



Prion infections a crash course

28th IPFA/PEI workshop on blood-borne pathogens
Porto, September 21st 2022

Hans L. Zaaijer, medical microbiologist

Sanquin Blood Supply Foundation - Blood-borne Infections

Amsterdam University Medical Center - Clinical Virology

Amsterdam NL

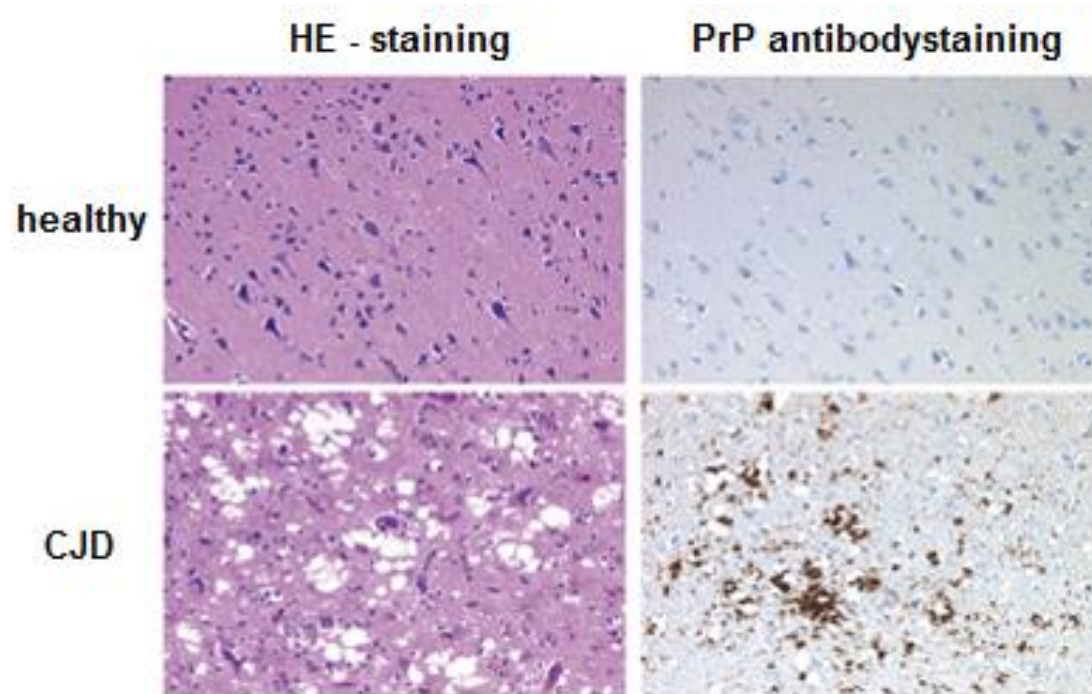
Let's brush up our knowledge of:

1. the mechanism of prion diseases
2. the prion diseases
3. potential transmission of
Alzheimer and Cerebral Amyloid Angiopathy

prion disease

- spongiforme encephalopathy, **presenile dementia**.
- accumulation in the brain of a misfolded version of your prion protein.

Brain shrinkage and deterioration occurs rapidly



Nature Reviews | **Molecular Cell Biology**

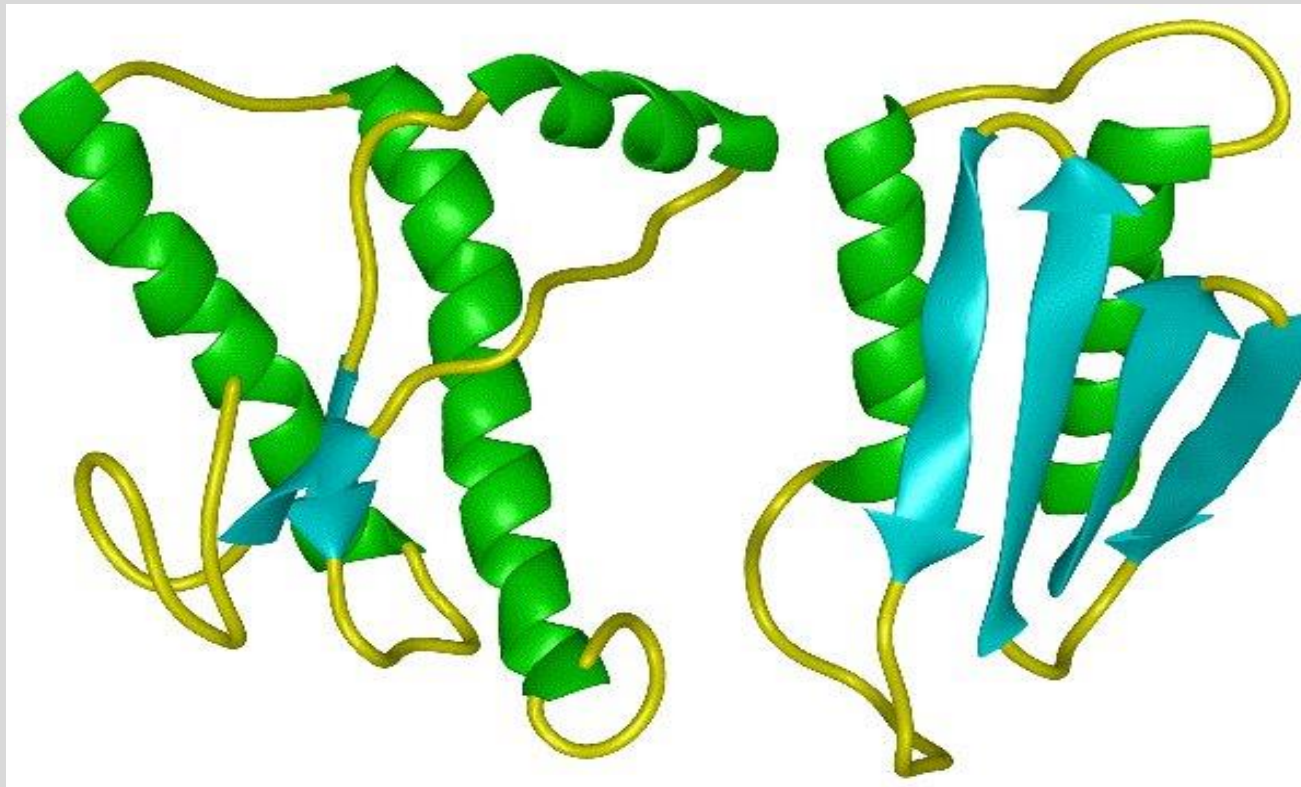


the misfolded protein is called: prion, and it is infectious!

Stanley Prusiner, 1982: proteinaceous infectious particle = “PrP”

prions are infectious proteins, without DNA or RNA.
infectious, but not contagious.

- normal, healthy version of the protein: PrP^C (c = cellular or common).
- pathological, misfolded, infectious proteins: PrP^{CJD}, PrP^{BSE}, etc.



PrP^c

normal prion protein

253 amino acids

proteinase K sensitive

PrP^{CJD}

misfolded prion protein

the same 253 amino acids

proteinase K **resistant**, non-degradable

(resistant to sterilization, alcohol, safe chlorine concentrations)

binds strongly to stainless steel

pathogenesis of prion disease

a brain cell:



the abnormal protein (PrP^{CJD}) causes a **chain reaction**.

it is non-degradable → accumulation, plaques →
brain cells die → spongiform encephalopathy →
presenile dementia and death

