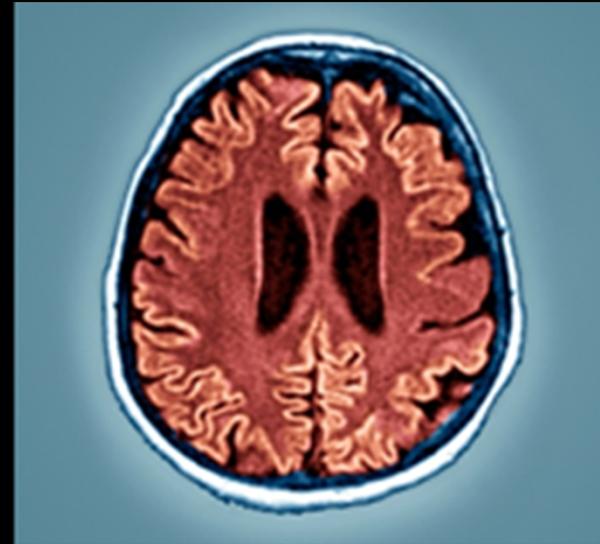


# DSHS Grand Rounds

April 2

## Creutzfeldt-Jakob Disease (CJD) and the Importance of Infection Prevention

Presenters: Beau Ances, MD, PhD, MSc, Washington University, Saint Louis;  
Deana M. Simpson, RN, St. John Providence Health System and Founder/Director CJD Insight



# Logistics

Registration for free continuing education (CE) hours or certificate of attendance through TRAIN at:

<https://tx.train.org>

Streamlined registration  
for individuals not requesting CE hours  
or a certificate of attendance

1. webinar: <http://www.dshs.state.tx.us/grandrounds/webinar-no-CE.shtm>
2. live audience: sign in at the door

For registration questions, please contact Annette Lara,  
[CE.Service@dshs.state.tx.us](mailto:CE.Service@dshs.state.tx.us)

# Logistics (cont.)

**Slides and recorded webinar available at:**

<http://www.dshs.state.tx.us/grandrounds>

## Questions?

There will be a question and answer period at the end of the presentation. Remote sites can send in questions throughout the presentation by using the GoToWebinar chat box or email [GrandRounds@dshs.state.tx.us](mailto:GrandRounds@dshs.state.tx.us).

For those in the auditorium, please come to the microphone to ask your question.

**For technical difficulties, please contact:**

GoToWebinar 1-800-263-6317(toll free) or 1-805-617-7000

# Disclosure to the Learner

## **Requirement of Learner**

Participants requesting continuing education contact hours or a certificate of attendance must register in TRAIN, attend the entire session, and complete the online evaluation within two weeks of the presentation.

## **Commercial Support**

This educational activity received no commercial support.

## **Disclosure of Financial Conflict of Interest**

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David Lakey, MD  
DSHS Commissioner  
is pleased to introduce today's  
DSHS Grand Rounds speakers

# Creutzfeldt-Jakob Disease (CJD) and the Importance of Infection Prevention



Beau Ances, MD, PhD, MSc,  
Associate Professor, Departments of  
Neurology, Radiology, and Biomedical  
Engineering, Washington University,  
Saint Louis



Deana M. Simpson, RN, Chief  
Clinical Transformation Officer, St.  
John Providence Health System and  
Founder/Director CJD Insight

**Beau M. Ances, MD, PhD, MSc, FANA**  
**Associate Professor**  
**Departments of Neurology, Radiology,**  
**Biomedical Engineering, and Microbiology**  
**Washington University in St. Louis**

**April 2, 2014**  
***Department of State Health Services***  
***Austin, TX***



# Beau M. Ances, MD, PhD, MSc

## Disclosure of Interest



**National Institute of Nursing Research (NINR) (R01NR012657, R01NR012907, R01NR014449)**

### Clinical Trials

**National Institute of Aging (NIA) (RC2AG036535)-  
Alzheimer's Disease  
Neuroimaging Initiative (ADNI)**



**National Institute of Mental Health (NIMH) (R21MH099979)**

### Consultant

**None**



**WUSTL Institute for Clinical and Translational Science (ICTS)-  
Inaugural SPIRiT Award**

### Speakers Bureau

**None**



**Alzheimer's Association New Investigator in Research Grant (NIRG)**

**I own no stocks or equity in any pharmaceutical company**



Creutzfeldt-Jakob Disease  
Foundation, Inc.

## A Clear and Important Message

- © There is no reason for a patient with a TSE to be denied any procedure, as any associated risks should be reduced to negligible levels by following the recommendations made by the World Health Organization (WHO) as slightly modified by the CDC:

[http://www.cdc.gov/ncidod/dvrd/cjd/qa\\_cjd\\_infection\\_control.htm](http://www.cdc.gov/ncidod/dvrd/cjd/qa_cjd_infection_control.htm)



341 W. 38<sup>th</sup> Street, Suite 501, New York, NY 10018 ★ 212.719.5900 ★ HelpLine 1.800.659.1991  
[help@cjd.foundation.org](mailto:help@cjd.foundation.org) ★ [www.cjd.foundation.org](http://www.cjd.foundation.org)

# “Patient 24”

- A 53 year old female admitted with a rapidly progressive cognitive decline
- 3 months prior to admission was noted to have inappropriate actions
  - Symptoms first started at rehabilitation facility after knee surgery
  - Was noted to drive on wrong side of the road
  - Repeatedly put her clothes on backwards
  - Repeated same sentence in a conversation
- Past Medical History: hypothyroidism, bipolar disorder, OSA and osteo-arthritis
- No known family history of similar symptoms

# “Patient 24”

- 2 months prior to admission
  - Because of increased difficulties with activities of daily living, she was moved in with her daughter
  - Had increased difficulty feeding herself
  - Overall speech output diminished
  - Progressive balance problems with multiple falls. She began to use a walker for ambulation
  - Repeated confusion at night with inability to discern her dreams from reality.

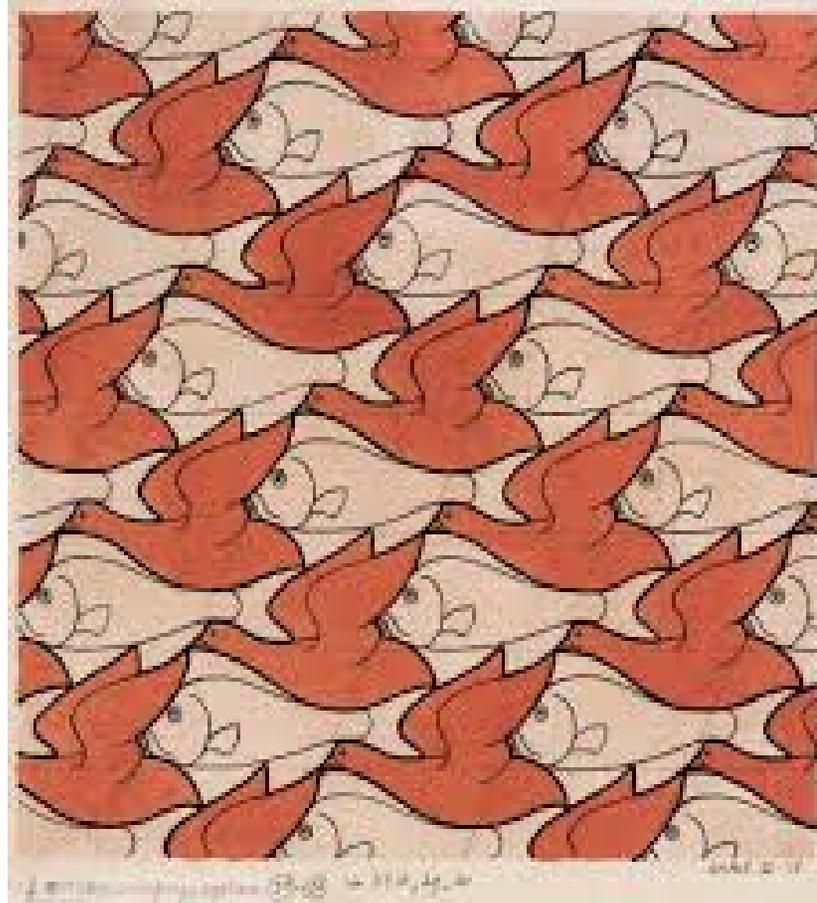
# Neurologic Exam at Admission

- Mental Status
  - Could open eyes spontaneously and would regard but not track for the examiner
  - Intermittently she would follow 1-step midline commands
  - Only oriented to name after given a choice selection
  - 0/3 immediate recall
  - Unable to perform simple calculations
- Language
  - No spontaneous speech output
  - She would occasional say “yes/no” to certain questions
  - She was unable to name objects or repeat a phrase

# Neurologic Exam at Admission

- Cranial nerves
  - Left homonymous hemianopsia
  - Decreased left nasolabial fold
- Motor
  - Mildly increased tone on the left side compared to the right
  - Left thumb fixed in an adducted position
  - 3/5 strength throughout but greater weakness in the left arm and leg than on the right (drift present)
- Startle myoclonus
- Reflexes
  - 2+ symmetric, extensor response seen in the toes
- Coordination/Gait
  - Unable to sit or stand without assistance
  - Unable to take any purposeful steps

# CJD - 'The Great Imitator'



Michael Geschwind MD, UCSF

# Differential Diagnosis for RPD

**TABLE 2-3** Recommended Initial Screening Tests for Evaluation of a Rapidly Progressive Dementia

Category	Required Tests	Sometimes Helpful	
Blood tests	Complete blood count	Cancer screen	
	Basic metabolic panel (including calcium, magnesium, phosphorus)	Blood smear	
	Liver function tests	Coagulation profile	
	Rapid plasma reagin	Hypercoagulability testing	
	Rheumatologic screen (erythrocyte sedimentation rate, antinuclear antibody, and C-reactive protein)	Homocysteine	
	Thyroid function tests	Copper and ceruloplasmin	
	Antithyroglobulin and antithyroperoxidase antibodies	Methylmalonic acid	
	Vitamin B <sub>12</sub>	Additional rheumatologic tests	
	HIV		
	Lyme disease		
	Paraneoplastic/autoimmune antibodies		
	Urine	Urine analysis	Urine culture
			Copper (24 hours, if Wilson disease suspected)
		Heavy metal screen (24 hours)	
CSF	Cell count and differential protein	Cryptococcal antigen	
	Glucose	Viral PCRs and cultures	
	IgG index	Bacterial, fungal, acid-fast bacilli stains, and cultures	
	Oligoclonal bands	Cytology	
	VDRL	Flow cytometry	
		Whipple PCR	
		14-3-3 test	
		Total tau	
		Neuron-specific enolase	

**TABLE 2-3** *Continued*

Category	Required Tests	Sometimes Helpful
Imaging	Brain MRI (including FLAIR and DWI) with and without contrast	CT head
		CT chest, abdomen, and pelvis with and without contrast
		MR angiography
		Brain angiogram
		Mammogram
		Body PET scan
		MR spectroscopy
Other tests	EEG	Carotid ultrasound
		Echocardiogram
		EMG/nerve conduction study
		Brain biopsy (especially if above tests are nondiagnostic)

HIV = human immunodeficiency virus; CSF = cerebrospinal fluid; PCR = polymerase chain reaction; IgG = immunoglobulin G; VDRL = Venereal Disease Research Laboratory (test); MRI = magnetic resonance imaging; FLAIR = fluid-attenuated inversion recovery; DWI = diffusion-weighted imaging; CT = computed tomography; PET = positron emission tomography; EEG = electroencephalogram; EMG = electromyogram.

