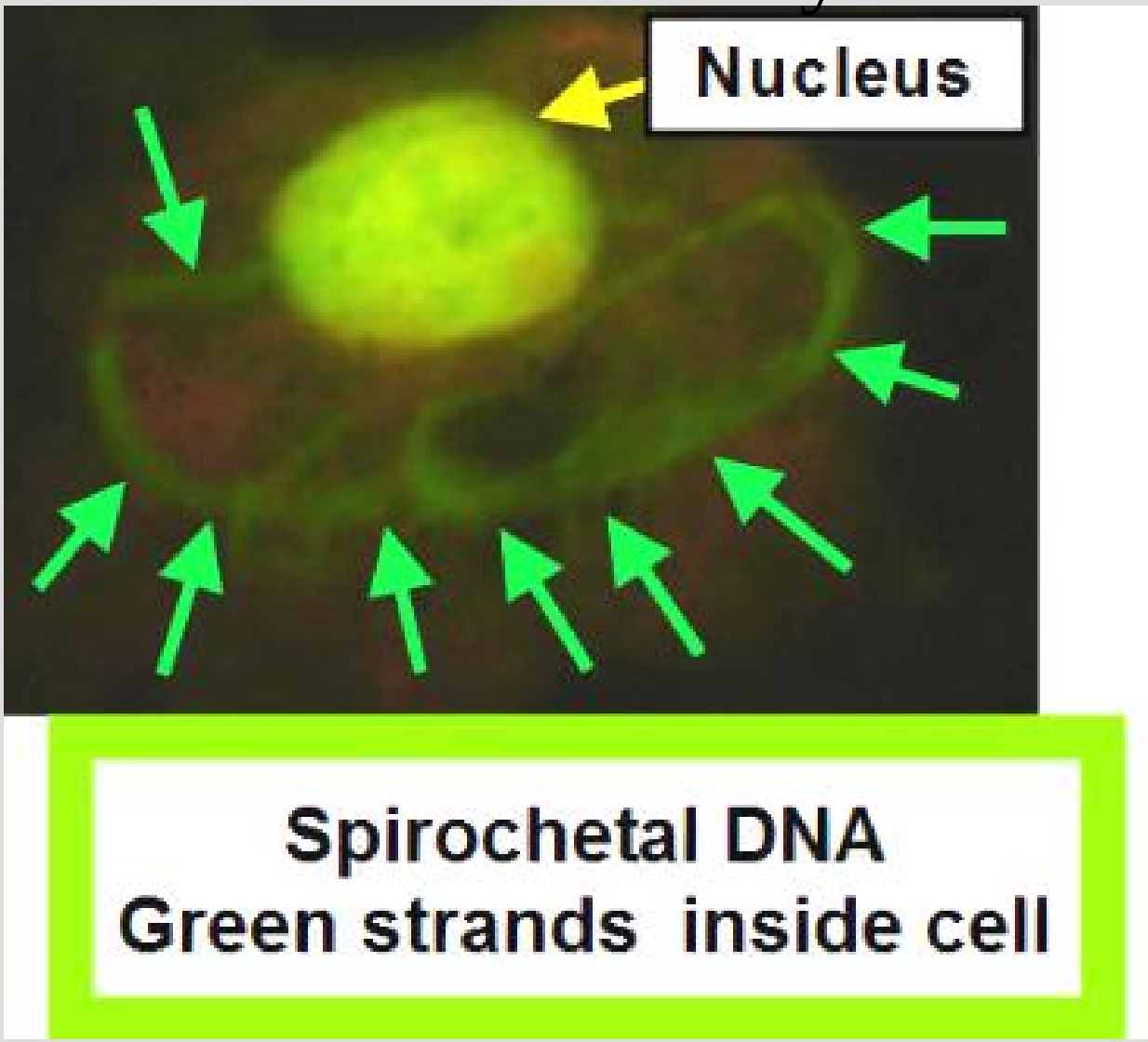
Double Strand DNA stains Yellow

Diseased Nerve cell

Hint: Round Thing Containing DNA

Single Strand DNA stains Green

Single Strand DNA in Cytoplasm is Never seen in Healthy Neuron



Braak Stages of Alzheimer's

Normal
Brain

Size

On Left

Ellison & Love: Neuropathology 2e © 2004 Elsevier Ltd.

