ABCD of CJD

(the big picture of Creutzfeldt-Jakob disease)

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Canadian Dementia Resource and Knowledge Exchange

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Presentation goals

- Explain: prion diseases
- Explain CJD Surveillance System (CJDS)
- Discuss our collaboration

"The Alzheimer Society provides support, information and education to people with Alzheimer's disease and related dementias, families, physicians and health-care providers" (Alzheimer Society of Canada website, Nov. 2011).

You answer the phone on a Monday morning and the husband of a suspect CJD patient says he has several questions about CJD – he needs to speak to someone before he sees the doctor later today. He says his wife's disease is progressing rapidly, the 14-3-3 protein test was positive and the doctor asked him to meet him to discuss test results, genetic testing and a possible autopsy

How comfortable do you feel answering his questions?

0 not comfortable

1

2

3

5 very comfortable

CJD:

- Rare degenerative brain disease
- Rapid progressive decline
- Always fatal
- Transmissible →notifiable disease
- Cause of inaccurate information & myths

CJD

Rare brain disease…

Rate

- ~1 case per million population in Canada

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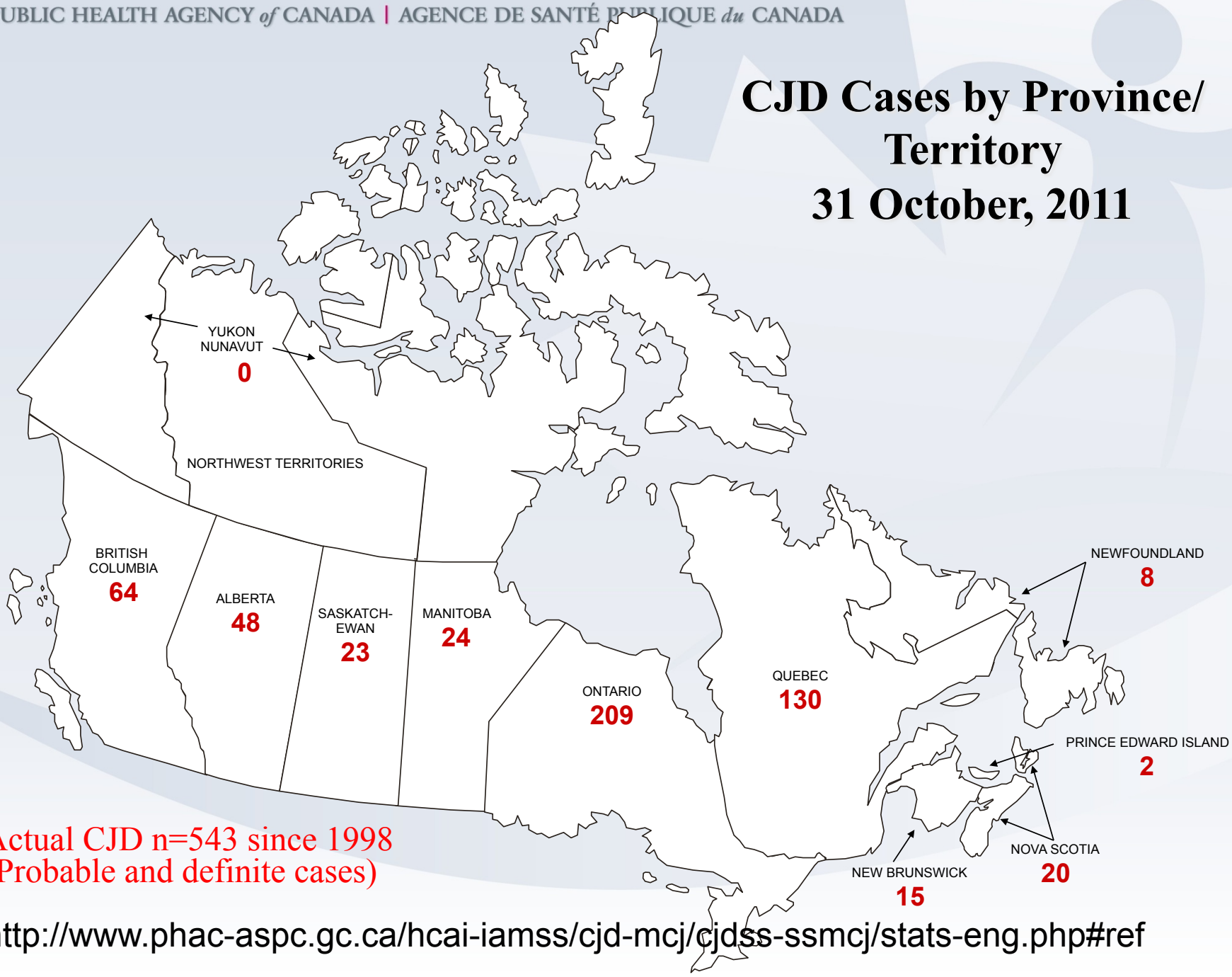
CJD Cases by Province/ Territory 31 October, 2011