Modified with permission from Geschwind MD, Shu H, Haman A, et al. Rapidly progressive dementia. *Ann Neurol* 2008;64(1):97-108.

Geschwind MD, *Continuum* April 2010

# Treatable Neurological Disorders Misdiagnosed as CJD

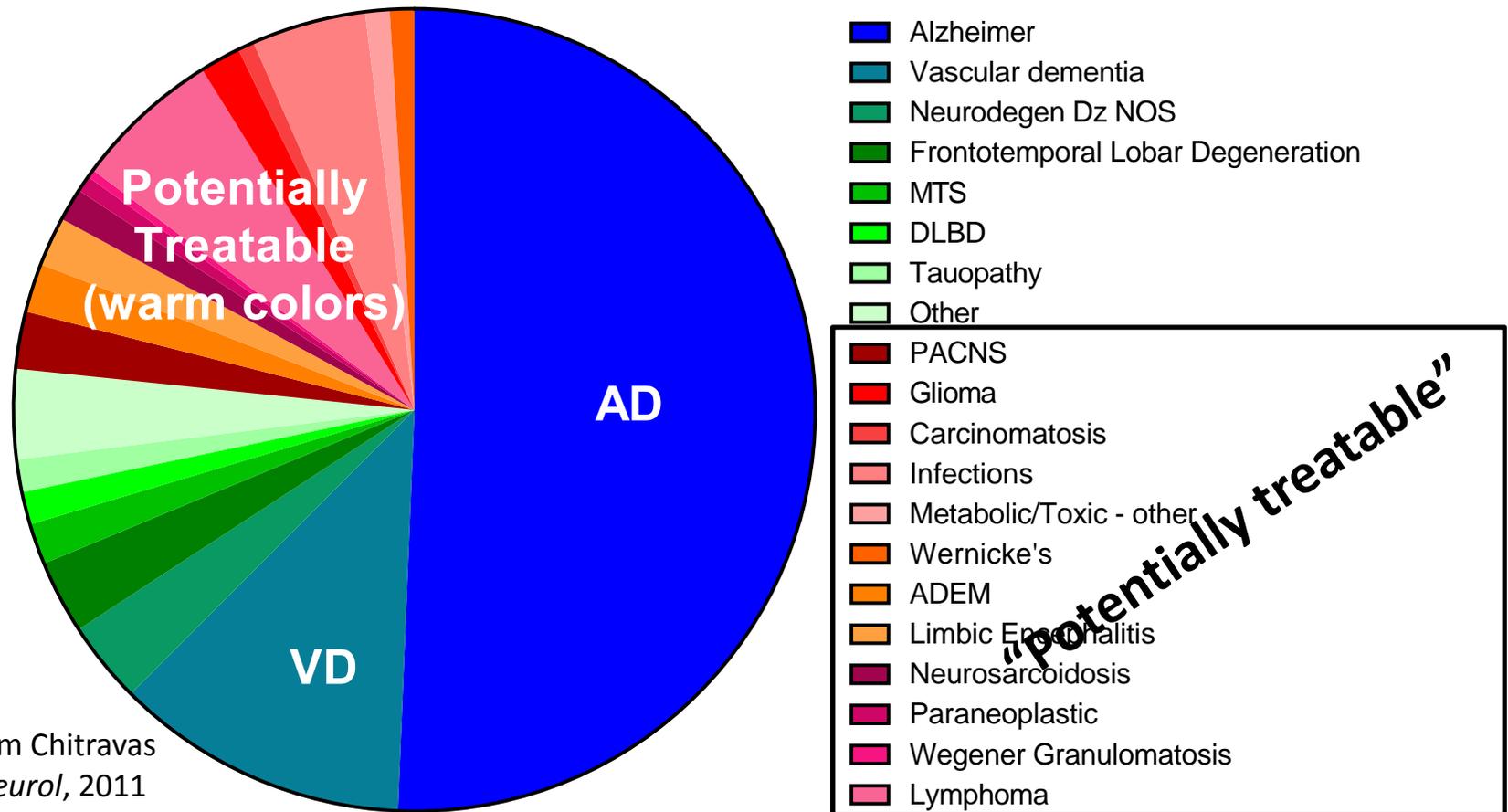
National Prion Disease Pathology Surveillance Center (NPDPSC)

352/1106 (32%) Brain autopsies negative for prion disease

(77%) "Incurable" Neurological disorders

(23%) "Treatable" Neurological disorders

(35% Neoplasm; 37% Immune; 20% Infections, 8% Metabolic)



Modified from Chitravas  
et al., *Ann Neurol*, 2011

# Proposed Work-up for RPD

**First Line**

Blood tests	CSF	Imaging	Urine/Other
<b>Basic panel of tests</b>			
<ul style="list-style-type: none"> <li>- Complete blood count</li> <li>- Basic metabolic panel (+Ca,P,Mg)</li> <li>- Liver function tests (including ammonia)</li> <li>- Renal function tests</li> <li>- Thyroid function tests</li> <li>- Anti-TG and Anti-TP antibodies</li> <li>- Vitamin B12/MMA/homocysteine</li> <li>- Rheumatologic screen (ANA, ESR, CRP, RF, ANCAs, SSA, SSB)</li> <li>- Rapid plasma reagin (RPR)</li> <li>- HIV serology</li> <li>- Paraneoplastic/autoimmune antibodies</li> </ul>	<ul style="list-style-type: none"> <li>- Cell count and differential</li> <li>- Protein</li> <li>- Glucose</li> <li>- IgG index</li> <li>- Oligoclonal bands</li> <li>- VDRL</li> <li>- 14-3-3/NSE/total tau</li> </ul>	<ul style="list-style-type: none"> <li>- Brain MRI (including FLAIR, DWI and ADC sequences), at least one scan with and without contrast</li> </ul>	<ul style="list-style-type: none"> <li>- Urine analysis (and culture if indicated)</li> <li>- EEG</li> </ul>

**Second Line**

<b>Tests to consider in selected cases</b>			
<ul style="list-style-type: none"> <li>- Lyme disease (in endemic areas)</li> <li>- Cancer screen</li> <li>- Blood smear</li> <li>- Coagulation profile</li> <li>- Hypercoagulability testing</li> <li>- Copper and ceruloplasmin</li> <li>- Additional rheumatologic tests (complement, dsDNA, anti-Sm, anti-RNP, anticardiolipin, anti-SCL 70, Anti-Jo, anti-centromere antibodies)</li> </ul>	<ul style="list-style-type: none"> <li>- Bacterial, fungal, acid-fast bacilli stains and cultures</li> <li>- Cytology</li> <li>- Flow cytometry</li> <li>- Whipple PCR</li> <li>- Cryptococcal antigen</li> <li>- Viral PCRs and cultures</li> </ul>	<ul style="list-style-type: none"> <li>- Cancer screen (CT chest, abdomen, and pelvis with and without contrast; mammogram; body PET scan)</li> <li>- MR angiography or brain angiogram</li> <li>- MR spectroscopy</li> <li>- Carotid ultrasound</li> <li>- Echocardiogram</li> </ul>	<ul style="list-style-type: none"> <li>- Heavy metal screen (24h urine)</li> <li>- Copper (24h urine)</li> <li>- Porphobilinogen (PBG)/delta-aminolevulinic acid (ALA) in urine (24h)</li> <li>- EMG/nerve conduction study</li> <li>- Brain biopsy</li> </ul>