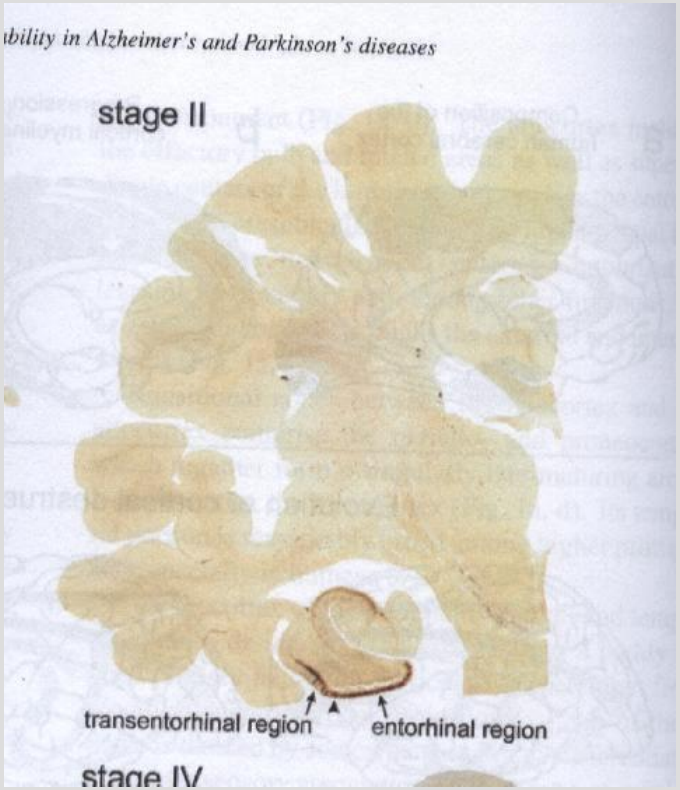
Alzheimer's

Disease

Brain size

On Right

Braak Stages of Alzheimer's



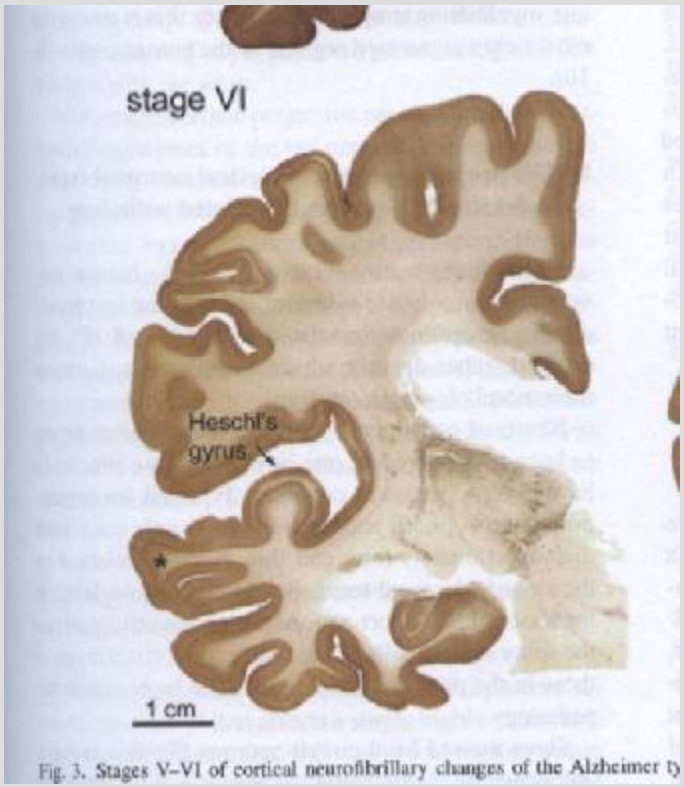