Actual CJD n=543 since 1998
(Probable and definite cases)

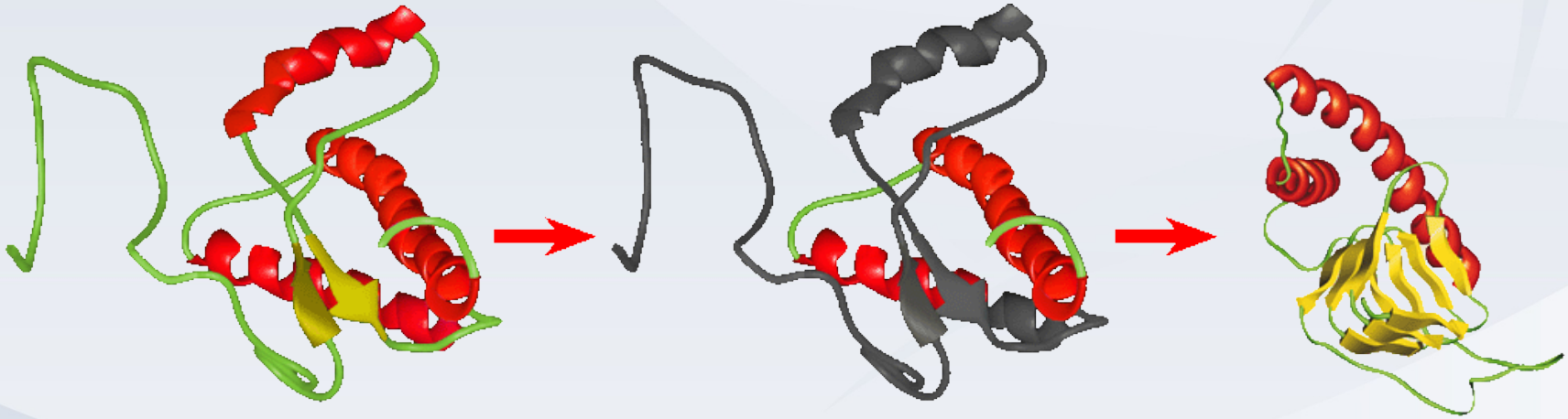
http://www.phac-aspc.gc.ca/hcai-iamss/cjd-mcj/cjdss-ssmcj/stats-eng.php#ref

Infectious agent

- Prion protein – 2 shapes →normal and abnormal
- Abnormal shape→ associated with prion diseases

Misfolded protein→cascading effect

(courtesy Dr. G. Jansen)



Symptoms

Depends on:

- region of the brain affected
- type of CJD

Rapid decline with symptoms of:

- Dementia
- Ataxia
- Myoclonus
- Etc.