# Diagnosics Tests for “Patient 24”

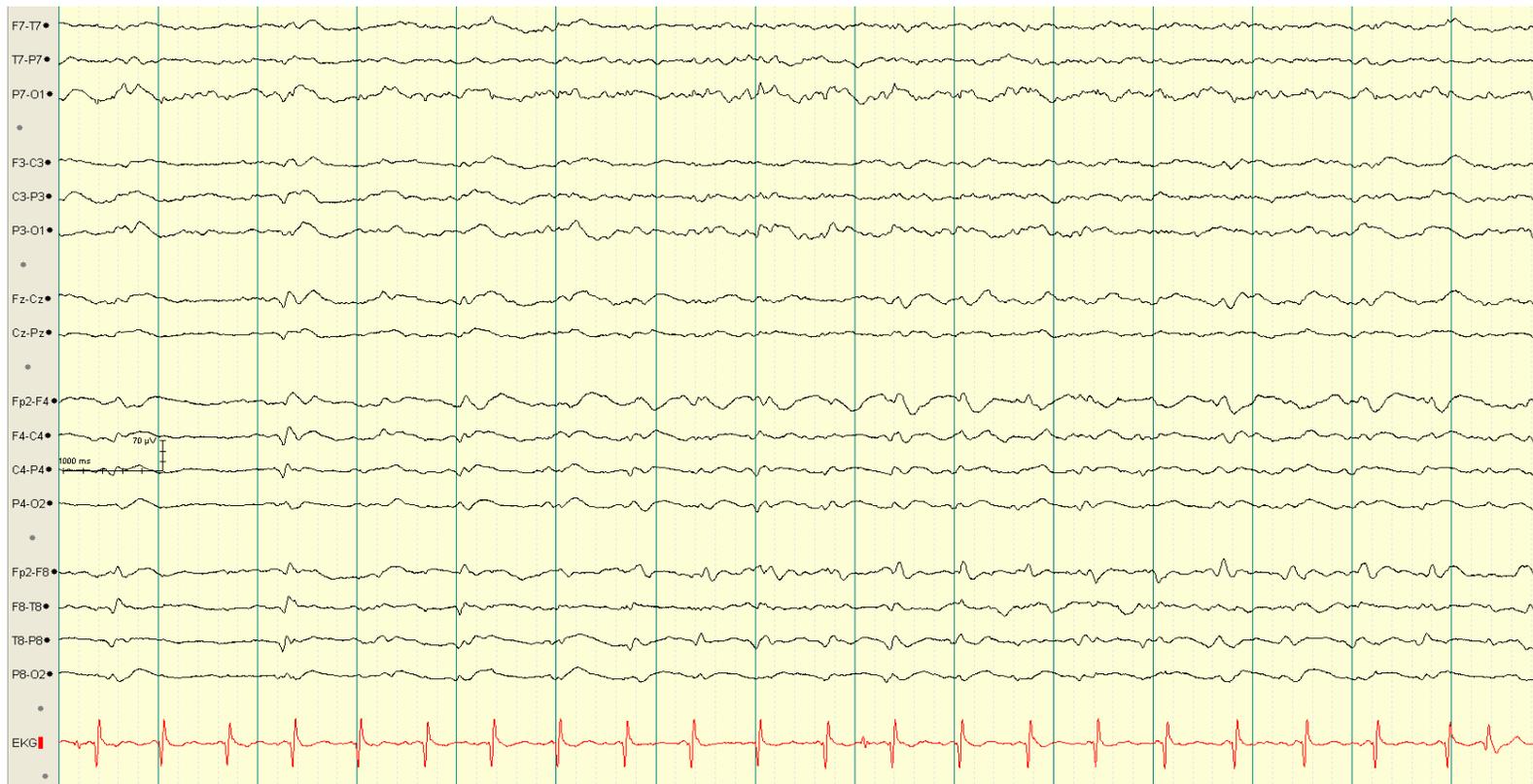
- CMP and CBC- normal
- Thyroid panel-normal
- Ammonia = 35
- Blood gas = 7.44/37/75
- UA = negative
- UDS = negative
- Vit B12 = 937
- Folic acid = 8.1
- RPR = negative
- HIV = negative
- Serum thyroid antibodies:
  - Anti-Thyroglobulin < 1.8
  - Anti – thyroperoxidase = 662.2 (< 9) (steroids at OSH)
- ANA/ENA/ANCA/anti-dsDNA = neg
- Paraneoplastic panel (serum): negative
- Chest/Abdomen/Pelvis CT: no evidence of malignancy

# CSF Studies for “Patient 24”

- Tube 1: TC = 0 NC = 0
- Tube 4: TC = 0 NC = 0
- Prot = 66; Glu = 65 (serum = 103)
- Micro: Bacterial, fungal and mycobacterial Cx = negative; AFB neg. Crypto neg. Mycoplasma PCR negative; CMV/EBV/toxo/enterovirus/HSV/VZV negative
- VDRL = negative
- ACE < 5
- 14-3-3 = “positive”
- Tau = 4743 (<1200 = “negative”)

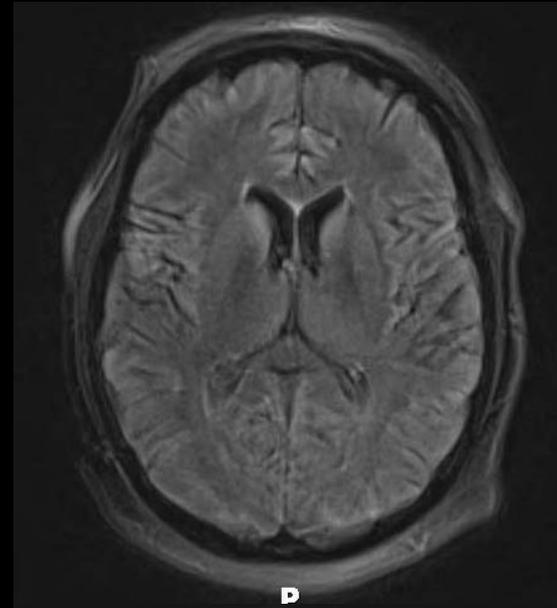
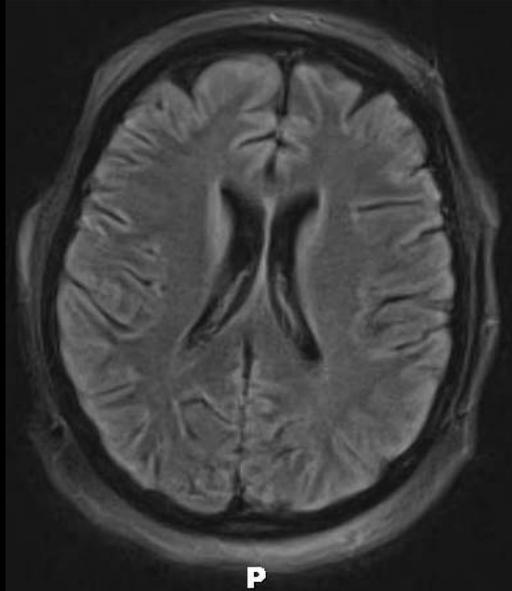
# EEG of “Patient 24”

- Report from outside hospital noted moderate generalized slowing
- EEG performed at admission to our hospital- periodic sharp and wave complexes (PSWC)

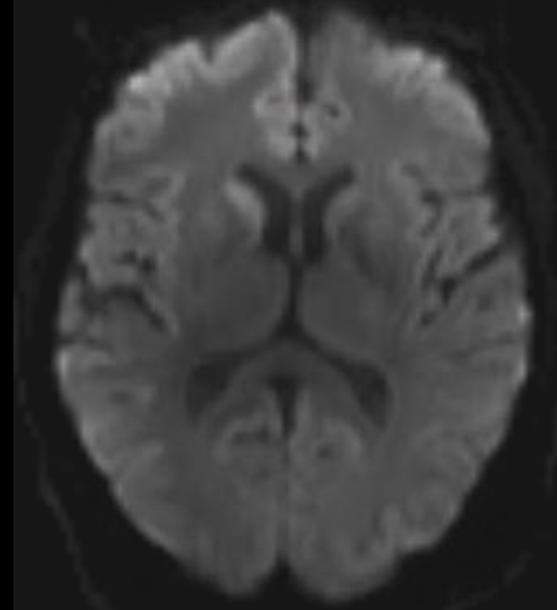
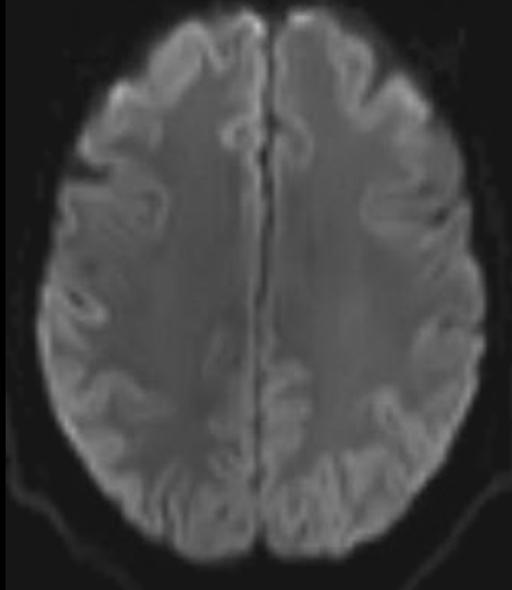


# Neuroimaging of Patient 24

**FLAIR**

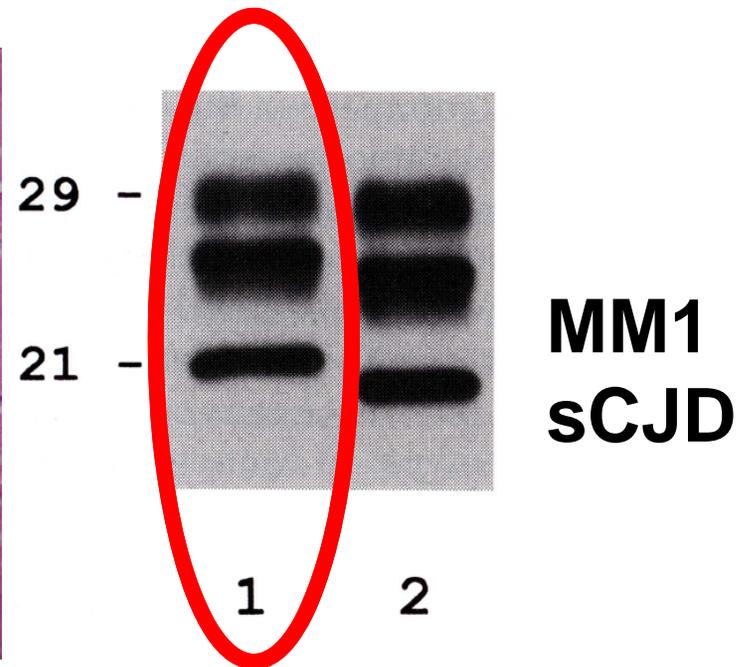
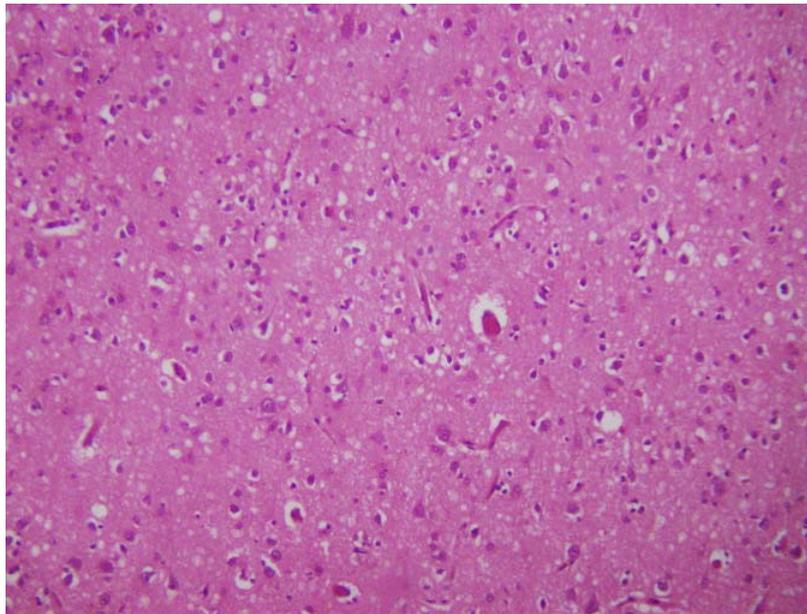