Fig. 3. Stages V–VI of cortical neurofibrillary changes of the Alzheimer ty

Braak Stages of Alzheimer's

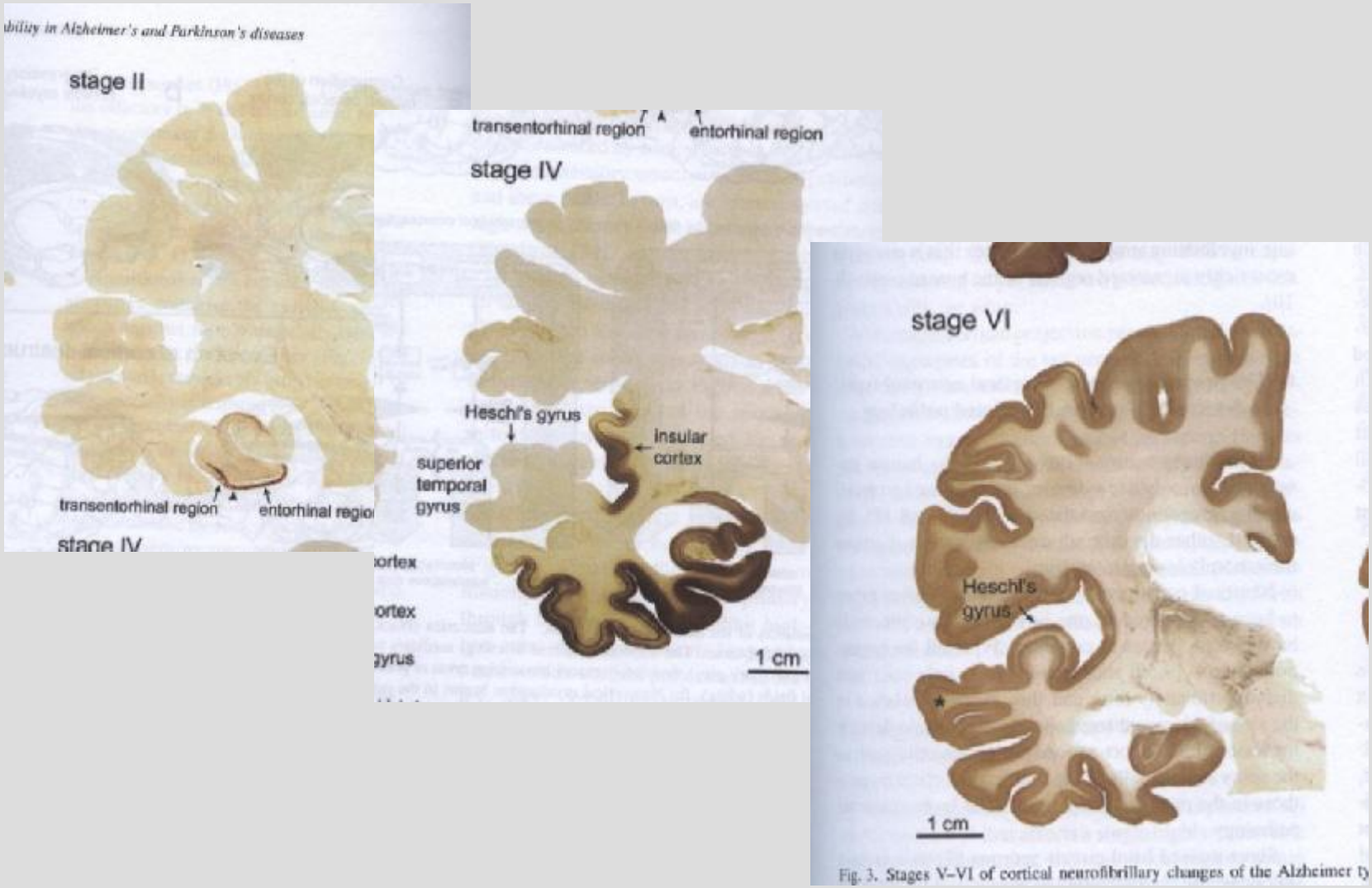
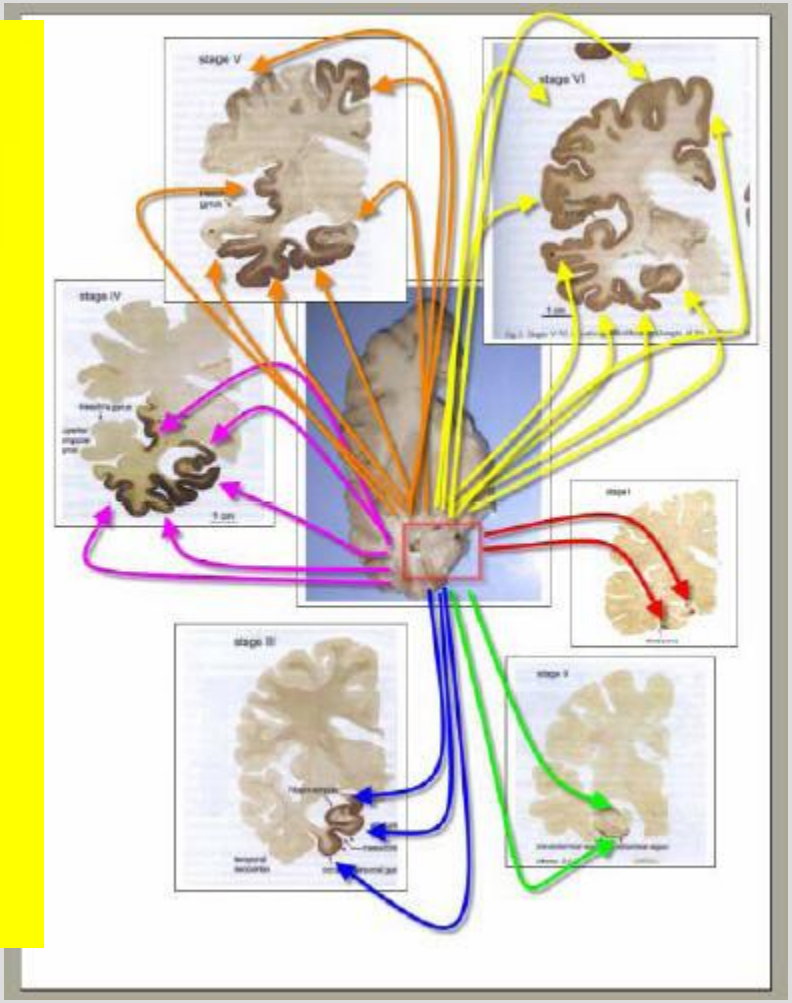