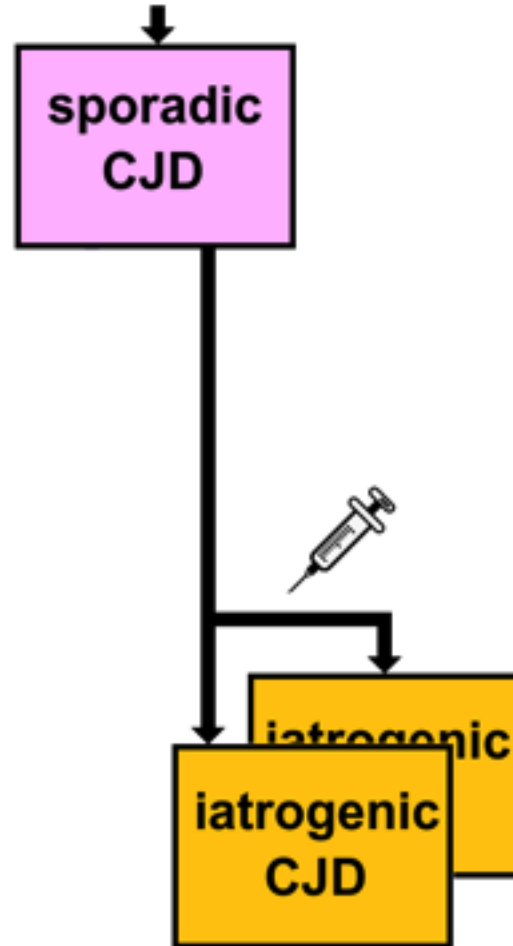
bad luck:
~ 1 per million per year



sporadic
CJD

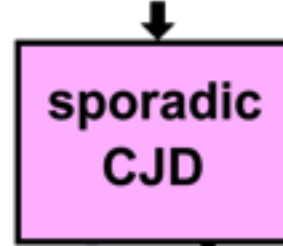
CJD = Creutzfeldt-Jakob disease

bad luck:
~ 1 per million per year



eg: growth hormone from
(CJD) pituitary glands

bad luck:
~ 1 per million per year



No transmission via transfusion

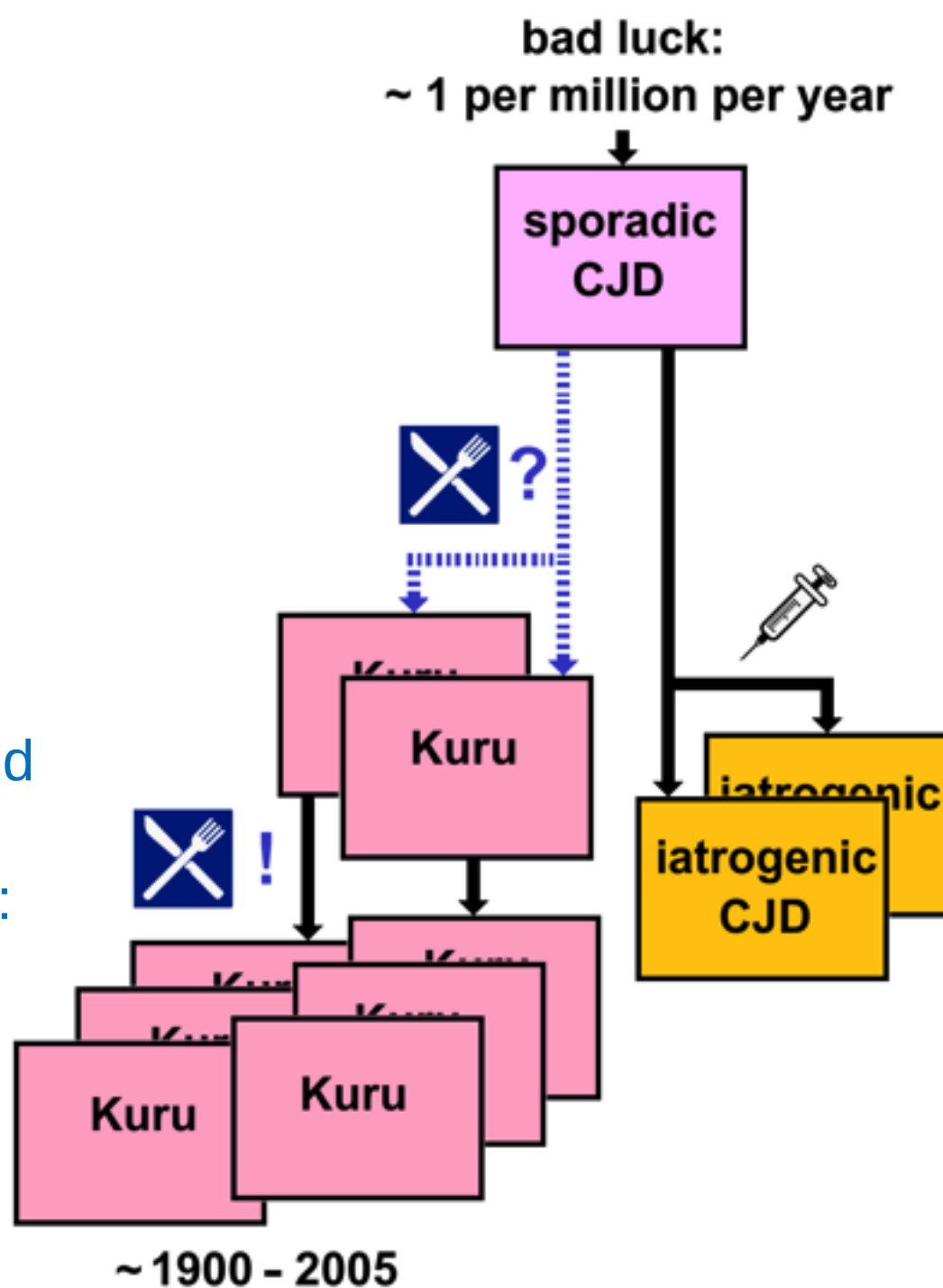
Edgren ae, Annals of Internal Medicine, 2016
Holmqvist ea, Transfusion 2020

eg: growth hormone from
(CJD) pituitary glands

Kuru:

caused by ritual
consumption of
brain material
from the deceased

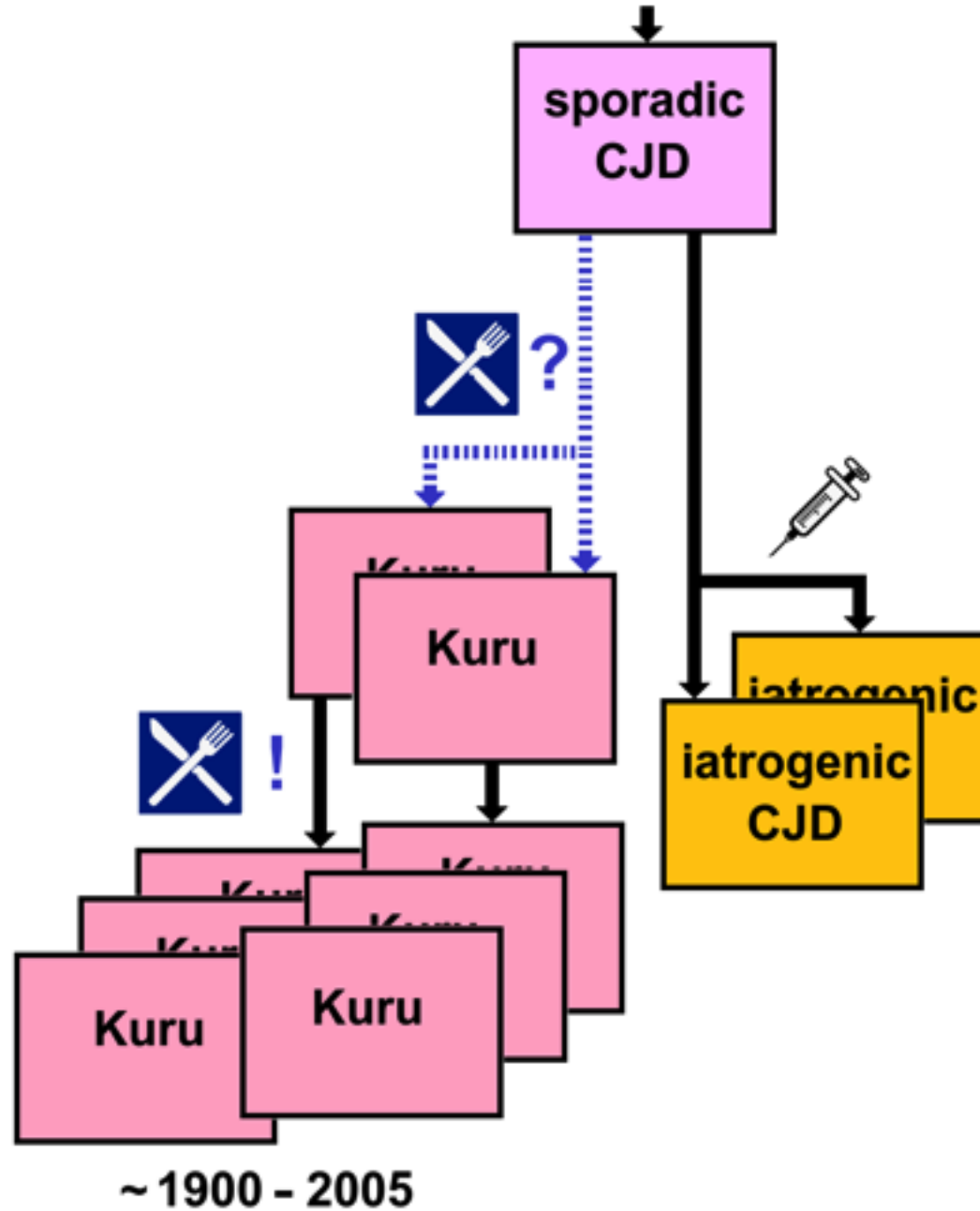
incubation period:
~5 to 56 years (!)