Treatment

- No cure
- Some experimental clinical trials
- Depends on person`s symptoms and views of the family and type of institution/ home

Types of CJD

- Sporadic
- Genetic
- Acquired

Sporadic

- Cause unknown
- 85% of cases
- Mostly > 50 y.o. (mostly 60-70)
- Rapidly progressive dementia
- Duration < 24 months (median 6 mo)
- Cerebellar ataxia
- Myoclonus
- Other:
  - (extra)pyramidal signs
  - central visual loss
  - akinetic mutism

Genetic CJD

- Familial
- GSS (Gerstmann-Straussler-Scheinker)
- FFI (Fatal Familial Insomnia)

Genetic (cont.)

- 7% of Canadian cases
- Autosomal dominant →50 %
- Like sCJD clinically → gene mutation

Acquired CJD

- Kuru
- Iatrogenic
- Variant

Kuru (Courtesy Dr. G. Jansen)

Funeral ritual: cannibalism

Iatrogenic CJD

Related to some medical procedures involving certain tissues

Iatrogenic CJD (cont.)

- Occurred when today's decontamination methods and donor screening did not exist
- 4 cases in Canada

Variant CJD

- Related to BSE contaminated meat
- Blood transfusions from a vCJD donor

Variant CJD (cont.)

(Courtesy, Dr. G. Jansen)

- 65% →onset psychiatric presentation:
  - Younger onset (mean 27 y.o.)
  - Behavioural/personality changes
  - Attention deficit
  - Depression
- Later weeks - months:
  - Dysaesthesia
  - Ataxia
  - Myoclonus
  - Progressive dementia

sCJD Tissue infectivity (PHAC, 2007)

- High
- Low
- No detected infectivity

sCJD High Infectivity Tissues

(PHAC, 2007)

- Brain
- Dura mater
- Pituitary gland
- Posterior eye (including optic nerve and retina)
- Spinal cord
- Cranial and spinal cord ganglia
  (including dorsal root ganglia and trigeminal ganglia)

sCJD Low infectivity tissue (PHAC, 2007) (cont.)

- Cerebrospinal fluid (CSF)
- Anterior eye (includes cornea)
- Kidney
- Liver
- Lung
- Lymph nodes
- Placenta
- Spleen

(sCJD) No Detected Infectivity Tissues (PHAC, 2007)

- Adipose tissue
- Adrenal gland
- Appendix
- Blood
- Blood vessels
- Bone marrow
- Breast milk
- Dental pulp
- Epididymis
- Feces
- Gingival tissue
- Heart muscle
- Intestine
- Ileum
- Jejunum
- Large intestine
- Nasal mucous
- Oesophagus
- Ovary
- Pericardium
- Peripheral nerves
- Placental fluids
- Prostate
- Saliva
- Semen
- Seminal vesicle
- Skeletal muscle
- Skin
- Sweat
- Tears
- Testis
- Thymus
- Thyroid gland
- Tongue
- Tonsil
- Trachea
- Urine
- Uterus

Mr Smith is a construction worker and says he has cuts on his hands. He takes care of his wife at home including feeding and toileting. Their daughter-in-law is expecting their first child. He asks if they are at risk of catching CJD?

Are the people living in his home at risk of catching CJD?

a) No-If gloves and masks are worn

b) No- No precautions needed

c) Yes, because CJD is transmissible

No detected infectivity tissue (cont.)

- Ø CJD precautions for social contact with the person
- Ø CJD precautions for routine patient care
- Reprocess instruments, clean surfaces as usual

CJD precautions (PHAC, 2007)

- Recommended by WHO (http://www.who.int/bloodproducts/tablestissueinfectivity.pdf)
- Based→tissue infectivity and type of instrument/surface
- Discard instruments or 4 step CJD decontamination

CJD precautions (cont.)