Fig. 3. Stages V–VI of cortical neurofibrillary changes of the Alzheimer ty

Braak Stages of Alzheimer's Redefined as Infection in Neural Networks

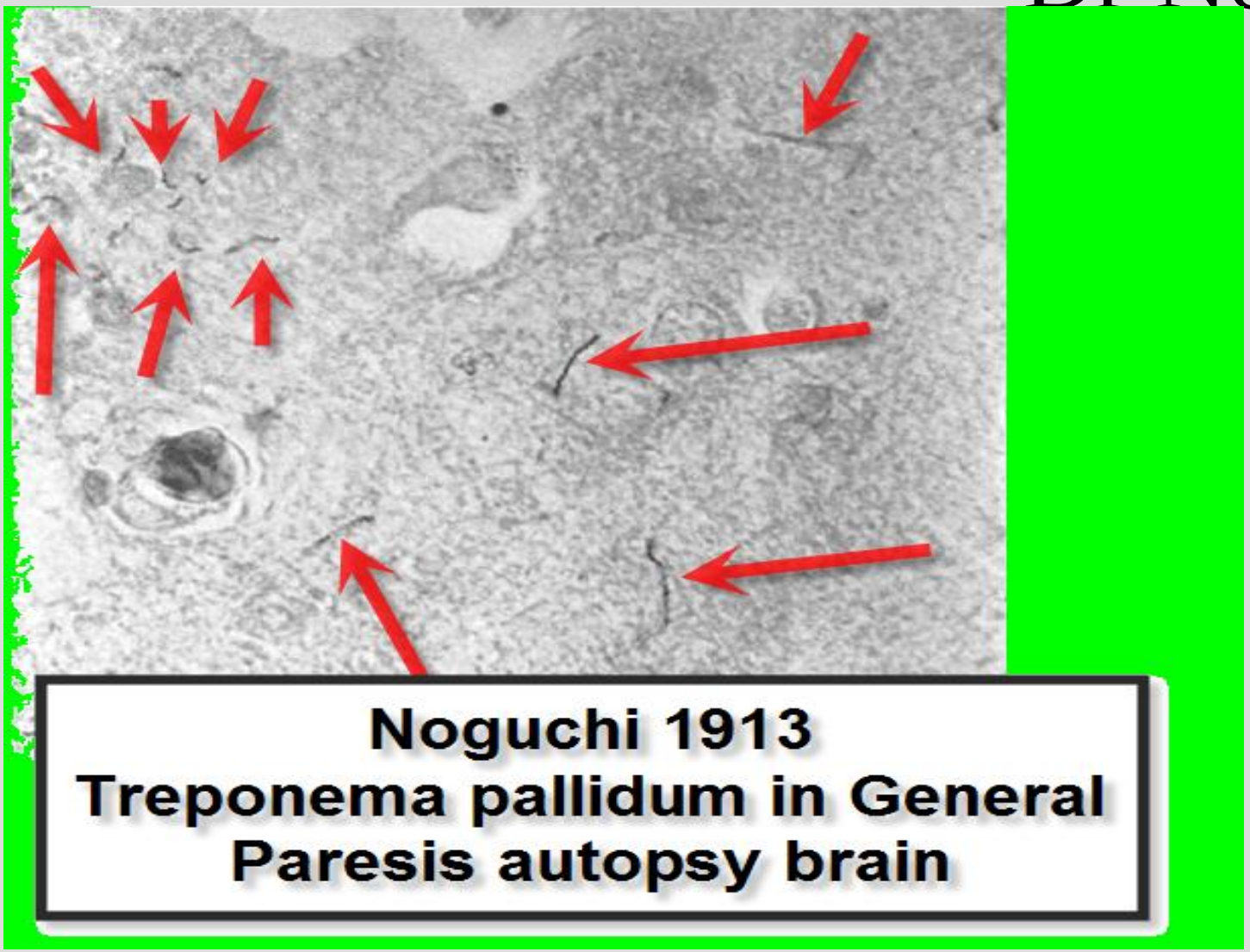


Escalator Model for Ascending Braak Stages

Escalator Schema for Infection movements through neural Circuits

Dr Noguchi

Dr Noguchi


Noguchi 1913
Treponema pallidum in General
Paresis autopsy brain

Negative Reviews
Borrelia/Alzheimer's

Marques et al – PCR Study using 16S target

Result***All Alzheimer's brains Negative for PCR product

Miklossy Rebuttal – PCR Alzheimer 16 S PCR – Positive Results in Alzheimer brains – Plus DNA Sequence Positive Evidence

Bergstrom Rebuttal – 16 S Nucleotides of Borrelia Differ among Strains of Borrelia Spirochetes – Wrong Strain Primers Yield Negative PCR when Borrelia are still present

Negative Reviews-Borrelia/Alzheimer's

Pappolla and Burgdorfer –

Pathology study of Alzheimer's Brain tissues for-Corkscrew Borrelia spirochetes.

Result ***No Borrelia corkscrew forms identified in Alzheimer Brain tissues – *Fragmentary Forms in Tissue Declared Artefacts*

MacDonald Rebuttal –

1. No Positive Controls—No tissues known to show Borrelia Spirochetes in Brain tissue were utilized by Pappolla.

2. No "truncated" forms" – in plane of Section Allowed by Pappolla and Burgdorfer.

Negative Reviews-Borrelia/Alzheimer's

Dr Dennis Dickson's Letter of Protest 1987 Human Pathology

******* Dickson's Allegations of "False Hope" for Alzheimer's Patient's.. based on a Single Case Study published by MacDonald and Miranda**

"Concurrent Neocortical Borreliosis and Alzheimer's Disease"

MacDonald Rebuttal – The Case of

Mr Paul Christensen

Mr Paul Christensen Lyme disease in Spinal Fluid 8 years before Death from Alzheimer's disease

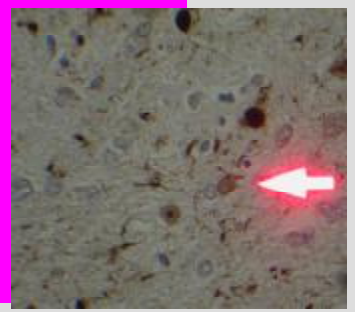
All Spinal Fluid testing Positive for Lyme disease – SUNY School of Medicine Stony Brook

8 years prior to Death from Dementia

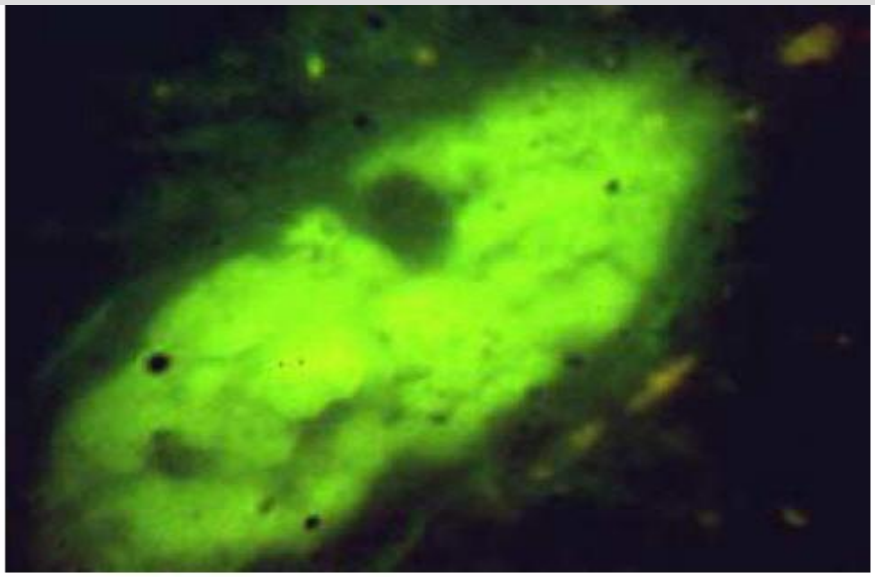
Autopsy Confirmed Alzheimer's Disease –

SUNY School of Medicine, Stony Brook, New York

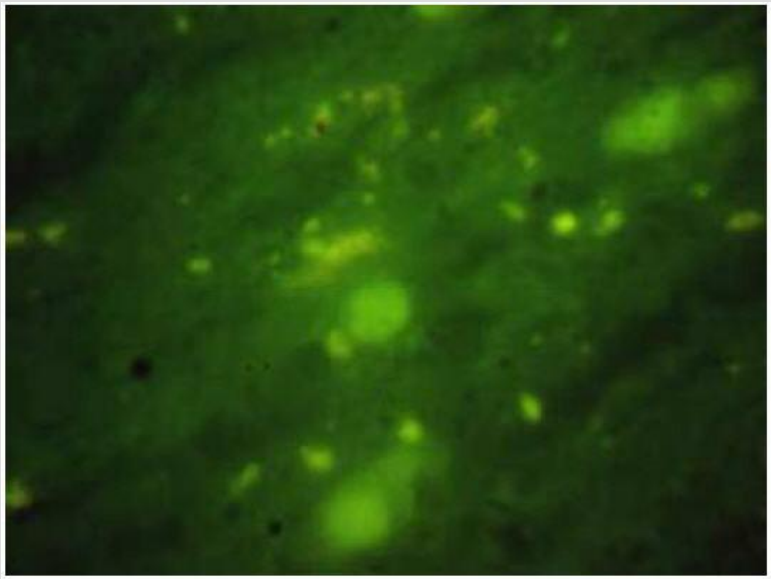
by Faculty Pathologist with Subspecialty Board Certification in Neuropathology-