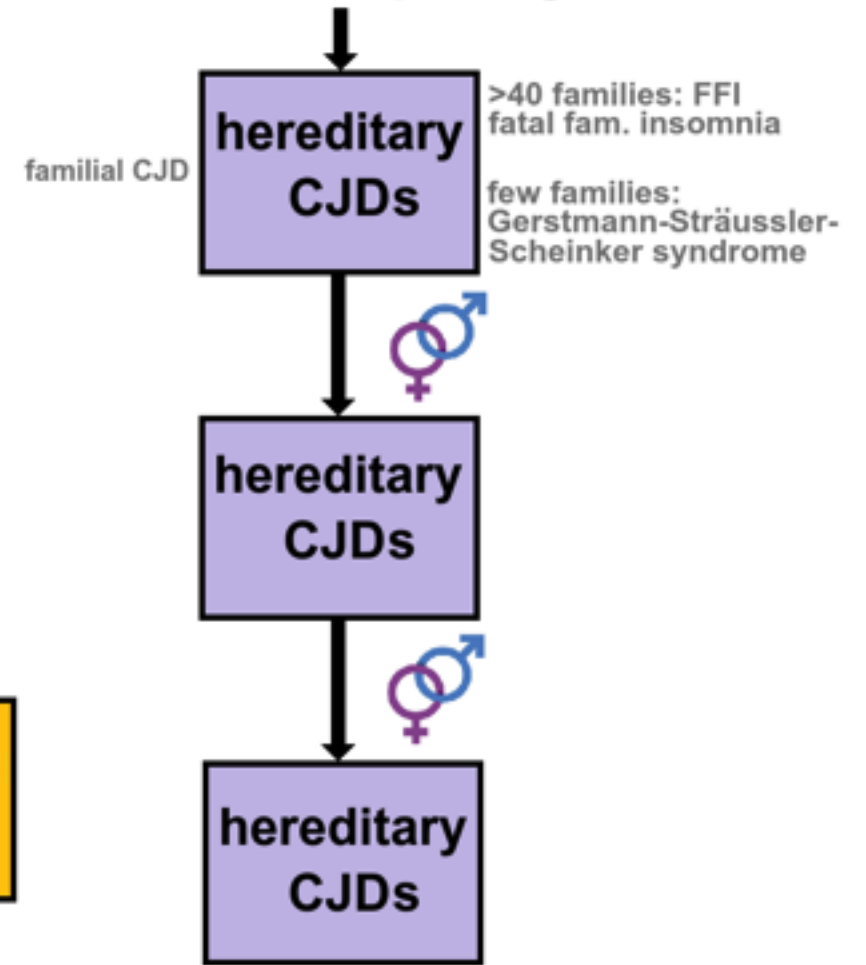
Kuru



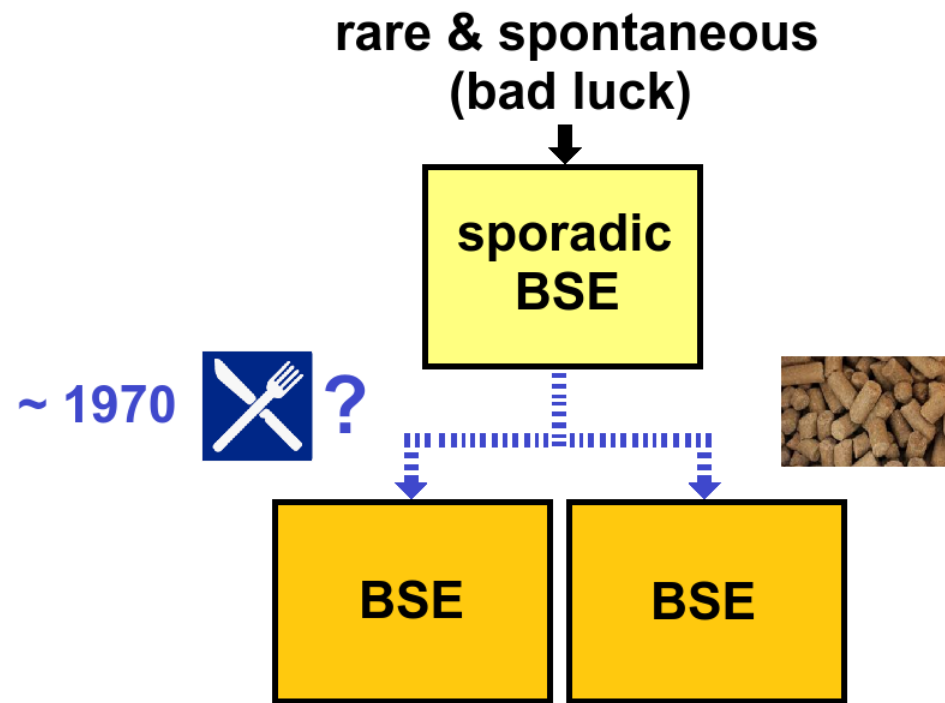
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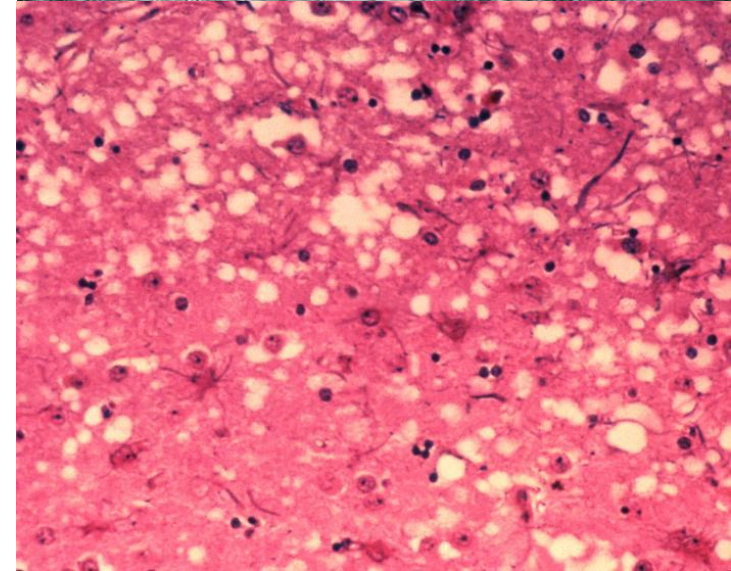
mutation in prion gene