- OR
- Lab
- Funeral services workers

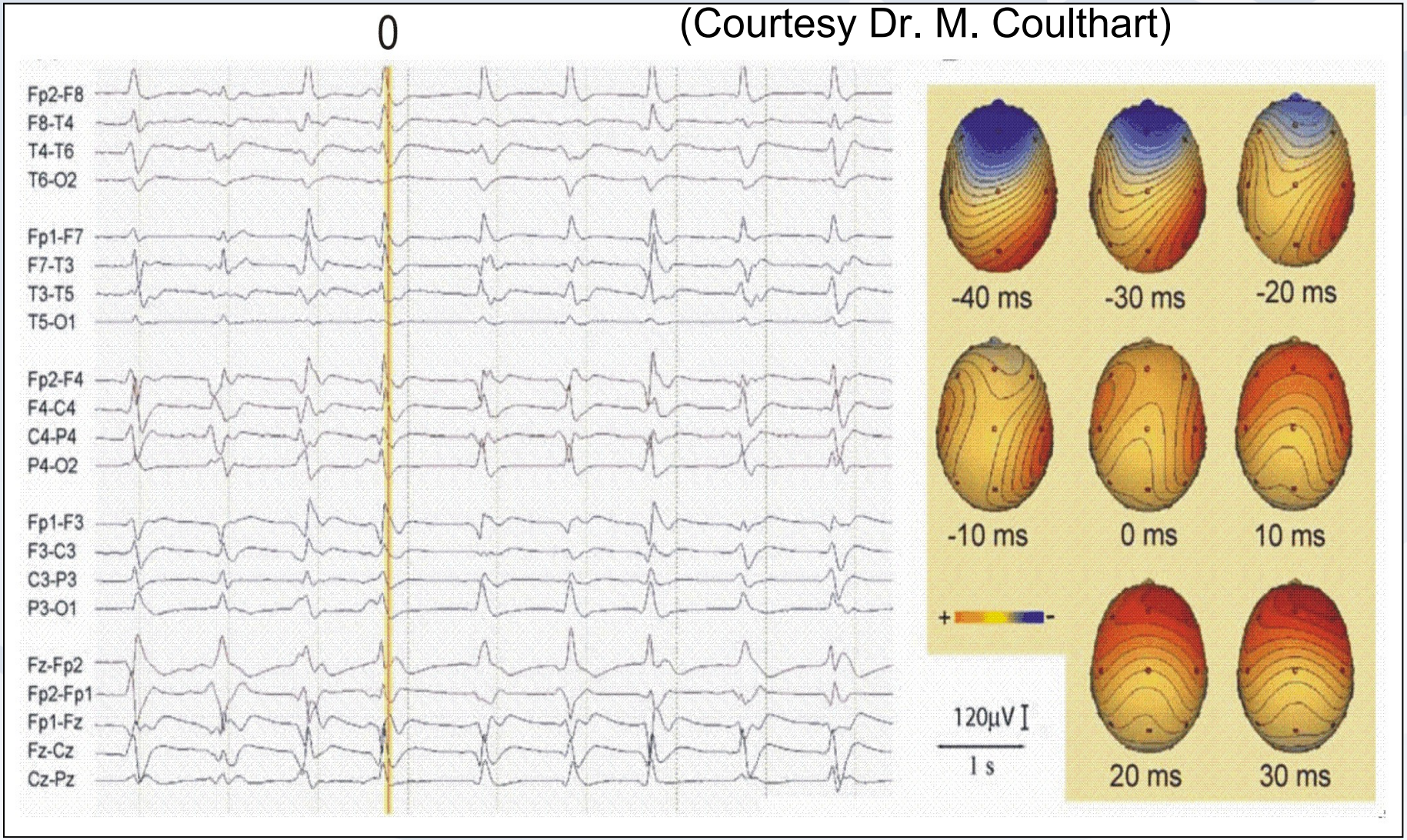
Tests results…

Blood tests

- No blood test to diagnose CJD
- Genetic test to find genetic mutation

EEG

- May show changes « periodic sharp wave complexes »
- Other conditions too
- Not useful for variant CJD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(Courtesy Dr. M. Coulthart)
Fp2-F8
F8-T4
T4-T6
T6-O2
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F4
F4-C4
C4-P4
P4-O2
Fp1-F3
F3-C3
C3-P3
P3-O1
Fz-Fp2
Fp2-Fp1
Fp1-Fz
Fz-Cz
Cz-Pz
-40 ms
-30 ms
-20 ms
-10 ms
0 ms
10 ms
+
-
120µV
1 s
20 ms
30 ms