Mr Paul Christensen Alzheimer's At Autopsy 8 years after Spinal Fluid + for Borrelia burgdorferi at Stony Brook



Borrelia burgdorferi **Flagellin DNA , In situ hybridization, Large Plaque**
1000x original magnification



Borrelia burgdorferi **flagellin DNA in situ DNA hybridization, Alzheimer hippocampus**
1000x magnification.

Mr Paul Christensen Alzheimer's at Autopsy
8 years after Spinal Fluid positive
for Borrelia burgdorferi Antibodies at SUNY Stony Brook School of Medicine

Key points: Infection in Spinal Fluid – Lyme Positive

Atypical Facial pain at presentation – later onset of Normal Pressure Hydrocephalus –

Shunt Placement – Shunt Infection – Antibiotics – Clinical improvement – Antibiotics discontinued – Dementia again develops – Deterioration to Death – Alzheimer's Disease at Autopsy

CERAD criteria satisfied at Medical School SUNY-

DNA Probes for Flagellin DNA – Positive hybridization signals in Alzheimer Plaques

Opportunities for Improvement in Alzheimer's Patient Care

****

Contributions from the Molecular version of the Autopsy

Website

http://www.molecularalzheimer.org

Special Thanks to : Turn the Corner Foundation

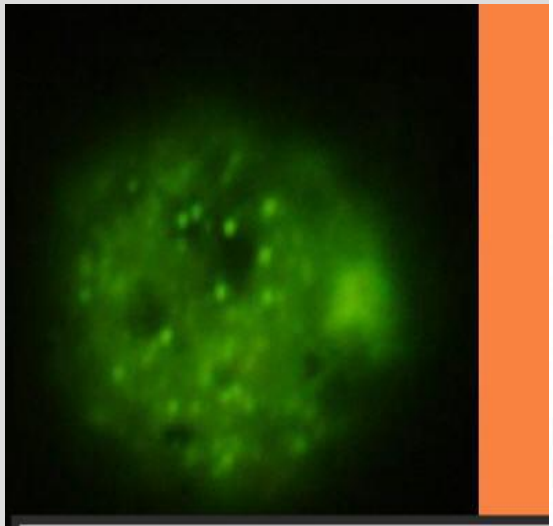
New York City, New York

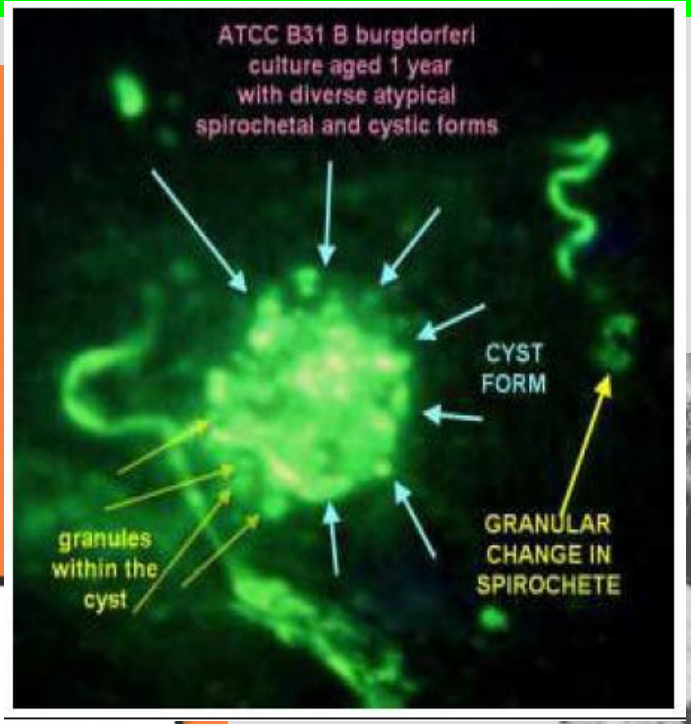
Turn the Corner Foundation
The Fight against Lyme Disease