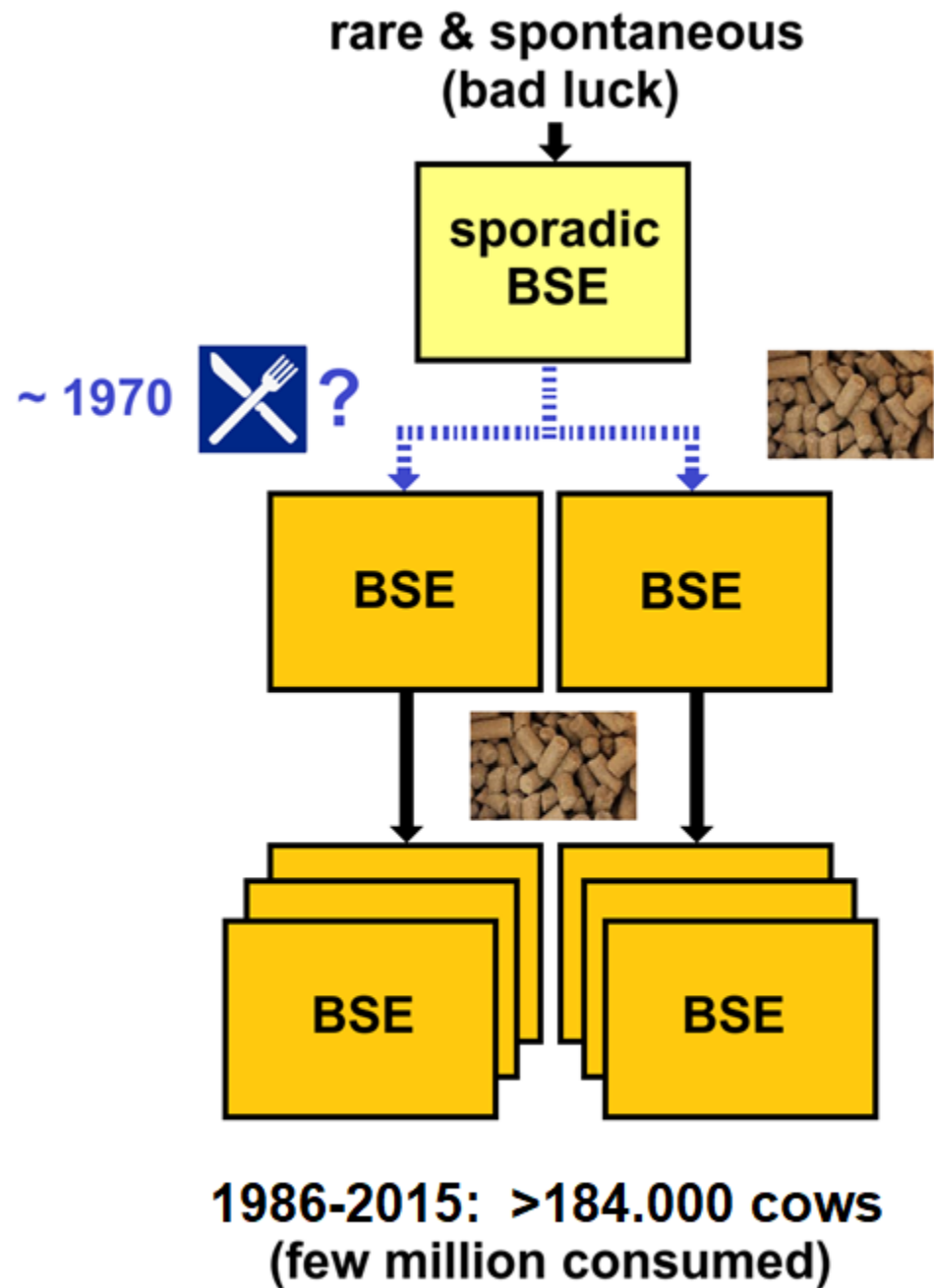


1,2,3,4

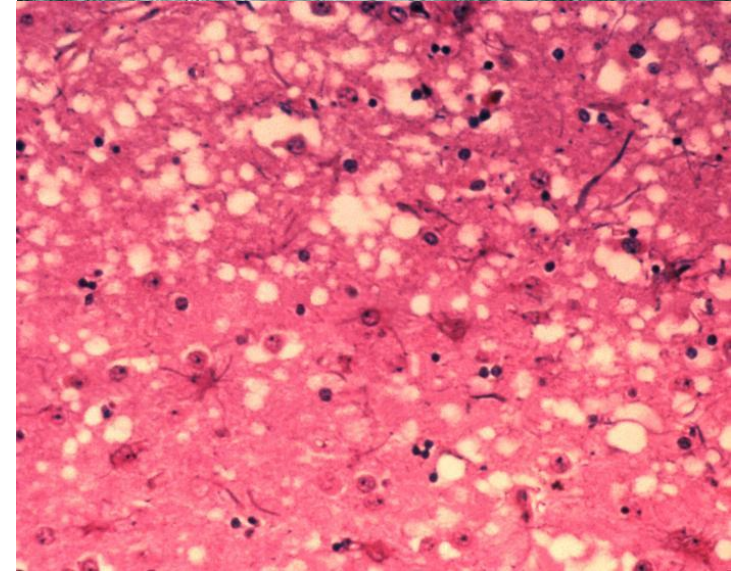


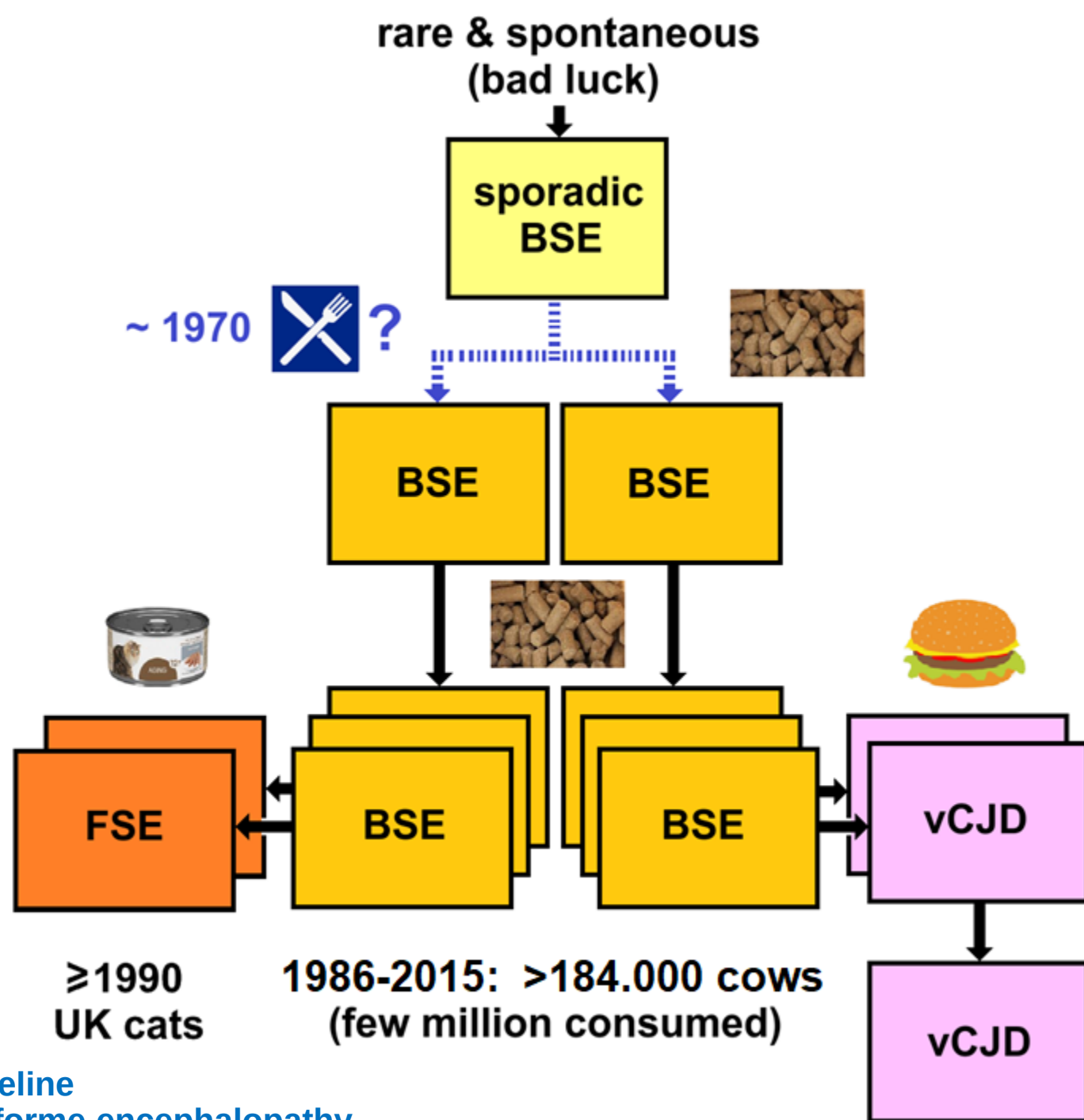
BSE =
bovine spongiform
encephalopathy





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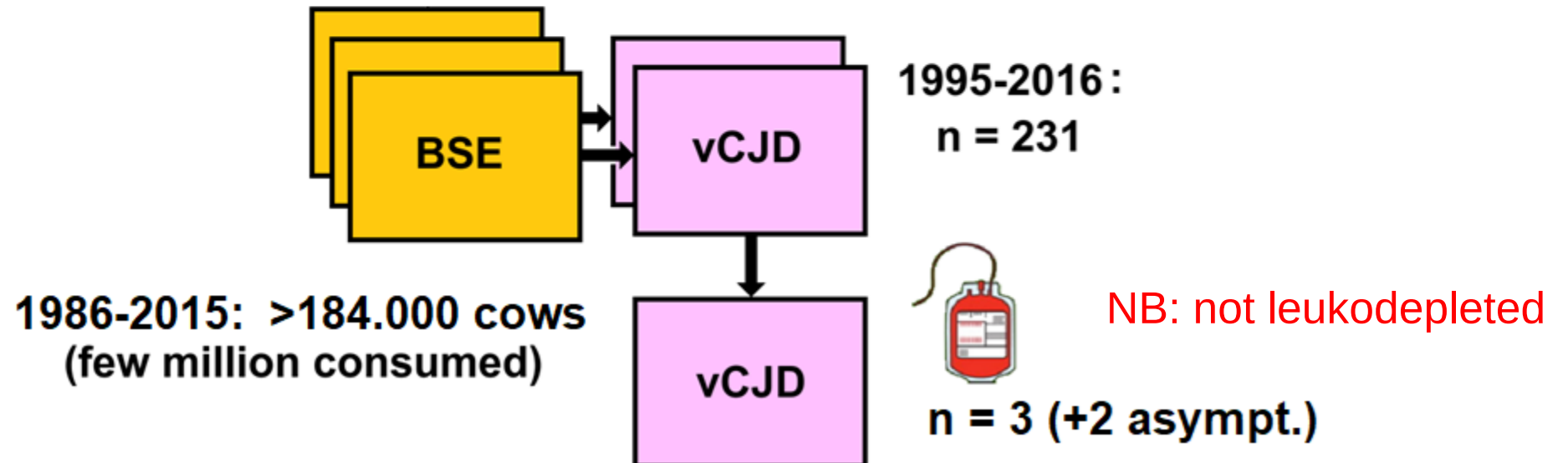




FSE = feline
spongiforme encephalopathy

Prevention of transfusion transmitted vCJD:

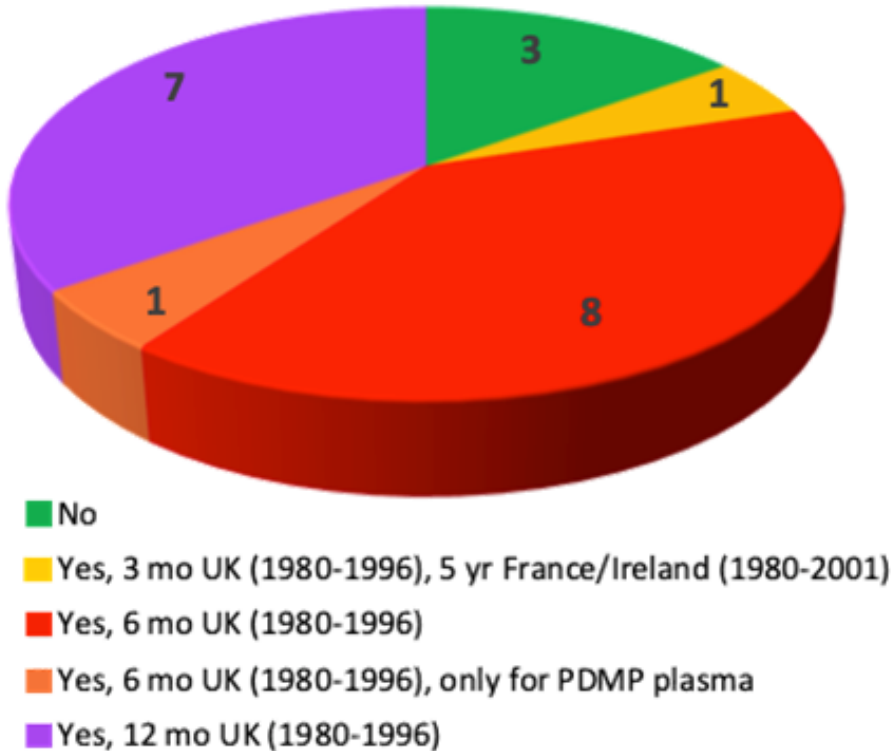
- leukodepletion.
- defer donors who lived in country where food was contaminated, or who received a **local** blood transfusion.