MRI

- Important to rule-out other conditions
- Particular MRI changes: strong indication of CJD

(courtesy Dr. M. Coulthart)

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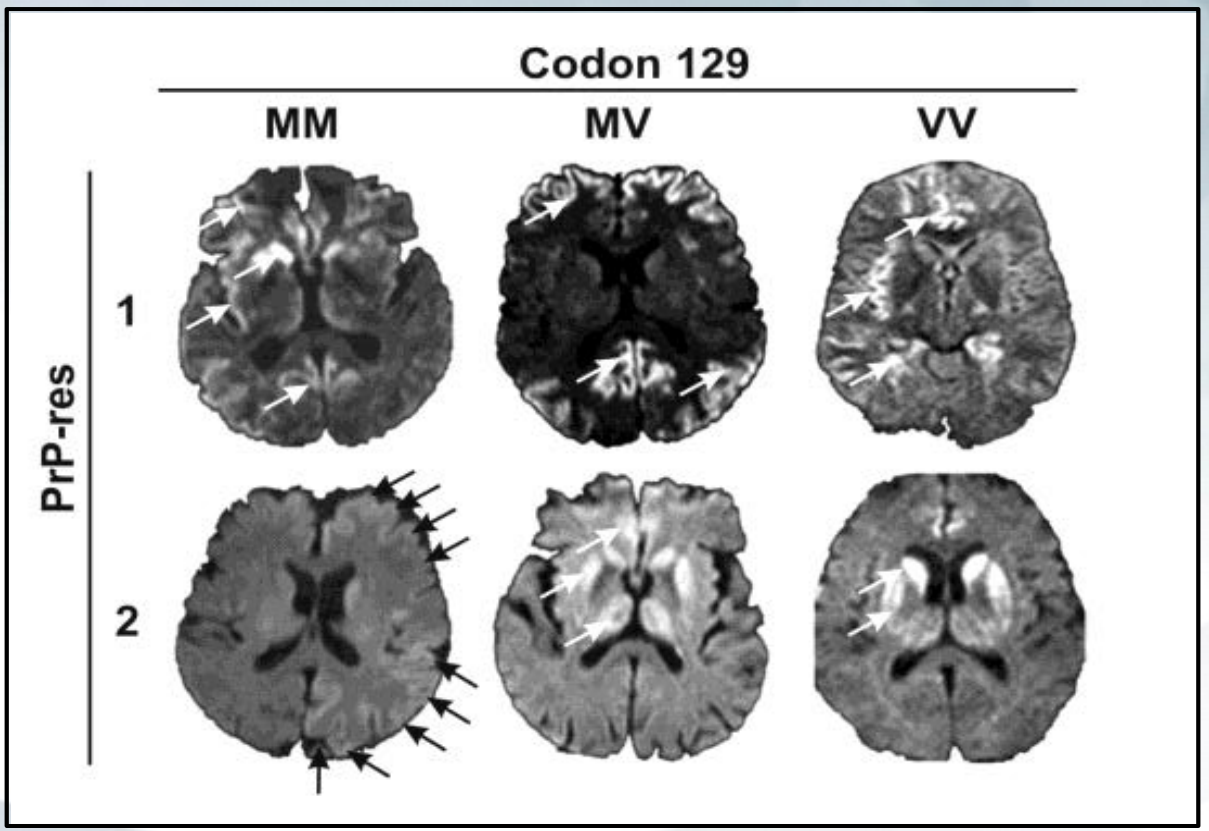
3. MRI: lesion profiles (probable sporadic)



Meissner B et al 2009, Neurology 72:1994

CT

- Rule-out other conditions
- Does not show distinctive changes seen on MRI

Lumbar puncture

- Done to exclude infection (viral, bacterial encephalitis) of the brain
- 14-3-3, tau and S100B protein tests→CSF to NML in Winnipeg

CSF,14-3-3 protein test (cont.)