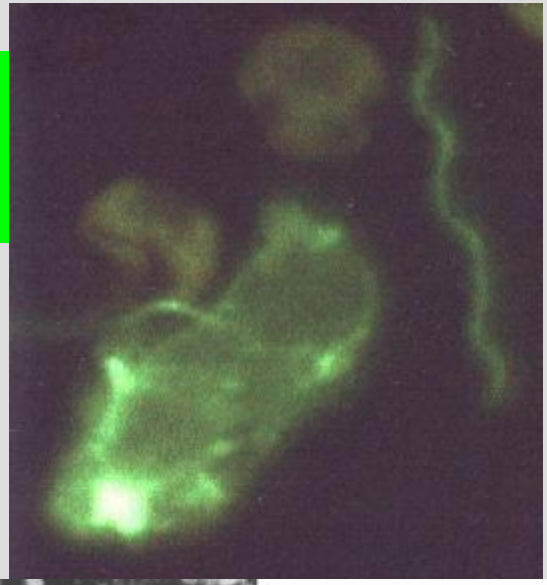
St Catherine of Siena Medical Center,

Smithtown, New York

Walking on Thin Ice



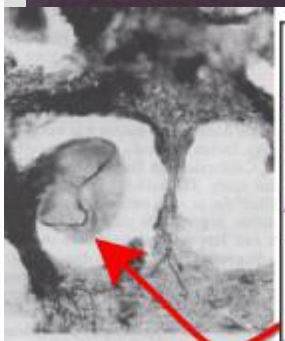




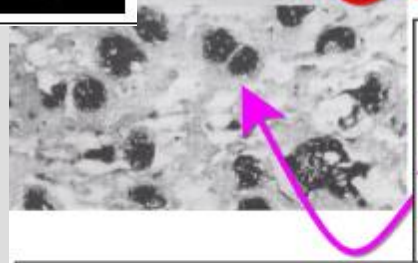
DLB

Diffuse Lewy Body Disease

Cystic Borrelia Form



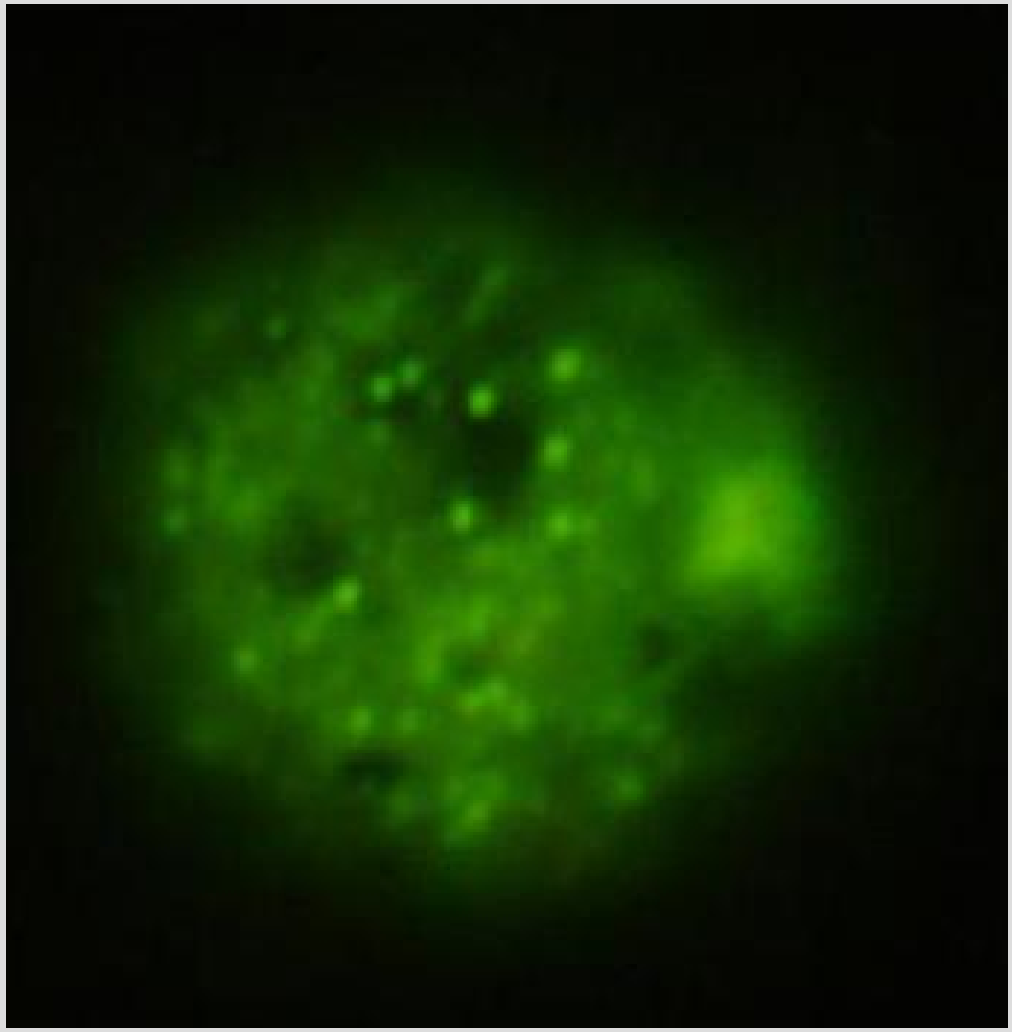
Cystic Borrelia in Alzheimer Autopsy Brain 1987



Plaques Alzheimer Disease

Concurrent Neocortical Borreliosis and Alzheimer's Disease 1988 Ann. New York Acad Sci, vol 539 p. 468-470