**DWI**



# Hospital Course of “Patient 24”

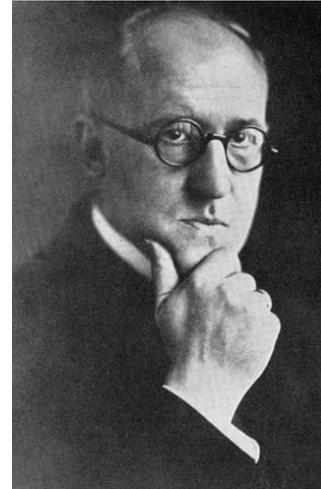
- Over a period of 2 weeks she progressed to a state of akinetic mutism
- She expired 3 weeks into her admission
- An autopsy (limited to brain) was performed



# CJD Clinical Features



**Hans Gerhard Creutzfeldt**



**Alfons Maria Jakob**

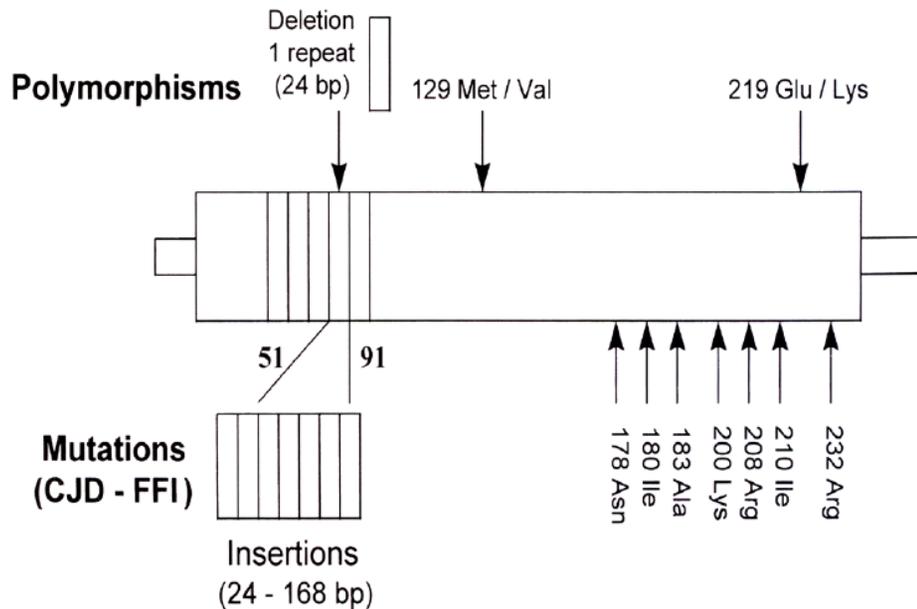


**Daniel Gajdusek**

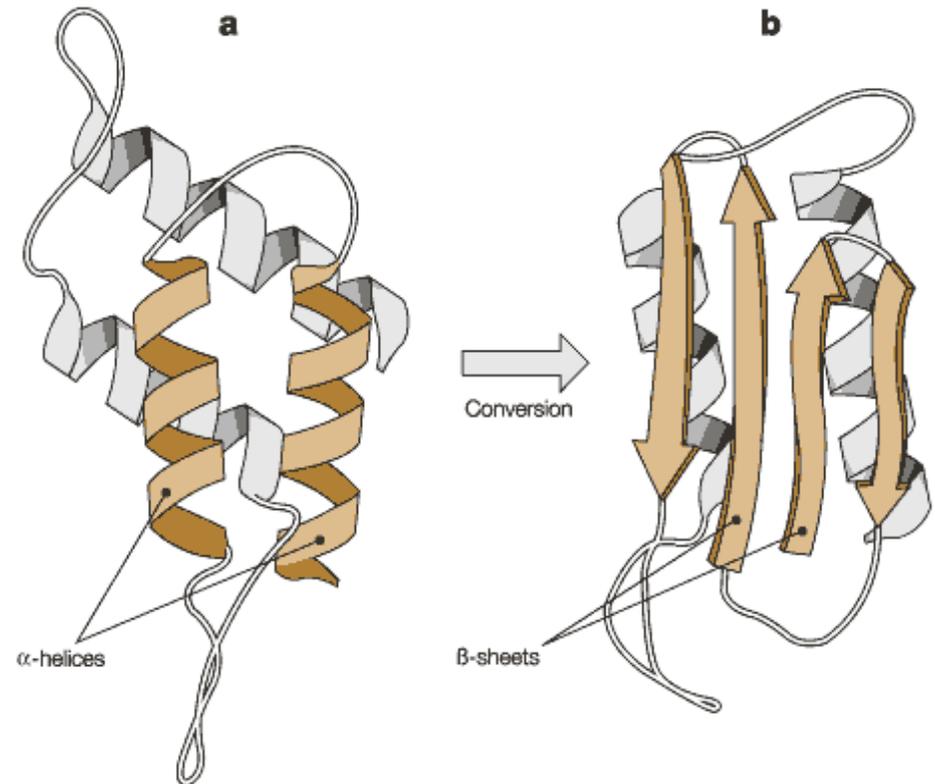


**Stanley Prusiner**

# Prion Pathophysiology



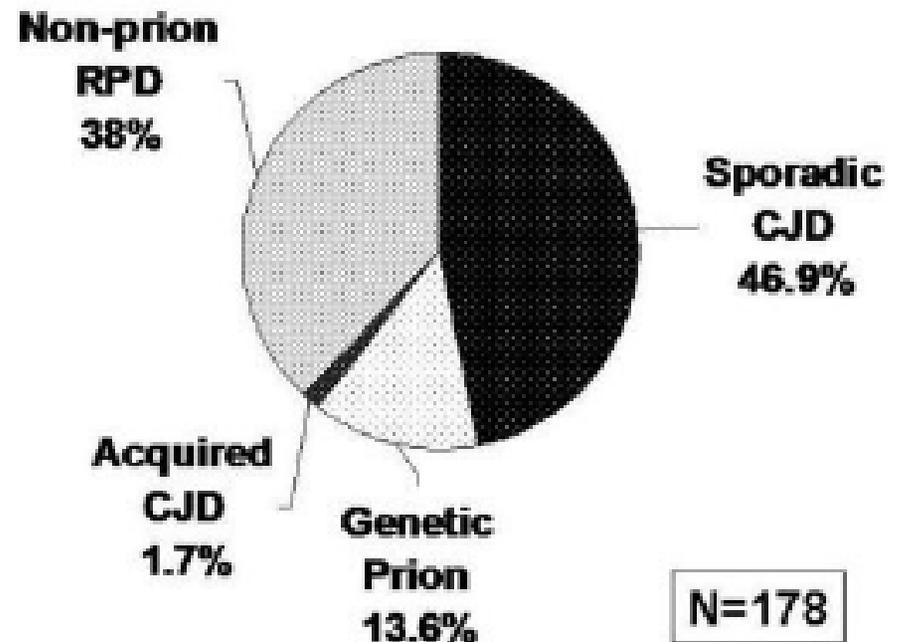
<http://www.bseinquiry.gov.uk/>



- Mechanism remains unknown. Mutation of the prion protein (PrP) gene cause protein misfolding
- A cluster of tangled, nonfunctional plaques of PrP<sup>Sc</sup> aggregate in the brain and proliferate

# CJD Statistics

- **US Incidence: 1-1.5 per million per year**
  - ~300 new cases a year
  - No evidence of change in incidence over the years
- **Three forms:**
  - *Sporadic*: 85%
  - *Genetic*: 14%
    - Gerstmann-Straussler-Scheinker (GSS), Fatal Familial Insomnia (FF)
  - *Acquired*: 1%
    - Iatrogenic or variant
- **Age of onset** - 55-75 years old
- **Median age of onset** – 62 years old
- **Male: Female** - 1:1
- **Median duration** – 4.5 months



Modified from Brown P, et al. *Ann Neurol* 1994 and Geschwind et al., *Ann Neurol*, 2008

# Diagnostic Criteria for Probable CJD

## World Health Organization Revised 1998<sup>19</sup>

Progressive dementia with any two of:

- Myoclonus
- Pyramidal/extrapyramidal
- Visual/cerebellar
- Akinetic mutism

AND

Typical EEG<sup>b</sup>, or if <2-year duration, positive CSF 14-3-3

AND no other condition to explain

MRI = magnetic resonance imaging; EEG = electroencephalogram; CSF = Cerebrospinal fluid.

<sup>a</sup>For example, aphasia, apraxia, acalculia, neglect.

<sup>b</sup>~1-Hz focal or diffuse periodic epileptiform discharges.

## University of California, San Francisco Modified<sup>3,18</sup>

Rapid cognitive decline with any two of:

- Myoclonus
- Pyramidal/extrapyramidal
- Visual
- Cerebellar
- Akinetic mutism
- Other focal higher cortical sign<sup>a</sup>

AND

Typical MRI and/or EEG

AND no other condition to explain

Geschwind MD,  
*Continuum*, 2010

**Possible CJD = 2 clinical signs without typical 14-3-3 or EEG**

# Clinical Signs of CJD

	Presenting	During*
Cognitive	40%	100%
Cerebellar	22%	70%
Constitutional	21%	N/A
Behavioral	20%	N/A
Sensory	9%	N/A
Motor (non-cerebellar)	9%	62%
Visual	7%	N/A

Modified from Rabinovici et al. *Neurology* 2006;  
Geschwind et al., *Ann Neurol*, 2008

**\*Myoclonus = 80%**

# Sensitivity and Specificity of Current Recommended Diagnostic Tests

Test	Sensitivity (%)	Specificity (%)
EEG (PSWCs)	38-64	74-91
CSF 14-3-3	74	95
CSF tau	95	100
MRI with tau	95	100
Biopsy	95	100

“...a positive test result ... should [not] reduce efforts to reach an alternative diagnosis”

**While the recent additions of MRI and other CSF biomarkers (e.g. tau) have improved diagnosis, there continues to remain a need for more reliable, consistent, safe and rapid diagnostic testing**

**Experiences from the Rapidly  
Progressive Dementia Consortium  
(RPDC) at Washington University  
in Saint Louis (WUSTL)**