- Sensitivity 90%
- Specificity 70%
- Result→ positive or negative

14-3-3 + (cont.)

→ Rapid neuron loss

Examples of conditions with 14-3-3+

- Alzheimer`s disease
- Cerebral vasculitis confirmed by biopsy
- Dementia with parkisonism
- Frontotemporal dementia
- Hydrocephalus
- Hypercalcemia
- Hypothyroidism
- Lewy bodies dementia
- Multiple infarcts
- Vascular dementia
- Almost everything “brain damage-like” (Jansen, 2011)

14-3-3+

- Can make difference between classifying as possible and probable CJD

Sometimes we find surprises

- Good clinical picture
- 14-3-3 positive

.....Not CJD

New protein markers at NML:

- Tau protein
- S100B

Tonsil biopsy

- May be useful in diagnosis of variant CJD
- Not useful for sporadic CJD
- Instruments→ CJD precautions

Brain biopsy

- Pt alive
- Not done routinely for CJD
- Can help to exclude other treatable dx
- Instruments→CJD precautions→ destroyed

Mr. Smith is wondering why they cannot just do a brain biopsy and get a diagnosis of CJD.

What do you tell Mr. Smith?

a) Negative biopsy cannot exclude CJD
b) Biopsy best way to confirm diagnosis

Brain biopsy (cont.)

- If biopsy +→ CJD+
- If biopsy - → CJD not excluded

Mr Smith will be discussing the topic of autopsy with the doctor later today. He asks you how much the autopsy costs. What do you tell him?

How much will the autopsy cost?

a) *The family pays for the autopsy and the government will reimburse them*
b) *The province pays for the autopsy*
c) *With a signed consent from the next of kin, the CJD Surveillance System pays for the autopsy*

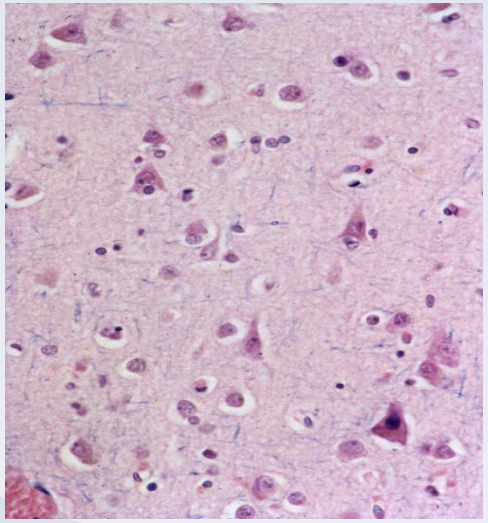
Autopsy

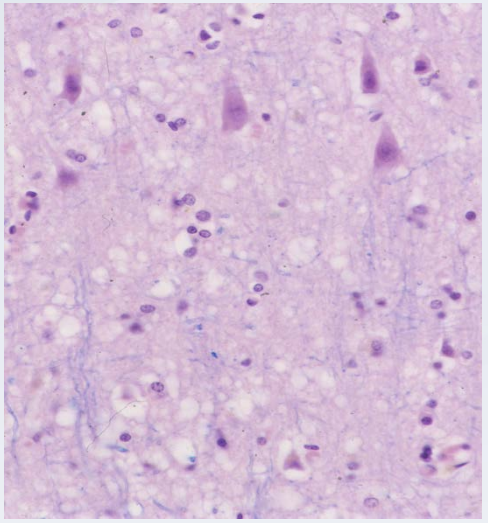
- Brain-only
- Best way to confirm diagnosis
- CJDSS consent required
- Performed in certain institutions, reviewed/ diagnosed in Ottawa