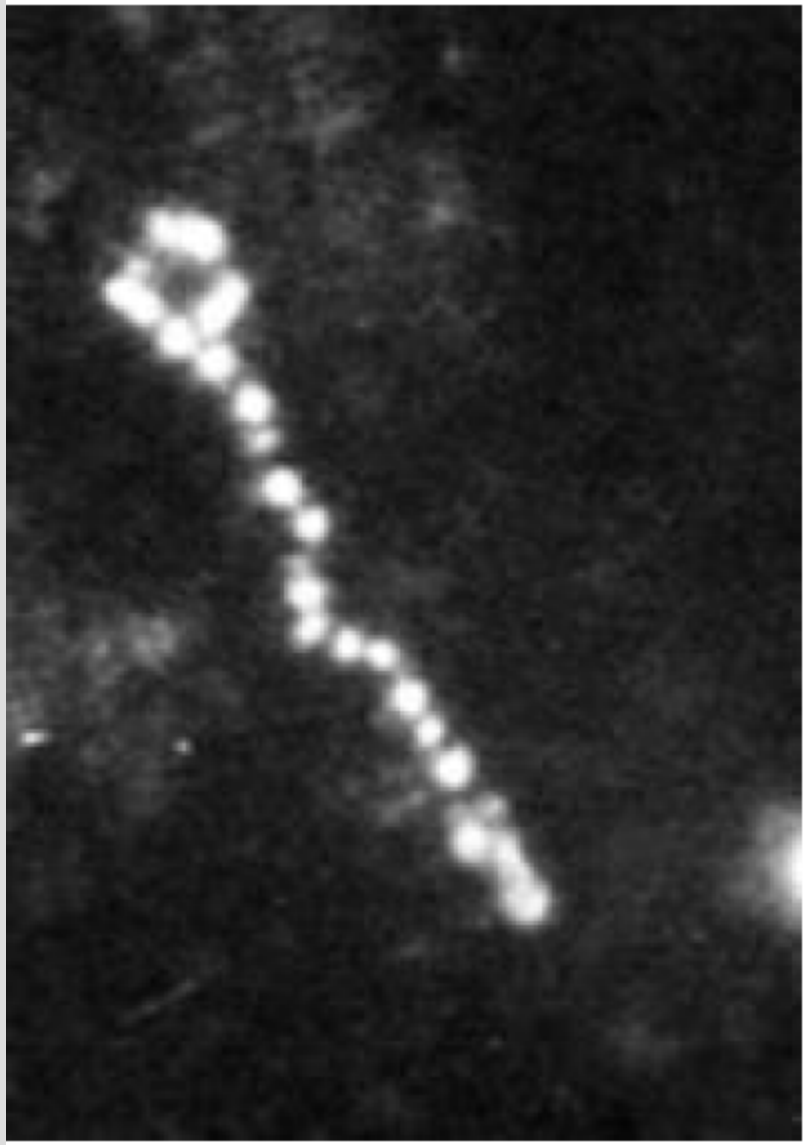
Ponder the Possibilities



Thank you

For

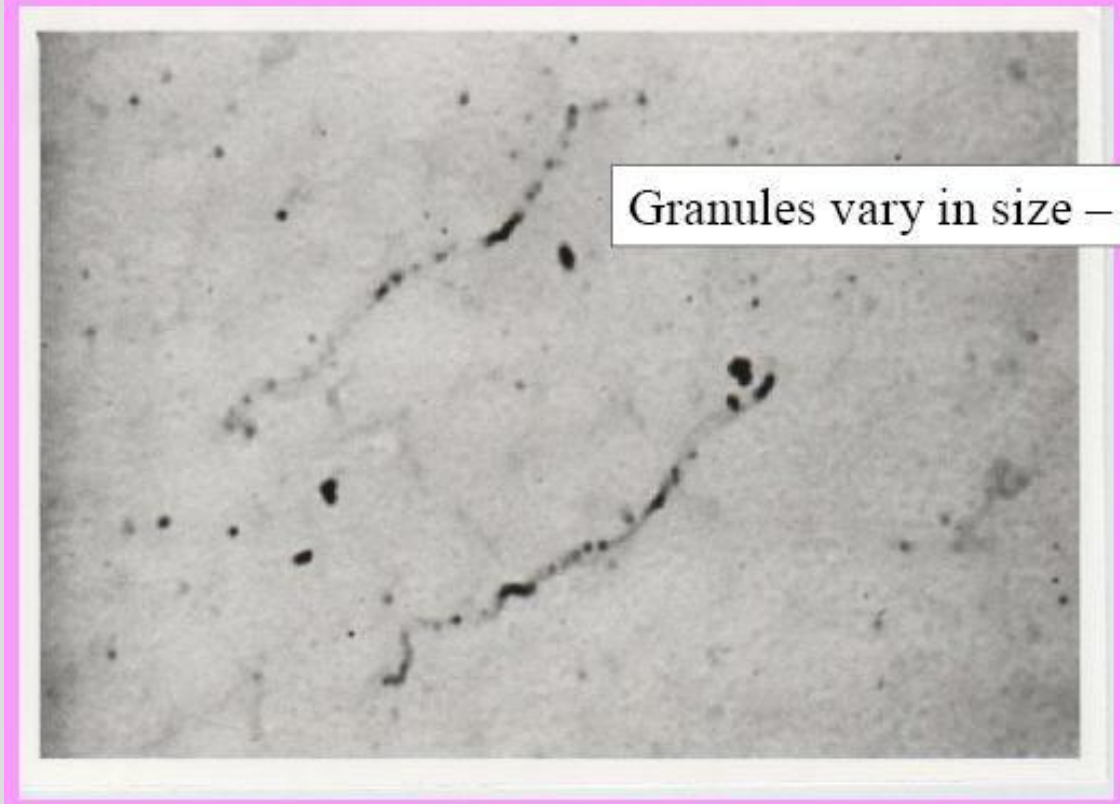
Your Kind Attention



Alzheimer's with GVB and ? Spirochetal form at 9 oclock

Granules vary in size – from little to big

Borrelia burgd. In transformation to granular forms