vCJD donor deferral policies in 20 EBA member states

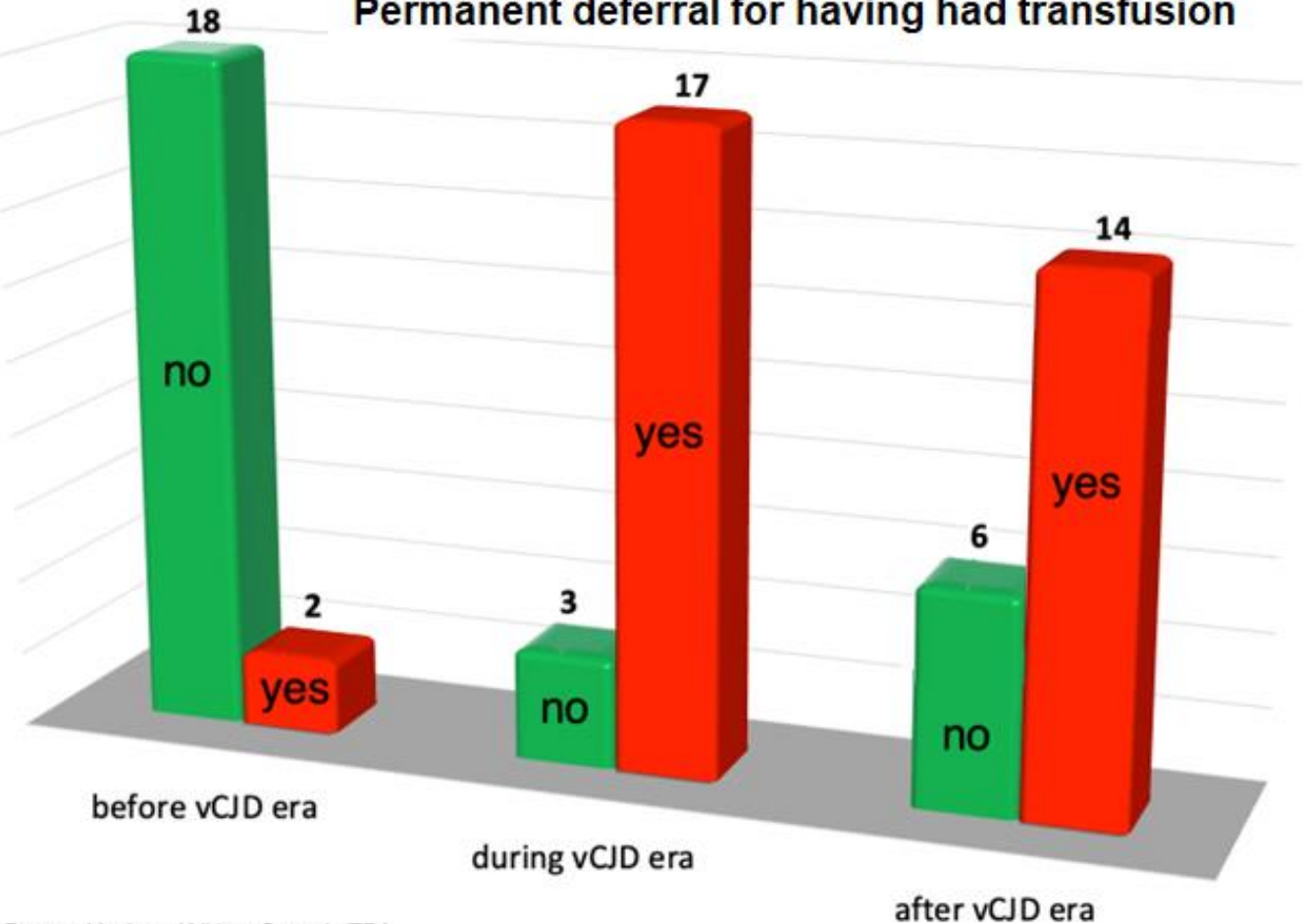
questionnaire by Ryanne Lieshout and colleagues (EBA-EID Monitor)

Deferral of donors for risk of exposure to BSE, based on time spent in specific countries



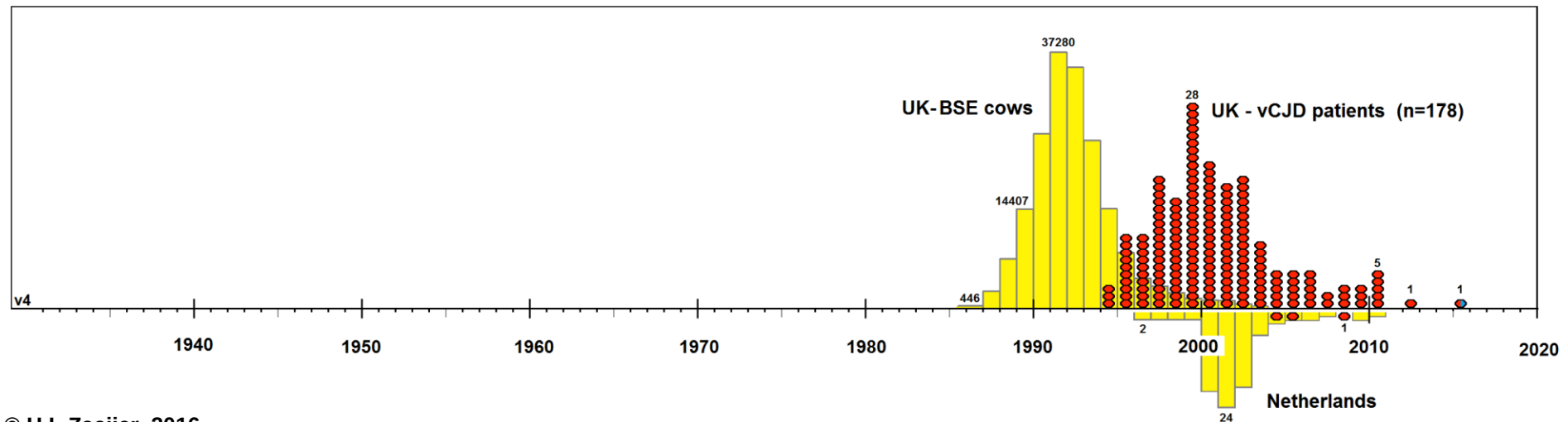
dr. Ryanne Lieshout-Krikke - Sanquin/EBA