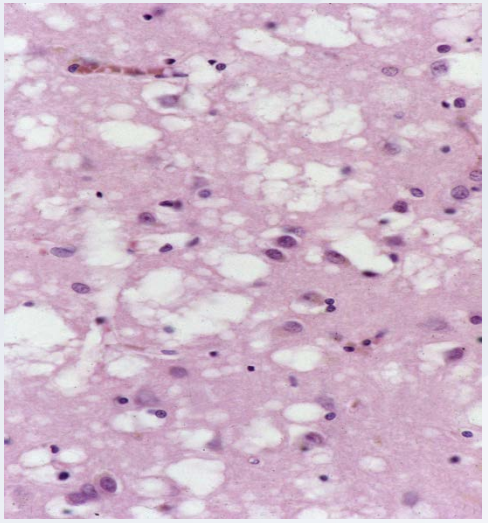
Transmissible spongiform encephalopathy

(courtesy Dr. G. Jansen)

Tissue looks like a sponge







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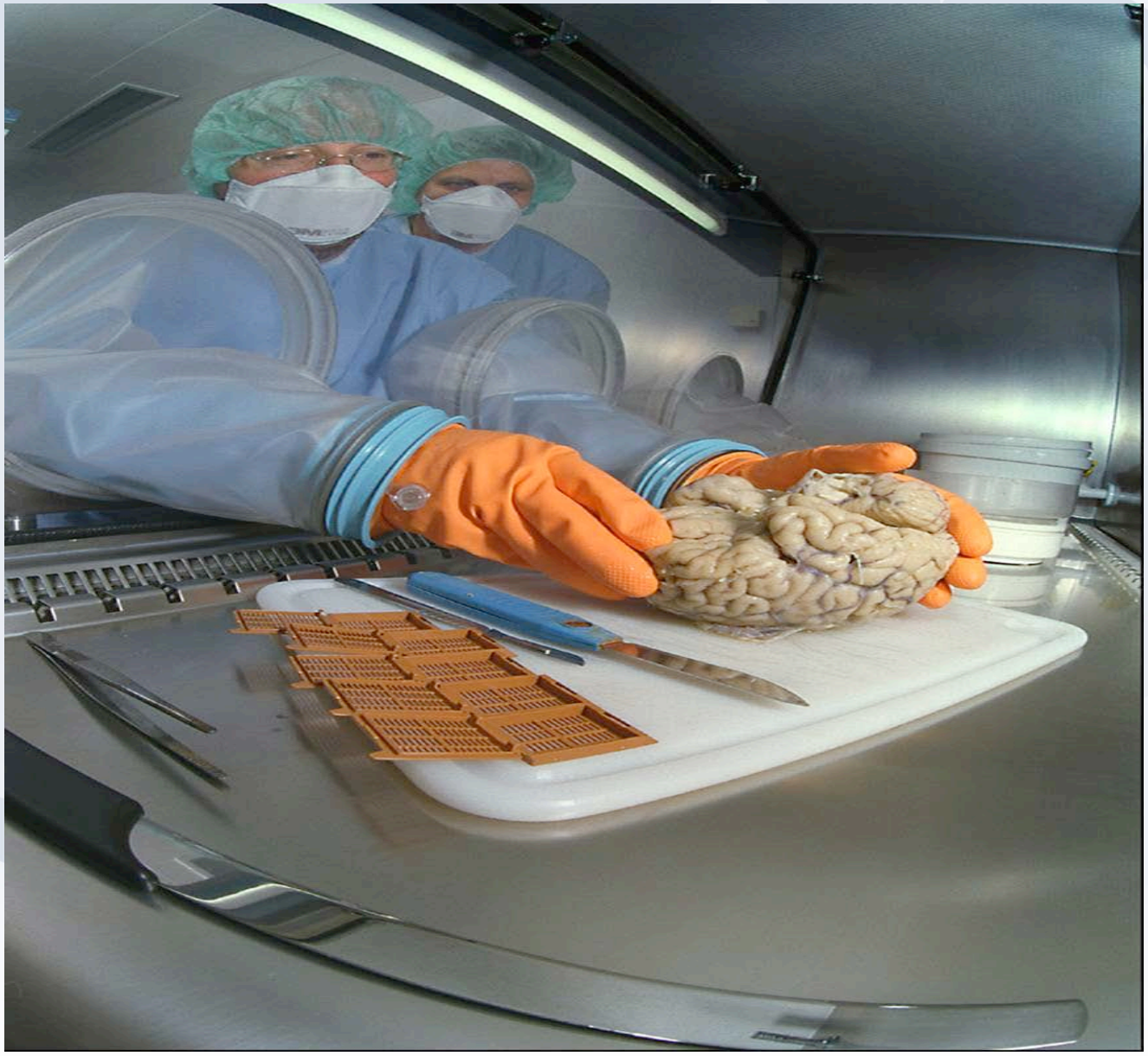