Granules vary in size – from little to big

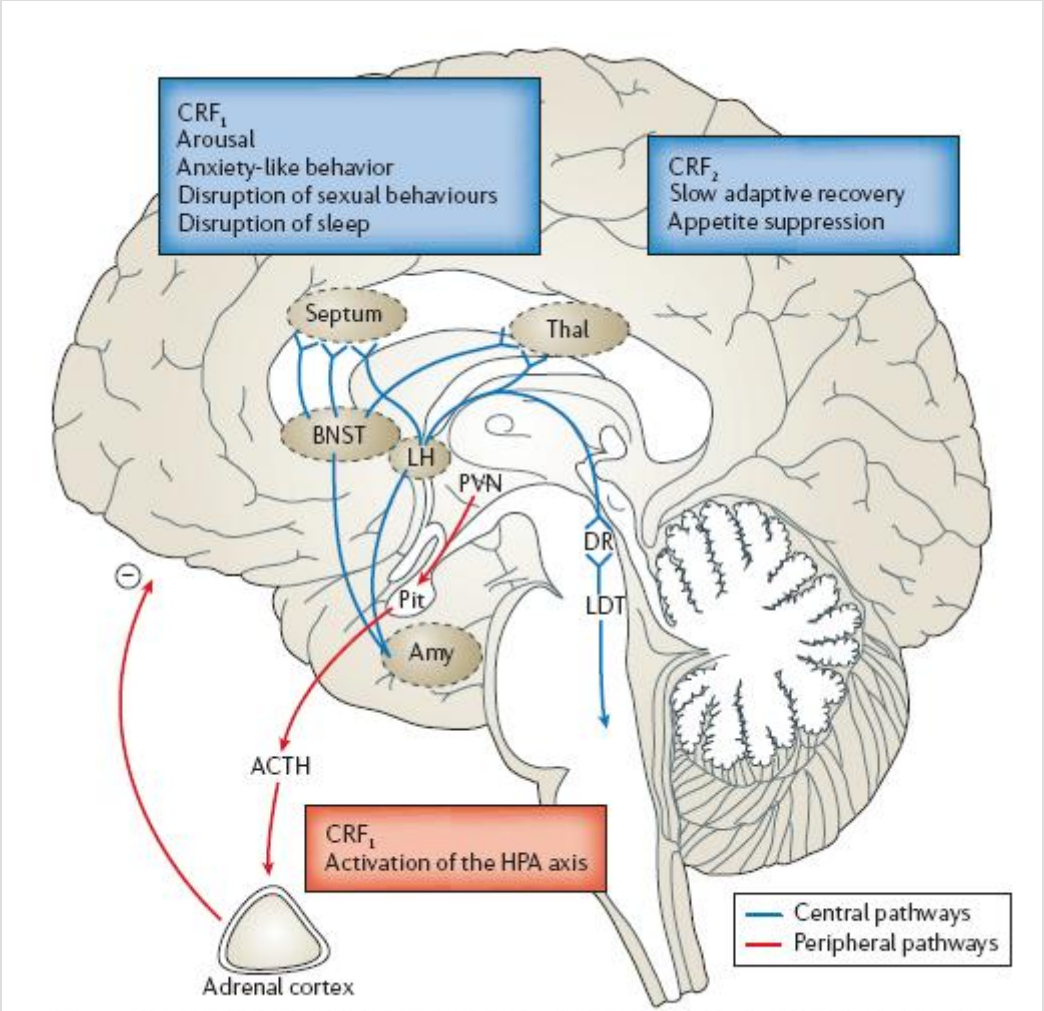
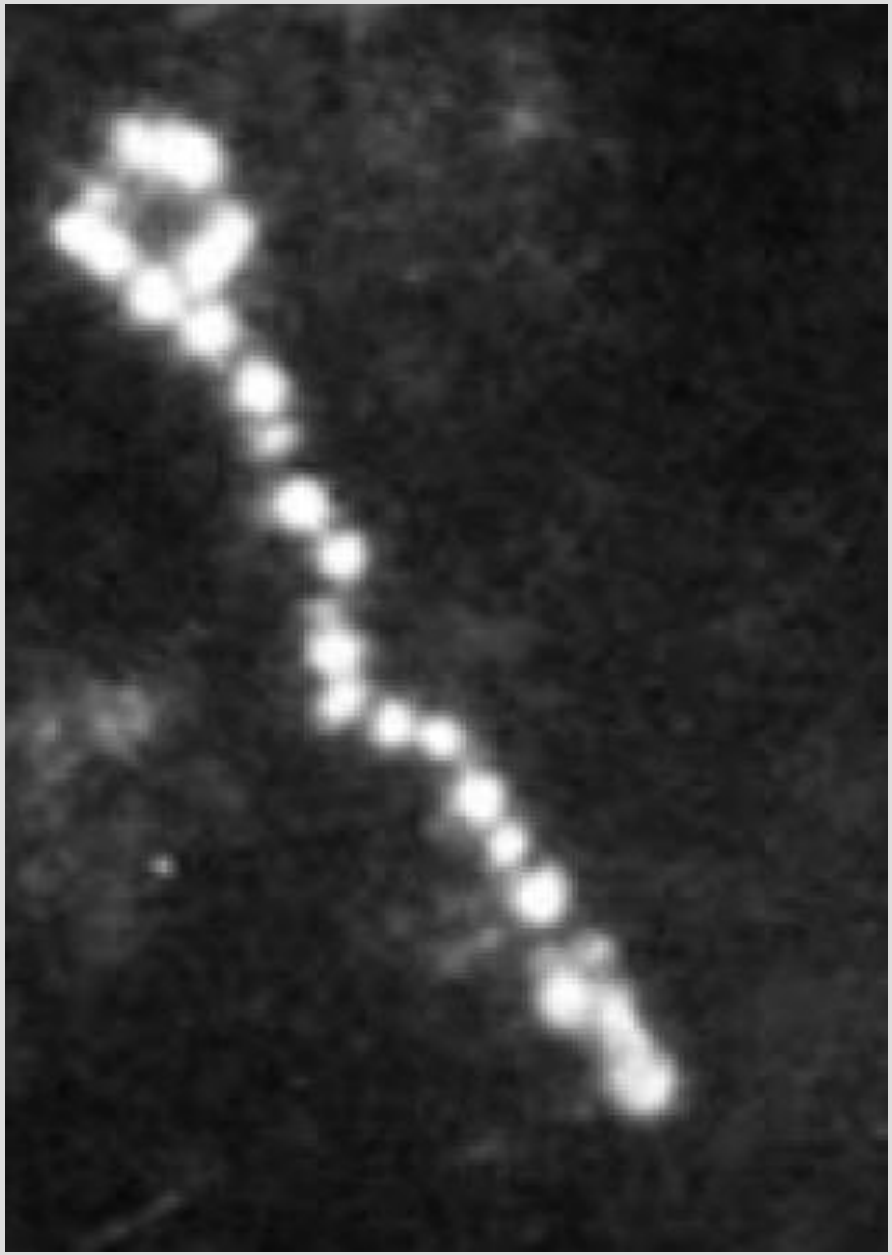


Figure 1 | **The corticotropin-releasing factor system in depression.** Corticotropin-



spirochete from culture of Alzheimer brain extract in culture
DNA stain
400 s original magnification