# The RPDC at WUSTL

- A combined retrospective/prospective review of patients evaluated at BJH between 2005-2014
- Inclusion criteria (n=50)
  - Rapid decline in cognition (< 2 years duration)
  - Absence of another condition on initial evaluation to account for symptoms
  - At least one other symptom to meet WHO criteria for “possible sCJD”

# The RPDC at WUSTL

- Two groups defined
  - “CJD” (n = 35) – patients meeting modified UCSF diagnostic criteria for probable/definite sCJD
  - “RPD” (rapidly progressive dementia, n=15) - a “disease control population”
    - Patients with a pathology proven alternative diagnosis or those eventually diagnosed with an alternative diagnosis after a full clinical assessment
- Compared results of the “recommended” diagnostic testing between the two groups
- Investigated the utility of diffusion tensor imaging (DTI) in hopes of further distinguishing the two group

# Demographics of RPDC Cohort at WUSTL

	<u>CJD</u>	<u>RPD</u>	<u>p</u>
Men (%)	18/35 (51)	9/15 (60)	0.75
Onset to Dx, d (SEM)	221 (42)	149 (22)	0.27
Age at Dx, yrs. (SEM)	62 (2)	65 (4)	0.46
Age Range	38 – 76	25 – 90	

## RPD Diagnoses

AD (4), Malignancy (2), Vascular Dementia (2), Psychiatric (2), Epileptic (2), Dementia with Lewy Bodies, Metabolic, Vasculitis

# Clinical Features of RPDC Cohort at WUSTL

<u>Clinical Signs, %</u>	<u>CJD (n=35)</u>	<u>RPD (n=15)</u>	<u>OR</u>	<u>95% CI</u>	<u>p</u>
Cognitive	100	100			
Extrapyr/Pyram	86	67	3	0.6 - 16	0.14
Akinetic Mutism	46	20	4	0.9 - 18	0.12
Cerebellar	80	13	26	4 - 219	< 0.0001
Visual	26	20	1.4	0.3 - 8	0.99
Higher Cortical	37	27	1.6	0.4 - 8	0.53
Myoclonus	63	47	1.9	0.5 - 8	0.36

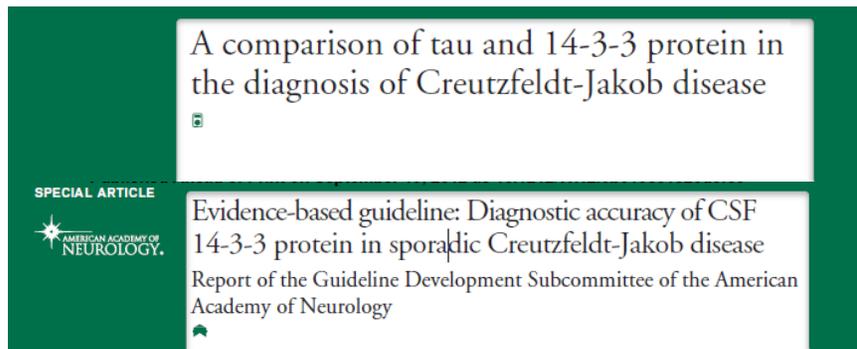
# MRI had Greater Sensitivity and Specificity than EEG in RPDC Cohort at WUSTL

	<u>CJD</u>	<u>RPD</u>	<u>Sens</u>	<u>Spec</u>	<u>OR (CI)</u>	<u>p</u>
PSWC on EEG (%)	32	40	32	60	0.7 (0.2 – 3)	0.7
DWI Changes (%)	94	20	94	80	58 (7 - 715)	< 0.0001

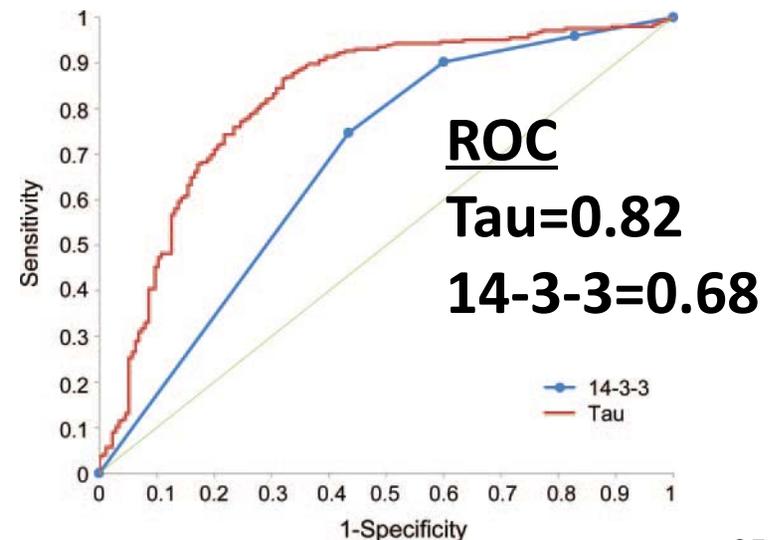
p values derived from 2-tailed Fishers exact

# Comparison of CSF Biomarkers in the RPDC Cohort at WUSTL

	<u>CJD</u>	<u>RPD</u>	<u>Sens</u>	<u>Spec</u>	<u>OR (CI)</u>	<u>p</u>
CSF 14-3-3 “+” (%)	74	29	74	71	7.2 (1.5 – 38)	0.007
CSF Tau “+” (%)	87	14	87	86	41 (5 – 421)	< 0.0001
Mean CSF Tau	4,594	718	NA	NA	NA	0.0004
Tau Range (pg/ml)	440 – 16,131	70 – 3,511	p values derived from 2-tailed Fishers exact or 2-tailed unpaired student t-test (for tau)			



9 studies, 1850 patients, the 14-3-3 pooled sensitivity was 93% and specificity was 80%

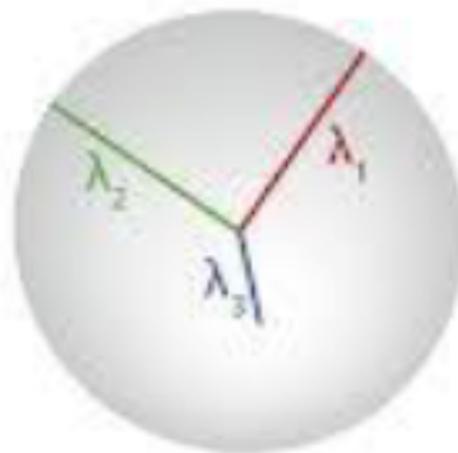
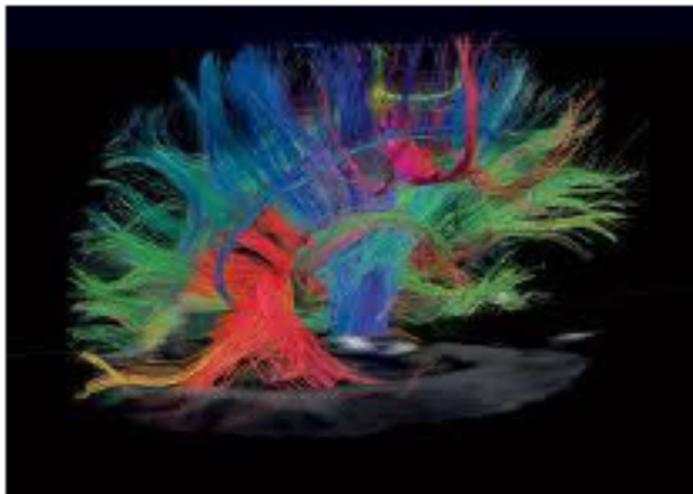


# Influence of Genotype in the RPDC at WUSTL

<u>Codon 129</u> <u>(n=24)</u>	<u>n (%)</u>	<u>Age at onset</u> <u>(yrs)</u>	<u>Onset to Death</u> <u>(d)</u>	<u>“Typical”</u> <u>EEG</u>	<u>14-3-3</u>	<u>tau</u>	<u>MRI</u>
MM1	11 (46)	64	111	7/10	8/8	8/8	11/11
VV1-2	3 (13)	63	138	0/3	3/3	3/3	2/2
MV1-2	4 (17)	62	574*	0/4	1/4	2/4	3/3
MM2	2 (8)	59	336	2/2	0/2	2/2	2/2
VV1	1 (4)	41.5	285	0/1	0/1	1/1	1/1
VV2	1 (4)	73.5	134	0/2	1/1	1/1	0/1
MM 1-2	1 (4)	68	106	0/1	0/1	0/1	N/A
VPSPr	1 (4)	74.5	514	0/1	1/1	1/1	1/1

\* = 267, 292, 297, 1440

# DIFFUSION TENSOR IMAGING (DTI) BASICS



Isotropic

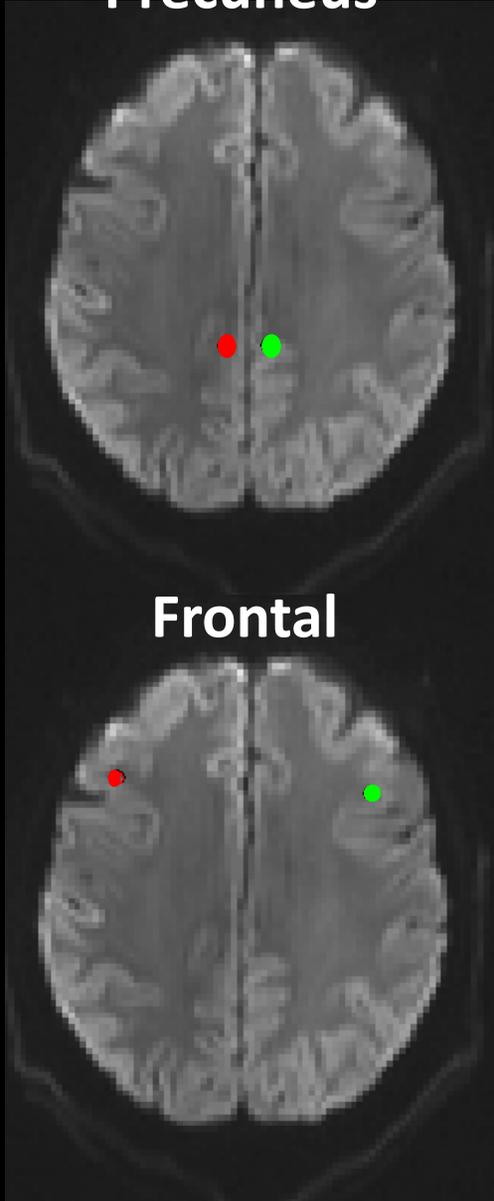


Anisotropic

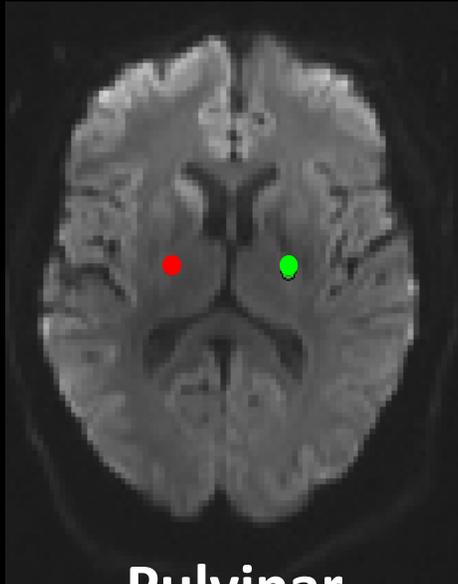
$\lambda_1$  = longitudinal (axial) diffusivity (AD)  
 $(\lambda_2 + \lambda_3)/2$  = radial diffusivity (RD)  
 $(\lambda_1 + \lambda_2 + \lambda_3)/3$  = mean diffusivity (MD)