What is the CJDSS?

- Canadian CJD Surveillance System
- Federal government
- Ottawa and Winnipeg laboratories
- Active surveillance since 1998
- Study of epidemiology of CJD in Canada and risk factors
- Protect public from risks

What the CJDSS does:

- 14-3-3, tau, S100B CSF protein tests
- Genetic testing
- Neuropathology (biopsy and autopsy)
- Family interview, medical record review
- Support to laboratories, health providers
- Outreach and education

EuroCJD/CJDSS surveillance definitions
EuroCJD: http://www.eurocjd.ed.ac.uk

- Possible CJD
- Probable CJD
- Definite CJD

Diagnostic criteria for sporadic CJD (EuroCJD/Dr. G.Jansen, 2010)

1.1 Definite:
neuropathology/immunocytochemically confirmed

1.2 Probable:
1.2.1 I + two of II + III
OR
1.2.2 I + two of II + IV
OR
1.2.3 Possible + positive 14-3-3

1.3 Possible:
I + two of II + duration < 2 years

I Rapidly progressive dementia
II A Myoclonus
B Visual or cerebellar problems
C Pyramidal or extrapyramidal features
D Akinetic mutism
III Typical EEG
IV High signal in caudate/putamen on MRI brain scan

Variant CJD dx criteria (WHO)

I A Progressive neuropsychiatric disorder
B Duration of illness > 6 months
C Routine investigations do not suggest an alternative diagnosis
D No hx of potential iatrogenic exposure
E No evidence of a familial form of TSE

II A Early psychiatric symptoms
B Persistent painful sensory symptoms
C Ataxia
D Myoclonus or chorea or dystonia
E Dementia

III A EEG without typical periodic sharp waves of sporadic CJD (or no EEG)
B MRI with bilateral symmetrical pulvinar high signal

IV Tonsil bx +

Definite: I A and neuropathological confirmation of vCJD
Probable: I and 4/5 of II and IIIA and IIIB OR I and IV A
Possible: I and 4/5 of II and III A

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You answer the phone on a Friday morning and the husband of a suspect CJD patient calls you saying he has many questions – he saw on the Alzheimer Society of Canada website that you give information about all types of dementia, including CJD. He wants to speak to someone before he sees the doctor later today. He says his wife's disease is progressing rapidly, the 14-3-3 protein test was negative and the doctor asked him to meet him to discuss test results, genetic testing and a possible autopsy.

How comfortable do you feel answering his questions?

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References

- EuroCJD: http://www.eurocjd.ed.ac.uk
- Public Health Agency of Canada (2007). *CJD and human prion diseases: http://www.phac-aspc.gc.ca/hcai-iamss/pdf/cjd_prion_disease-eng.pdf*
- Public Health Agency of Canada (2007). *Classic Creutzfeldt-Jakob disease in Canada. Quick reference guide. http://www.phac-aspc.gc.ca/nois-sinp/cjd/cjd-eng.php*
- World health organization (WHO), (2010). *WHO tables on tissue infectivity distribution in TSEs. http://www.who.int/bloodproducts/tablestissueinfectivity.pdf*

Une autre ressource pour vous – Another resource for you

Contactez-nous si vous avez des questions

Contact us anytime if questions from staff / family

To subscribe to the CJDSS newsletter:

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