Permanent deferral for having had transfusion

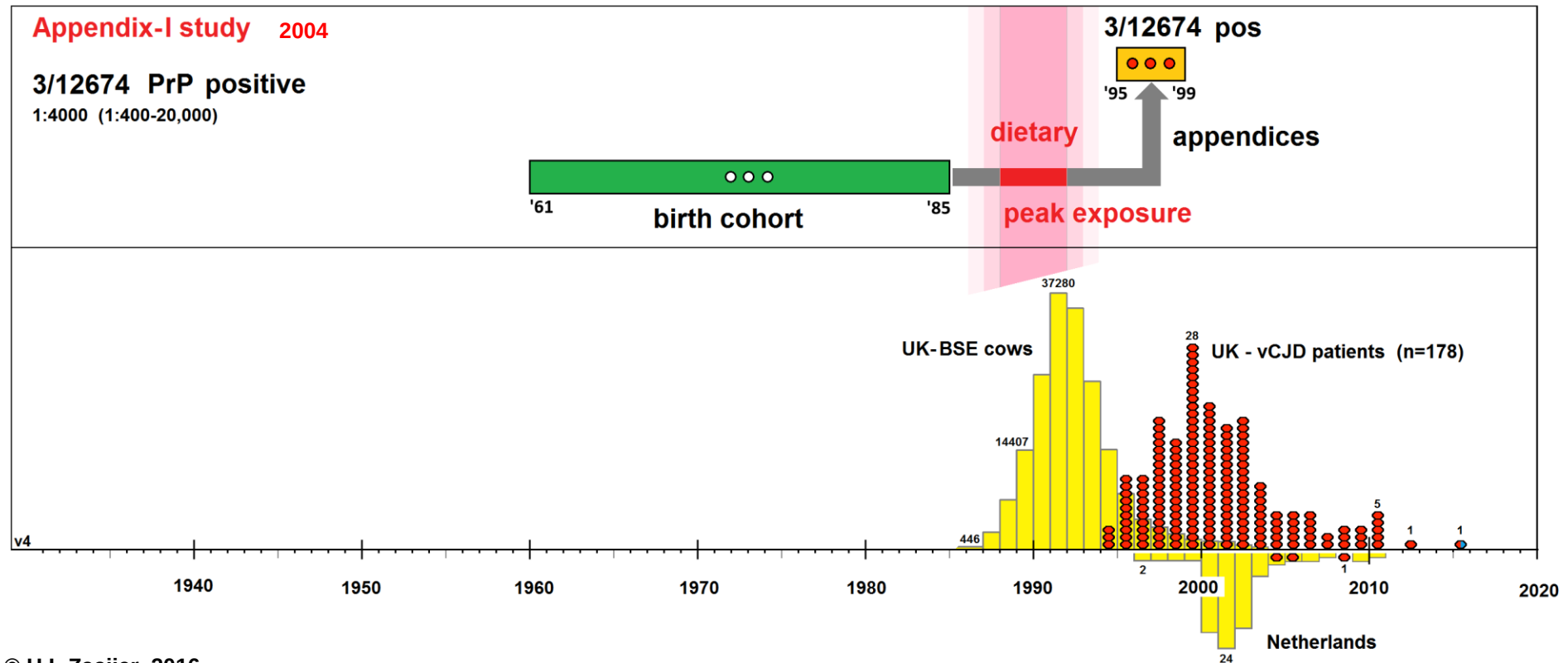


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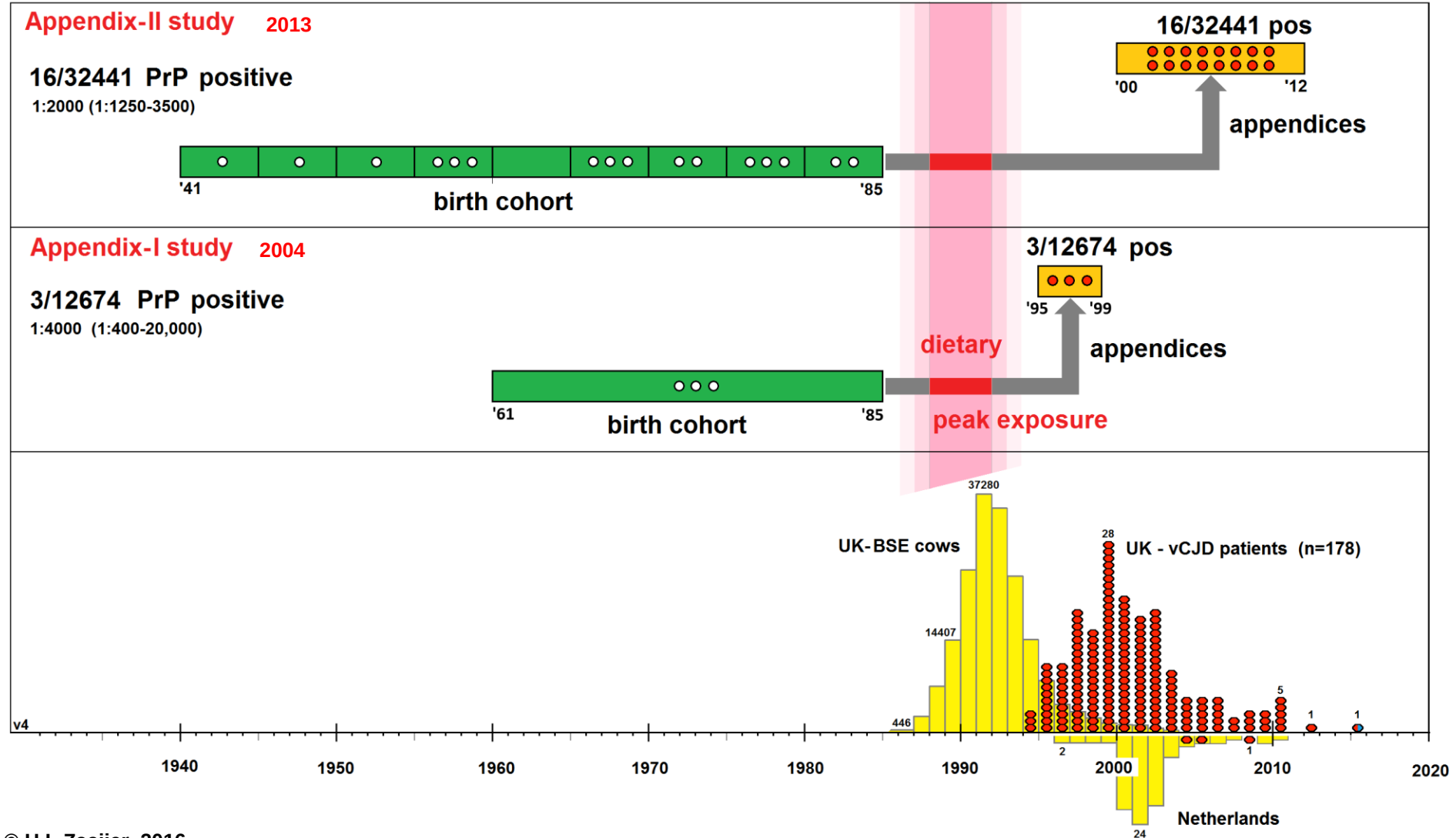
course of BSE and vCJD in UK and NL



Appendix-I study

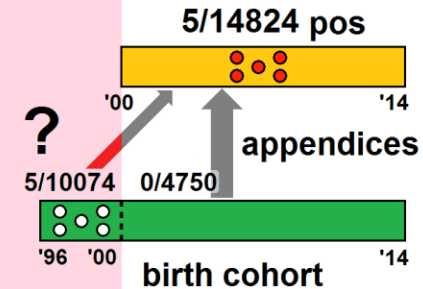
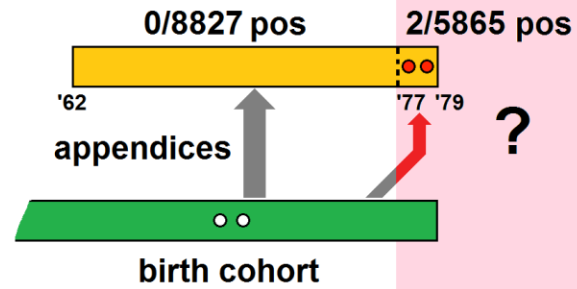


Appendix-I and -II studies



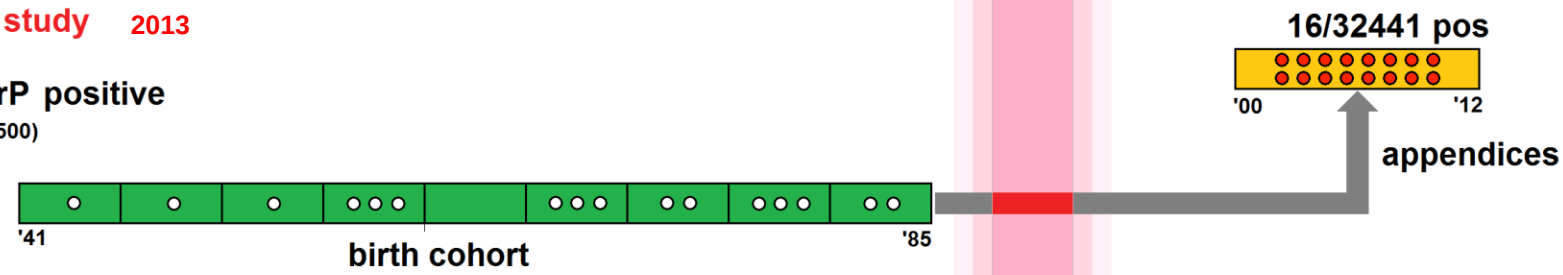
Appendix-III study 2016

7/29516 PrP positive
 1:7000 and 1:3000
 ↓
 (1:2050-62500)



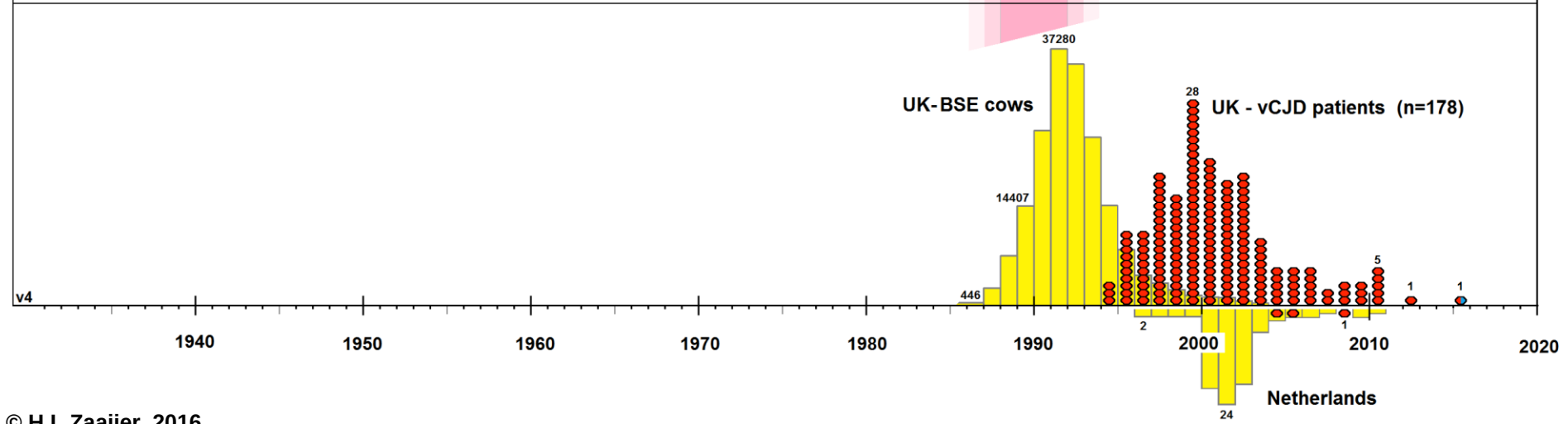
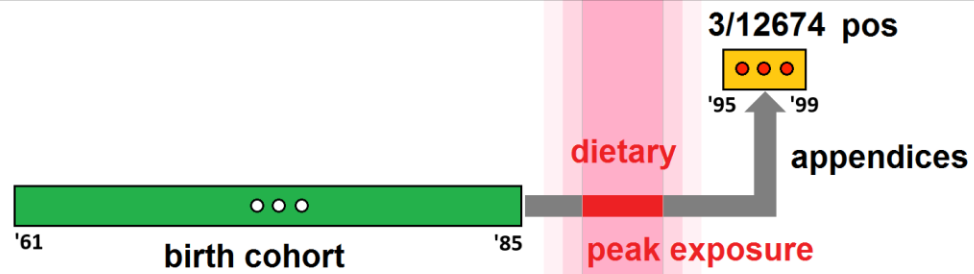
Appendix-II study 2013

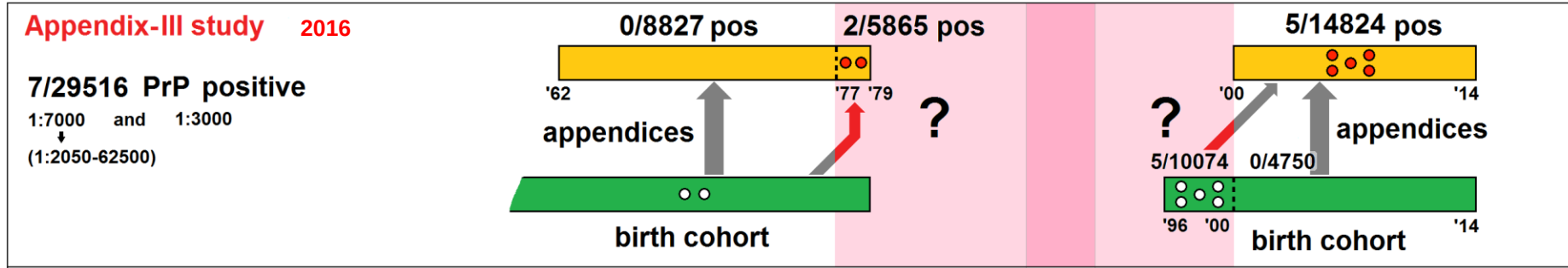
16/32441 PrP positive
 1:2000 (1:1250-3500)