# Regions of Interest for DTI – Patient 24

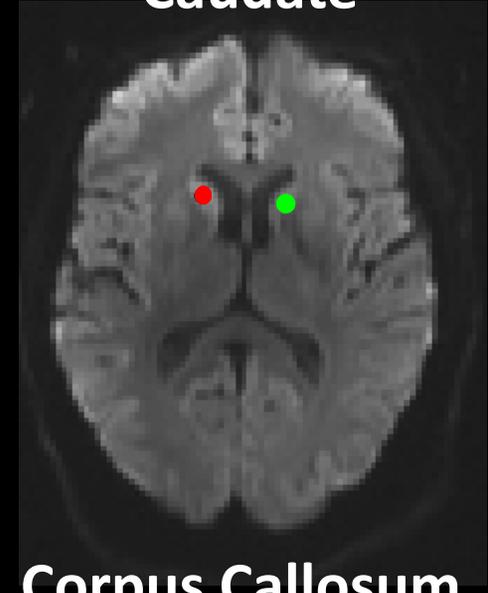
Precuneus



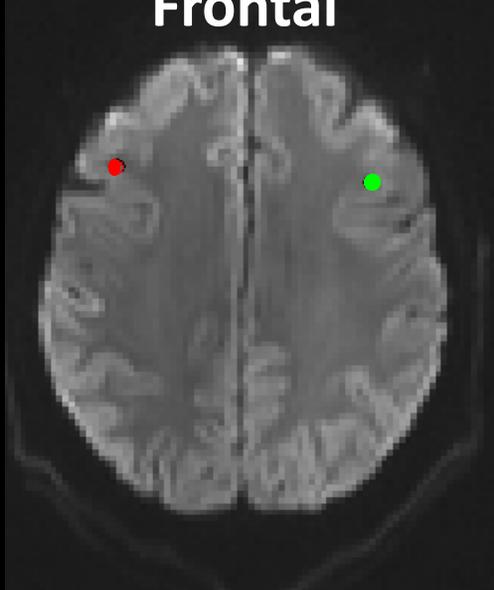
PLIC



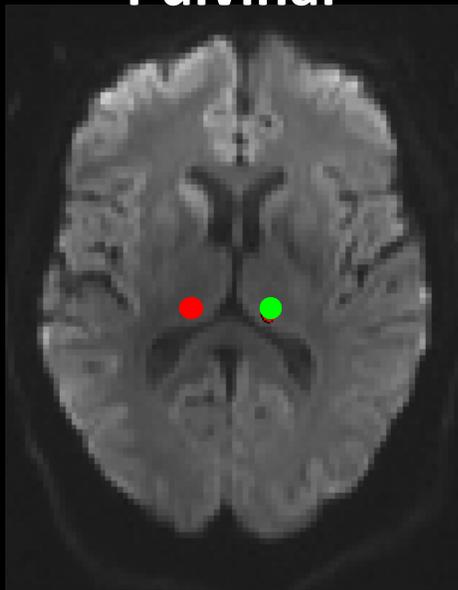
Caudate



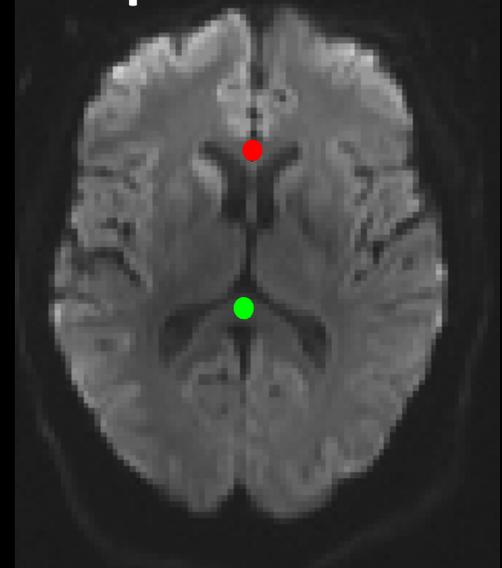
Frontal



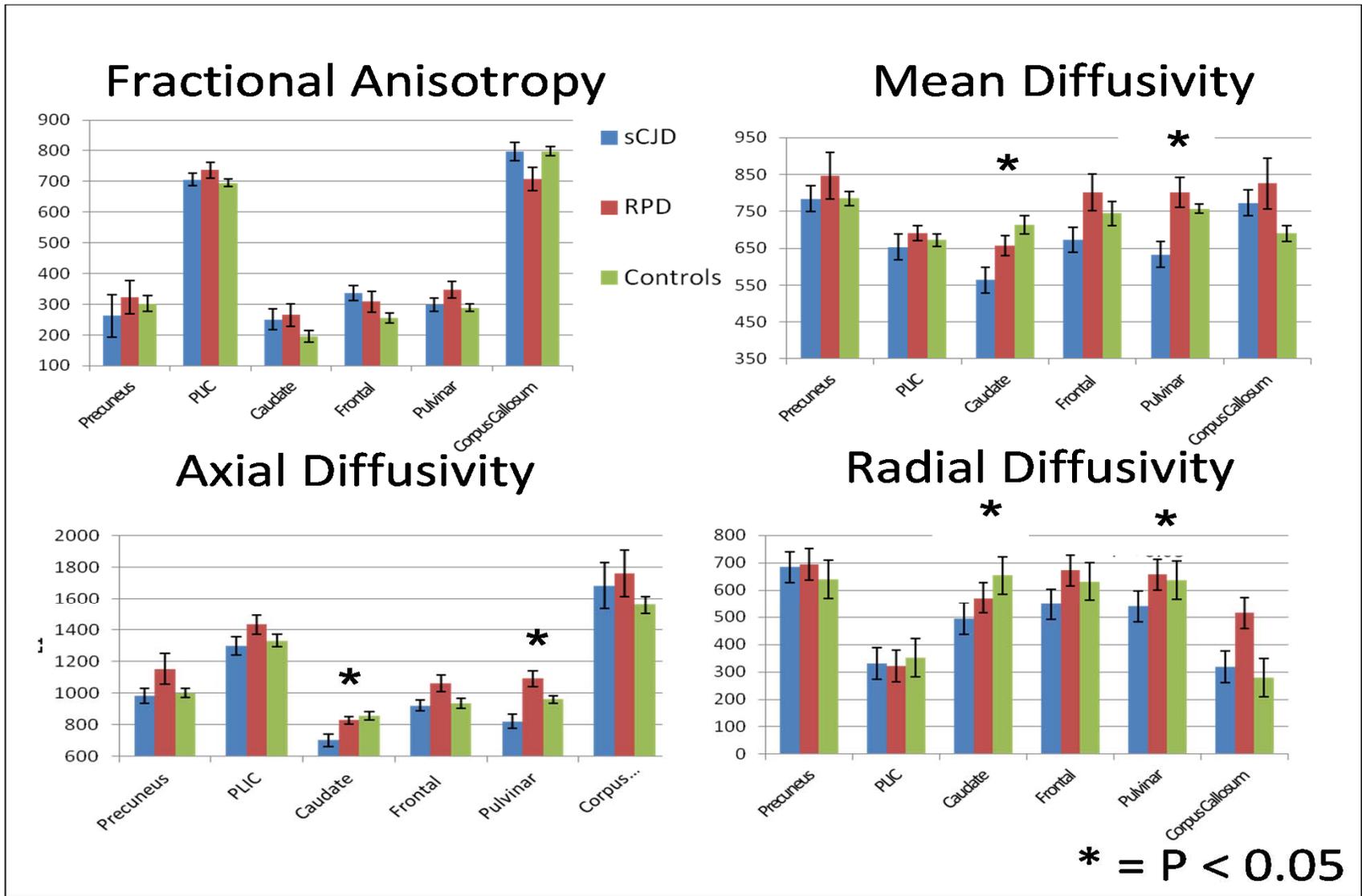
Pulvinar



Corpus Callosum

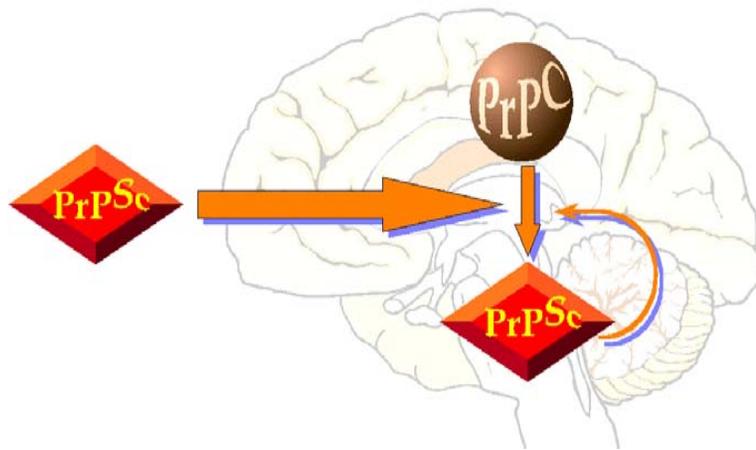


# DTI in CJD



Spongiform vacuoles may impair diffusion of water

# Real-time Quaking Induced Conversion (RT-QUIIC) in CJD



Atarashi et. al, *Nature Medicine*, 2011

- Method for detecting small amounts (fg) of PrP<sup>Sc</sup> in the CSF by using PrP<sup>c</sup> as a substrate for amplification
- CSF samples from 18 definite CJD vs. 35 other neurodegenerative dz
  - 87% sensitive
  - 100% specific
- Now performed on all CSF samples that are tau+ and 14-3-3 + by NPDPSC

# Treatment for CJD Has Been Unsuccessful

- No current therapies for CJD.
- No clinical trials currently being conducted for CJD (Clinicaltrials.gov).
- Recent study using Quinacrine (300 mg per day) did not improve 2-month survival of patients with sCJD, compared with placebo (Geschwind et al., *Neurology*, 2013).
- Recent study using Doxycycline (100 mg per day) was well tolerated but did not significantly affect the course of sCJD (Haik et al., *Lancet Neurol*, 2014).
- Intraventricular administration of pentosan polysulfate (iPPS) did not change overall neuropathological changes in the a sCJD patient (Newman et al., *JNNP*, 2014).