Appendix-I study 2004

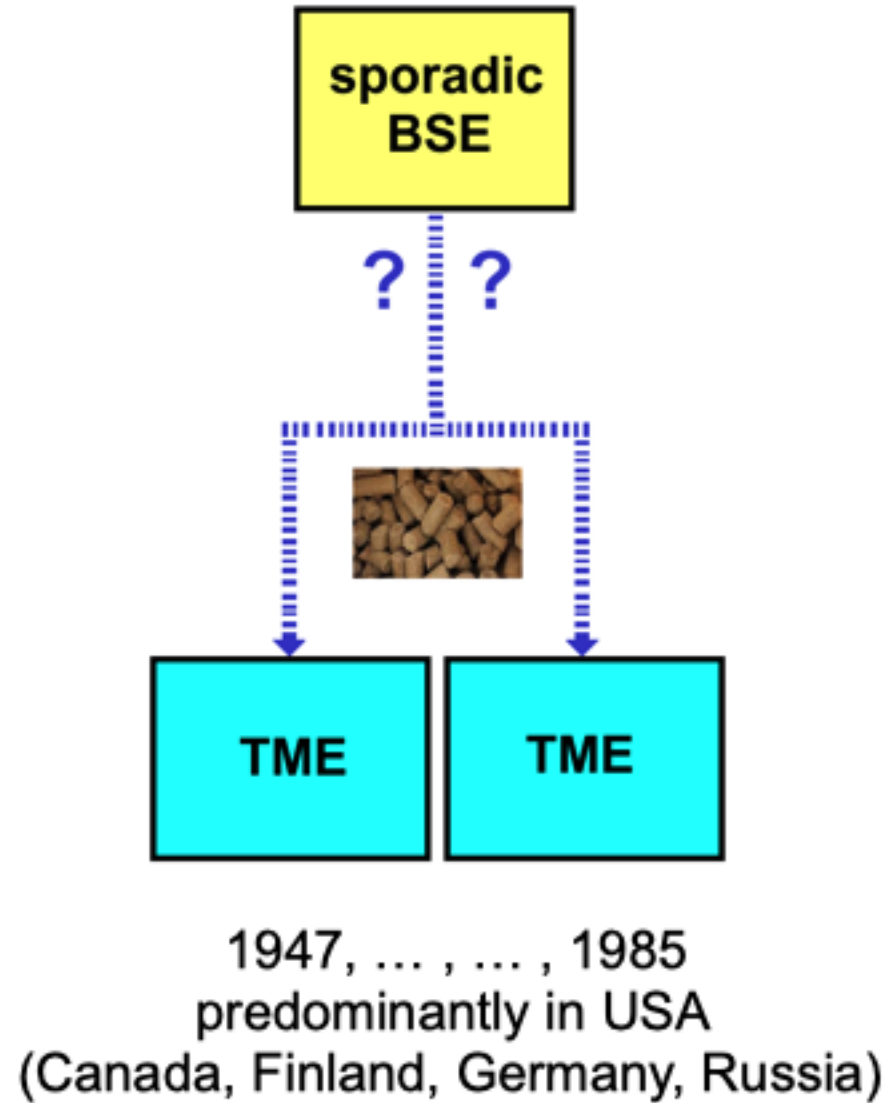
3/12674 PrP positive
 1:4000 (1:400-20,000)





Gill ea, Acta Neuropathologica, 30-3-2020:

...Two interpretations are possible. Either there is a low background prevalence of abnormal PrP in human lymphoid tissues that may not progress to vCJD. Alternatively, all positive specimens are attributable to BSE exposure, ...



TME =
transmissible mink
encephalopathy



scrapie

sheep
goats



scrapie

scrapie

- known since 1732 (UK).
- via placenta, milk, ... ,
grazing on contaminated soil
- under control.



scrapie

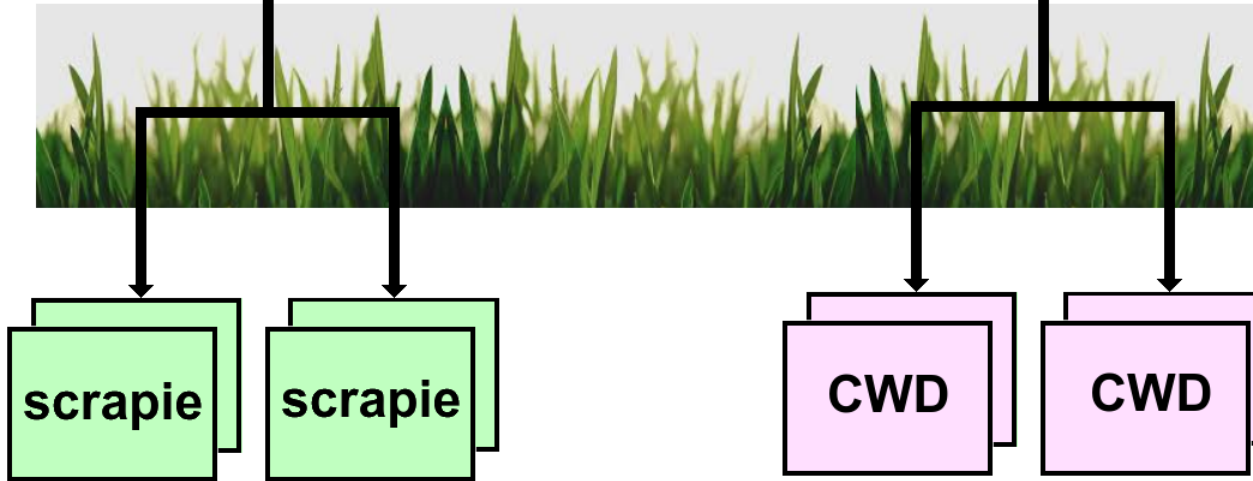
sheep
goats



CWD

elk
(rein)deer
moose

CWD =
chronic wasting
disease



- known since 1732 (UK).
- via placenta, milk, ... ,
grazing on contaminated soil
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- known since 1967 (Colorado).
- via urine, saliva, feces, ... ,
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scrapie sheep
goats



CWD elk
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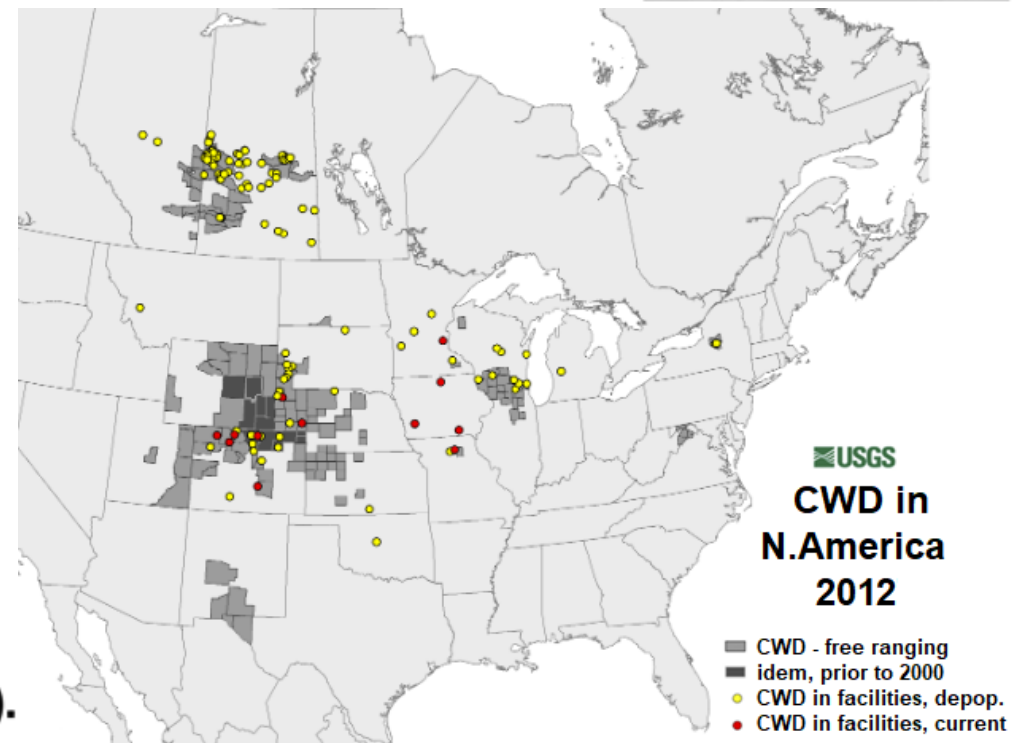


scrapie
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grazing on contaminated soil
- **emerging at this moment.**



Osterholm ea, mBIO 2019
 "... in 2018, with 894 (18%) testing positive.
 More than 18,500 deer harvested in these four Wisconsin counties were not tested for CWD, suggesting that the meat from at least 3,000 CWD-positive animals was consumed."