## CARE CONSIDERATIONS

- ⦿ Minimize turning and movement - touch gently
- ⦿ Encourage a calm, quiet approach and environment
- ⦿ Patient may be more aware of activity on one side of the body
- ⦿ Always assume that the patient can hear and understand what is being said
- ⦿ Frequent observations
- ⦿ Quick response to changes
- ⦿ Need for consistency
- ⦿ Facilitate family involvement in the patient's care quickly

## CARE CONSIDERATIONS

- ⦿ Address the physical, nutritional, psychological, educational, spiritual, and social needs of the patient and their family/significant other
- ⦿ Normal social and clinical contact, and non-invasive clinical investigations with CJD patients do not present a risk to healthcare workers, relatives or the community
- ⦿ Contamination of body fluids (no detectable infectivity tissues) poses no greater hazard than for any other patient
- ⦿ Universal precautions
- ⦿ Private room not required for Infection Prevention, but may be appropriate for compassionate reasons
- ⦿ Patient waste should be handled according to country, regional or federal regulations



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## CARE CONSIDERATIONS

- No special precautions are required for feeding utensils, feeding tubes, suction tubes, bed linens, or items used in skin or bed sore care
- Anticipate the possibility of labile psychiatric symptoms e.g. mood swings, hallucinations, or aggressive behavior
- Comfort care (music, touch, talk, etc.)
- Requires special sensitivity to confidentiality of written and verbal communications
- Recognize the potential for the staff to experience stress, sadness and grief

# Thank you for your attention

Questions please contact:  
**bances@wustl.edu**  
**(314) 747-8423**

Link to our list of recommended testing  
[http://neuro.wustl.edu/research/  
researchlabs/anceslaboratory/interests](http://neuro.wustl.edu/research/researchlabs/anceslaboratory/interests)



# CREUTZFELDT-JAKOB DISEASE (CJD) INFECTION PREVENTION PROGRAM

Department of State Health Services (DSHS)

Grand Rounds

April 2, 2014

Austin Texas

# SPEAKER



Deana M. Simpson, RN  
Chief Clinical Transformation Officer  
St. John Providence Health System, Detroit,  
MI

Founder and Director CJD Insight

Impacted Family Member (Genetic CJD)

# MY STORY

## DEDICATION



**Dedicated to my Mom  
and our extended  
family**

- ◉ Mother died in 1998 at the young age of 64 from Genetic CJD (gCJD)
- ◉ Aunt died 2001
- ◉ Cousin died 2004
- ◉ Brother died in 2012
- ◉ Lost 13 family members spanning five generations
- ◉ More to come unless a treatment or cure is found



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## THE FACTS

- ⦿ **There is no treatment/cure - the disease is 100% fatal today**
- ⦿ **Diagnosis may not be made before death**
- ⦿ **Initial diagnosis is often Alzheimers, stroke or unknown neurologic disease**
- ⦿ **Many physicians/clinicians are uninformed about CJD**
- ⦿ **If CJD is not on the death certificate and autopsy not performed - diagnosis may not be counted**
- ⦿ **Stable incidence patterns and absence of recognized transmission support theory of spontaneous occurrence**

# Symptomatic Treatment for CJD

Symptom	Suggested Treatment
Psychosis/Agitation	Low potency neuroleptics (e.g., quetiapine)
Myoclonus/Hyperstartle/ Sleep issues	Long acting benzodiazepines (e.g., diazepam) Anticonvulsants (e.g., valproic acid)
Seizures	Anticonvulsants
Dystonia/Contractures	Passive movement Long acting benzodiazepines
Constipation	Bowel regimen (e.g., ducolax)
Dysphagia/Rumination	Thickener, cueing, positioning

**Behavioral/environmental changes first**

**Start low and go slow**

**Evaluate frequently**

# WORRY LIST

- ◉ Do I have the mutation?
- ◉ Do I get tested?
- ◉ If I do get tested, do I tell my family?
- ◉ If I do get tested and I am positive for mutation, do I tell healthcare providers when I need care?
- ◉ Do I tell my children?
- ◉ If I have the mutation will I die from CJD?
- ◉ What do you mean I can't donate blood or my organs?
- ◉ What about life insurance?
- ◉ What about health insurance?
- ◉ Other life decisions
- ◉ Access to care
- ◉ I will see this again



# GENETIC TESTING: THINGS TO CONSIDER

- ◉ Samples provided can be used for research
- ◉ Ability to deal with a positive result
  - Psychosocial death - potential for family relationships to change
  - Level of uncertainty
  - Hypervigilance
  - Guilt of having passed on to future generations
- ◉ Ability to deal with a negative result
  - "Survivor's Guilt"
  - Will see again
- ◉ Role of fCJD family members
  - Role as advocate
  - Role as caregiver
  - Role as historian
  - Role of educator
  - Role as truth-teller - those who define reality
- ◉ Preparedness
- ◉ Possible prevention of transmission via organ donation or invasive testing





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# IATROGENIC & HEALTH CARE ASSOCIATE EXPOSURE

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## IATROGENIC CASES

- ◉ <1% of the cases - 267 documented cases
- ◉ Due to direct contact with high-risk tissues
- ◉ No new cases since preventive strategies put into place - *until:*

---

- ◉ *Possible* Exposure:

15 patients possibly exposed to rare and fatal brain disease  
(September 2013)

- 8 - New Hampshire
- 2 - Connecticut
- 5 - Massachusetts

# CONFIRMED IATROGENIC CASES WORLD WIDE



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<b>Mode of Infection</b>	<b># of patients</b>	<b>Agent entry into brain</b>	<b>Mean incubation period</b>
<b><u>Surgical Procedures</u></b>			
• Neurosurgery (Surgical Instruments)	4	Intracerebral	20 mo (15-28)
• Stereotactic EEG	2	Intracerebral	18 mo (16-20)
• Corneal Transplant	2	Optic Nerve	17 mo (16-18)
• Dura Mater Grafts	228	Cerebral Surface	5.5 yrs. (1.5-12)
<b><u>Medical Procedures</u></b>			
• Growth Hormone	226	Hematogenous	12 yrs (5-30)
• Gonadotropin	4	Hematogenous	13 yrs (12-16)
• Packed Red Blood Cells	2		

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# BASIS FOR INFECTION PREVENTION GUIDELINES



- Presence of pathogen does not mean that a disease will occur
- Need to complete the steps in “Chain of Infection” to enable transmission
- Patients do not ooze prions
- No instance of transmission acquired through non-iatrogenic environmental contact per CDC & WHO

# BASIS FOR INFECTION PREVENTION GUIDELINES



- Iatrogenic cases are linked to *direct exposure* to prion contaminated CNS tissues
- Prion is challenge to disinfection and sterilization
  - Many conventional products will inactivate the majority of the prions
  - Substrate can survive - Question is - is it pathogenic?
- Transmission via surgical instruments due to improperly cleaned and processed neurosurgical instruments
- No transmission from other procedures

# EVALUATING RISK



- Risk is dependent upon three considerations:
  - The probability that an individual has or will develop CJD
  - The level of infectivity in tissues or fluids of these individuals
  - The nature or route of the exposure to these tissues





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## LEVELS OF INFECTIVITY

### High

Brain

Spinal Cord  
(Dura Matter  
Penetration)

Posterior Eye

Pituitary gland

### Lower

CSF

Kidney

Liver

Lung

Lymph  
nodes/spleen

Placenta

### No Detectable

Adipose tissue **Blood\***

Thyroid gland Urine

Semen Tears

Adrenal gland Feces

Gingival tissue Nasal

mucous

Heart muscle Saliva

Intestine Sweat

Peripheral Nerve

Prostate

Serous exudate

Testis

Milk



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# SURGICAL PROCEDURE CONSIDERATIONS

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## TYPES OF SURGICAL PROCEDURES

- Patients with TSE may develop intercurrent illnesses that may require them to undergo diagnostic or surgical procedures
- Brain Biopsy for diagnostic purposes: CJD or other treatable illness



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## SURGICAL PROCEDURES

- ◉ Inform Infection Prevention team of intention to perform a surgical procedure on any person with confirmed or suspected TSE
- ◉ Schedule in advance to allow for obtaining suitable instruments and equipment (such as single use items)
- ◉ Schedule case at the end of the day

# PRECAUTIONS FOR SURGICAL PROCEDURES



- Perform procedure in an operating room
- Involve the minimum required number of healthcare personnel
- Personnel Protective Equipment:
  - Gloves
  - Mask
  - Visor or goggles
- Use single-use/disposable equipment as follows:
  - Liquid repellent operating gown, over plastic apron
  - Linens and covers
  - Biopsy Kits - disposable

# PRECAUTIONS FOR SURGICAL PROCEDURES



- Cover all non-disposable equipment
- Maintain one-way flow of instruments
- Treat all protective clothing, covers, liquid and solid waste by an approved method
- Mark samples with a "Biohazard" label
- Clean all surfaces according to recommendations



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# REPROCESSING OF INSTRUMENTS

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## KEY POINTS



- Asymptomatic Patient - Minimal Risk
- Symptomatic Patient - recommend following WHO guidelines
- Regular sterilization is somewhat effective
  - Each time instruments are put through a cycle, risk of infectivity decreases
- Transmissibility is rare

# QUARANTINE OF SURGICAL INSTRUMENTS



- ◉ Used while determining the final diagnosis of persons suspected of TSE
- ◉ Avoids needless destruction of instruments
- ◉ Must be cleaned by approved methods, sterilized, packed, dated and “Hazard” labeled, and stored in specially marked rigid sealed containers

# HANDLING OF SURGICAL INSTRUMENTS



- Instruments should be kept moist until cleaned and decontaminated (i.e. enzymatic cleaner; H<sub>2</sub>O)
- Instruments should be cleaned as soon as possible after use to minimize drying of tissues, blood and body fluids
- Avoid mixing instruments used on no detectable infectivity tissues with those used on high and lower infectivity tissues
- Recycle durable items for re-use only after TSE decontamination methods are carried out

# HANDLING OF SURGICAL INSTRUMENTS



- ◉ Instruments to be cleaned in automated mechanical processors must follow approved methods before processing
- ◉ The washers should be run through an empty cycle before any future routine use
- ◉ Cover work surfaces with disposable material which can then be removed and incinerated (With RMW)
- ◉ Be familiar with and observe safety guidelines when working with hazardous chemicals

# DESTRUCTION OF SURGICAL INSTRUMENTS



- Destruction of instruments is not recommended if they can be processed according to the guidelines
- If disposable, isolate in a rigid clinical waste container, labeled "hazardous"
- Transport to the appropriate area for removal to the incinerator or for transport by a hauler to a facility for incineration

# INFECTION PREVENTION GUIDELINES (BASED ON THE KNOWN AND UNKNOWN)



- Common disinfectants are ineffective against the prions, including:
  - sterilization
  - alcohol
  - boiling
  - dry heat
  - formalin and formaldehyde
  - Steam
  - Glutaraldehyde
  - Hydrogen peroxide
  - Phenolics

# EFFECTIVE DISINFECTANTS

(>4 LOG<sub>10</sub> DECREASE IN LD<sub>50</sub> WITH 1 HOUR)



- Sodium hydroxide  
1 N for 1h (variable results)
- Sodium hypochlorite  
5000 ppm for 15m
- Guanidine thiocyanate  
4M
- Phenolic (LpH)  
0.9% for 30m

## MEDICAL DEVICES



- ◉ Do not allow tissue/body fluids to dry on instruments (e.g., place in liquid)
- ◉ Some decontamination procedures (e.g., aldehydes) fix protein and this may impede effectiveness of processes
- ◉ Do not exceed 134°C
- ◉ Clean instruments but prevent exposure
- ◉ Assess risk of patient, tissue and device
- ◉ Choose effective process

# EFFECTIVE PROCESSES: STERILIZATION



- ◉ **Note:** Before instruments are immersed in sodium hypochlorite, the instrument manufacturer should be consulted about the instrument's tolerance of exposure to sodium hypochlorite
  - ◉ Instruments should be decontaminated by a combination of the chemical and recommended autoclaving methods before subjecting them to cleaning and processing in a washer- sterilizer and a sterilizer.
- 
- ◉ **Methods are listed in order of more to less severe treatments:**
    1. Immerse in a pan containing 1N sodium hydroxide (NaOH) and heat in gravity displacement autoclave to 121° C for 30 min; clean; rinse in water; and subject to routine sterilization according to manufacturer's instructions
    2. Immerse in 1NOH or sodium hypochlorite (20,000 ppm available chlorine for 1 hour; transfer instruments to water; heat in a gravity displacement autoclave at 121° C for 1 hour; clean; and subject to routine sterilization according to manufacturer's instructions
    3. Immerse in 1N NaOH or sodium hypochlorite (20,000 ppm available chlorine) for 1 hours; remove and rinse in water, and then transfer to open pan and heat in a gravity displacement sterilizer (121°C) or porous load (132°C) autoclave for 1 hour; clean; and subject to routine sterilization according to manufacturer's instructions



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# INFECTION PREVENTION: ENVIRONMENT

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# ENVIRONMENTAL SURFACES



- NO evidence of transmission from environmental surfaces If contaminated with blood or body fluids
- Regular thorough cleaning with OSHA approved disinfectant, detergents
- For spills: Apply 1 molar sodium hydroxide for 1 hour or Sodium hypochlorite 8500 ppm for 30 minutes (Evaluate risk)

# SPECIAL PROCEDURES



- ◎ Wear personal protective equipment when indicated to protect against exposure to high risk tissue
  - Spinal tap
  - Brain biopsy
  - Autopsy, especially if brain is to be examined
  
- ◎ Avoid puncture wounds

# IN THE MORGUE



- Restrict autopsy to removal of the brain
- Use mechanical saws
- Avoid penetrating wounds
- Avoid table surface contamination from fluids by using non-permeable, disposable sheets
- Fixed brain and the formaldehyde solutions are considered infectious
- Incinerate disposable materials
- Wet surface with bleach (1:2 dilution) or a 1-2 N NaOH solution for 1-2 hours
- Rinse thoroughly

# IN THE MORGUE



- Take care to avoid exposure
- **Percutaneous** Exposure to CSF or brain tissue of an infected individual
  - Rinse the wound with 0.5% (1-5) dilution of sodium hypochlorite or 1 N of sodium hydroxide for several minutes, then wash with soap and water - WHO Guidelines
- **Mucous Membrane Exposure**
  - Irrigate mucous membranes with saline for several minutes

# WASTE



- No evidence of transmission from handling medical waste
- Follow local or State Guidelines
- Use leak proof containers
- Incinerate pathological waste and contaminated disposable materials as appropriate
- Discharge liquids into sanitary sewer

# CONCLUSION



- ◉ Epidemiologic evidence suggests Health Care Associate CJD transmission via medical devices is very rare
- ◉ Guidelines are based on epidemiologic evidence, tissue infectivity, risk of disease via medical devices and inactivation data
- ◉ Risk assessment based on patient tissue and device
- ◉ Only critical/semi critical devices contacting high risk tissue from high risk patients require special prion reprocessing



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# POST EXPOSURE MANAGEMENT

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# OCCUPATIONAL EXPOSURE



- **NOTE:** No case of human TSE is known to have occurred through occupational accident or injury
- Cases of CJD in healthcare workers have been reported in which a link to occupational exposure is suggested
- Prudent to take a precautionary approach

# POST EXPOSURE MANAGEMENT



- Contamination of unbroken skin with internal body fluids or tissues:
  - Wash with detergent and abundant quantities of warm water (avoid scrubbing)
  - Rinse, and dry
  - Brief exposure (1 minute, to 0.1N NaOH or a 1:10 dilution of bleach) can be considered for maximum safety
  
- Needle sticks or lacerations
  - Gently encourage bleeding
  - Wash (avoid scrubbing) with warm soapy water, rinse, and dry
  - Cover with a waterproof dressing.
  - Report the injury according to normal procedures for your hospital

# POST EXPOSURE MANAGEMENT



- Splashes into the eye or mouth:
  - Irrigate with either saline (eye) or tap water (mouth)
  - Report according to normal procedures for your hospital
  
- Health and safety guidelines mandate reporting of injuries, and records should be kept for no less than 20 years



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# CLOSING

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## WHAT CAN YOU DO?

- ◉ Become educated
- ◉ Provide Compassionate Care/Support
- ◉ Act as Patient/Family/Significant Other Advocate
- ◉ Assist in educating and bringing awareness to colleagues
- ◉ Assist in identifying and/or become a physician champion

# RESOURCES: CJD FOUNDATION



- ◉ **Our mission is to support families and loved ones touched by CJD**
- ◉ One very important goal - track ALL CASES of CJD both suspected and confirmed - the ONLY organization keeping anecdotal information and statistics
- ◉ **Confidential Toll-Free Helpline - 1800 659-1991** answered 9-5 EST Monday through Friday, and calls returned usually within 1 hour on evenings and weekends.
- ◉ Website - [www.cjdfoundation.org](http://www.cjdfoundation.org)
- ◉ Email - [help@cjdfoundation.org](mailto:help@cjdfoundation.org)
- ◉ New Education programs:
  - Funeral Professional/Embalmers Education
  - Medical Education
- ◉ Free - pamphlets, tri-folds, DVDs, podcasts



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## RESOURCES: NPDPSC

- **The National *Prion* Disease Pathology *Surveillance* Center (NPDPSC)**
  - Established in 1997
  - Division of Neuropathology of Case Western Reserve University
  
- **Services:**
  - Tests CSF
  - Examines brain tissue
  - Genetic testing (blood vs. brain tissue)
  - Provides a definitive diagnosis of CJD and type
  
- **Autopsy (brain only) is at no cost to families - to any suspected or confirmed CJD case**
  - Myths about autopsy:
    - There can be no viewing at the funeral home. **FALSE**
    - Embalming is not possible. **FALSE**
    - The funeral will be delayed by days. **FALSE**

## RESOURCES: WHO



- The World Health Organization (WHO)
  - <http://www.who.int/en/>

# RESOURCES: CDC



## ○ The Centers for Disease Control and Prevention (CDC)

- The CDC is one of the major operating components of the Department of Health and Human Services
- **CDC's Mission** is to collaborate to create the expertise, information, and tools that people and communities need to protect their health - through health promotion, prevention of disease, injury and disability, and preparedness for new health threats.
- <http://www.cdc.gov/>

## ○ Resource Contact

- Ryan Maddox, PhD  
Epidemiologist  
Phone: 404-639-3838  
E-mail: [rmaddox@cdc.gov](mailto:rmaddox@cdc.gov)



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## RESOURCES: OTHER

- ◉ **CJD Insight - Familial CJD** - Deana Simpson, RN and Familial CJD Family Member  
Cell: 586-914-2215  
E-Mail: [deana.simpson@stjohn.org](mailto:deana.simpson@stjohn.org)
- ◉ **Infection Prevention** - Marie Kassai, RN, MPH, CIC  
Cell: 201-406-1430  
E-Mail: [mariek43@optonline.net](mailto:mariek43@optonline.net)
- ◉ **Funeral Home Services** - Robert Kassai, AS, BS  
Funeral Home Director  
E-Mail: [RJD793@aol.com](mailto:RJD793@aol.com)  
Home: 973-337-1058  
Cell: 201-406-1442

# Questions and Answers



Remote sites can send in questions by typing in the *GoToWebinar* chat box or email [GrandRounds@dshs.state.tx.us](mailto:GrandRounds@dshs.state.tx.us).

For those in the auditorium, please come to the microphone to ask your question.

Michael P. Fischer, MD, MPH & TM  
Emerging and Acute Infectious Disease Branch,  
Infectious Disease Control Unit, DSHS

# Our Next Grand Rounds

April 9

## Telepsychiatry: Breaking Barriers

**Presenter: Dr. Avrim Fishkind, president and CEO of JSA Health Telepsychiatry and past president of the American Association of Emergency Psychiatry**