scrapie sheep
goats



CWD elk
(rein)deer
moose

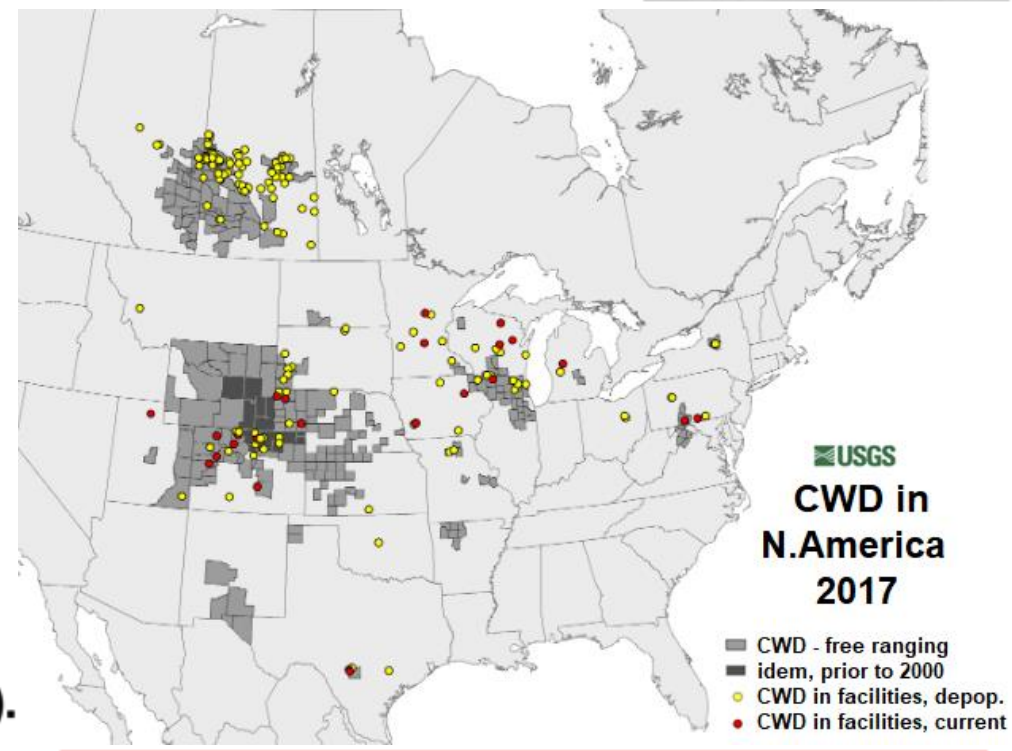


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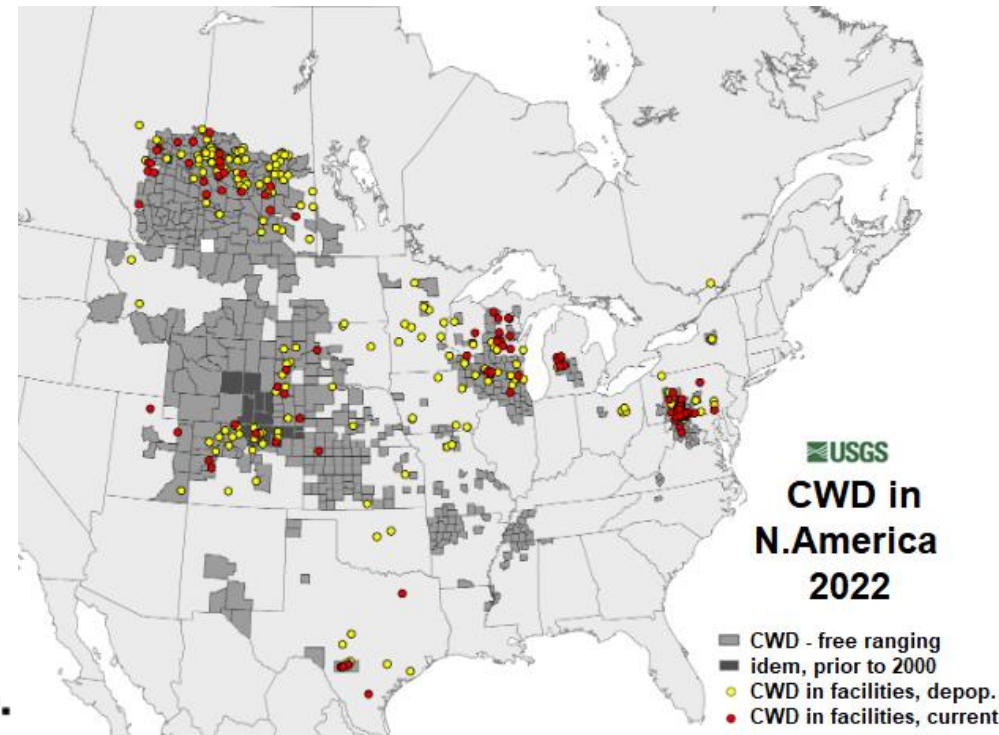


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Worry about CWD?

- highly contagious between cervids:
their urine contaminates plants,
weeks later plants can transmit PrP^{CWD}
- No evidence for transmission to humans.
- Affected area is expanding,
human consumption is increasing.



Alzheimer's disease and Cerebral Amyloid Angiopathy (CAA)

- ▶ accumulation of **amyloid- β** (extra-cellular plaques) and **tau protein** (intra-cellular tangles)
- ▶ CAA: only **amyloid- β** plaques

Alzheimer's disease:

- 60-70% of dementia cases
- starts >65y , 10% between 30y and 60y
- in 80% of cases also CAA:

Cerebral Amyloid Angiopathy:

- multiple lobar intracerebral hemorrhages

No evidence of transmission of Alzheimer's via transfusion

- Edgren ea, Annals of Int. Medicine, 2016
- Lauwers ea, Lancet Neurology 2020

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- ▶ CAA: only **amyloid- β** plaques

neurosurgery



iatrogenic
CAA



iatrogenic
CAA

11 CAA patients, age 30-57 y, after neurosurgery early in life:
neurosurgery: 10 patients $\leq$ 5y, 1 patient 17y

Lauwers ea, Lancet Neurology 2020

Edgren ea (Scandat), ISBT 2022 and lecture 12-7-22:

*... blood recipients of blood from donors who
eventually developed multiple intra cerebral hemorrhages:
3x higher risk of developing ICHs ...*

Prions - summary

vCJD:

No more vCJD cases 😊

France 2017: vCJD after needle stick lab accident in 2010. NEJM 2020.

Do 1:3000 Britons carry the vCJD agent? If so: is it a threat?

CWD:

Monitor the CWD outbreak, and the lack of human cases.

CAA:

amyloid- β may be transfusion transmittable, causing CAA.

Prion diseases are not 'stable', they come and go.
Sometimes they jump species barriers.

Chronic wasting disease of dinosaurs





Thank you

Blood-borne infections team at Sanquin:

Boris Hogema

Thijs van de Laar

Michel Molier

Ed Slot

Ryanne Lieshout-Krikke

Marco Koppelman

Hans Zaaijer

Disclosure of interests of Hans Zaaijer

No conflicts of interests:

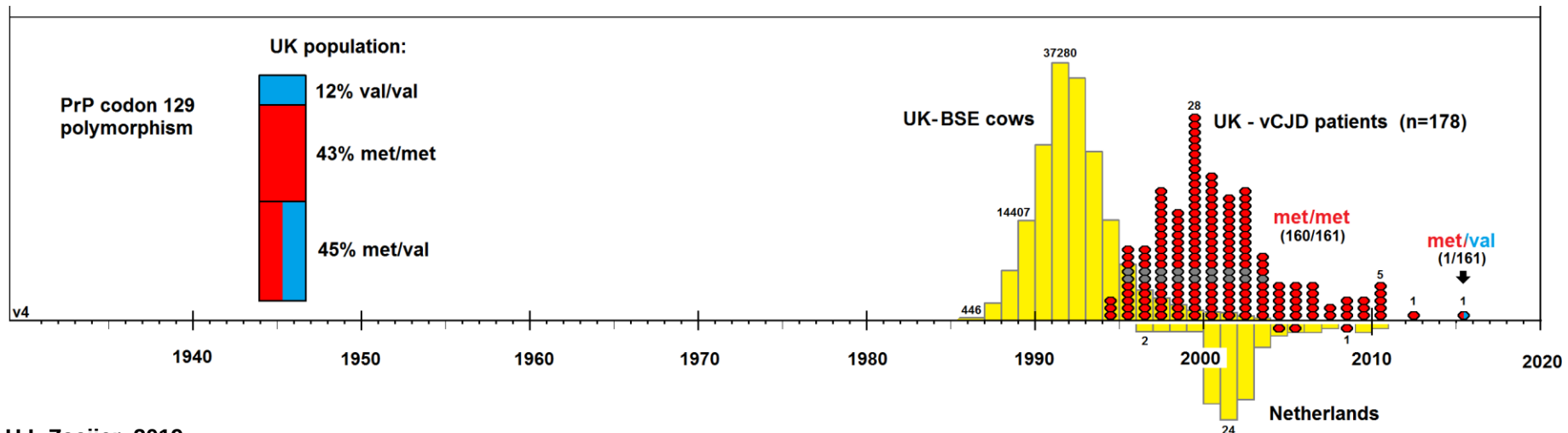
Hans Zaaijer is or was paid for *unrestricted* lectures and teaching by:

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No paid consultancy, no paid advisory boards, no shares, or other interests in companies.

course of BSE and vCJD in UK and NL

- Appendix-I study: Prevalence of lymphoreticular prion protein accumulation in UK tissue samples. Hilton DA ea., J Pathol 2004; 203: 733–739.
- Appendix-II study: Prevalent abnormal prion protein in human appendixes after bovine spongiform encephalopathy epizootic: large scale survey. Gill ON. BMJ. 2013 Oct 15; 347: f5675.
- Appendix-III study: Summary results of the third national survey of abnormal prion prevalence in archived appendix specimens. Public Health England. Infection report (weekly), vol 10, nr 26, published on: 12 August 2016.



vCJD via blood components: only in UK.

18th annual CJD report: 'beyond reasonable doubt'

non-leukodepleted transfusions:

- 3 cases of vCJD via blood transfusion
(met/met; exposure: 1996, 2x 1997);
- 1 asymptomatic infection
(met/val; exposure: 1999)

f VIII concentrate:

- 1 asymptomatic infection in hemofilia patient
(met/val; exposure: 1994-1996)