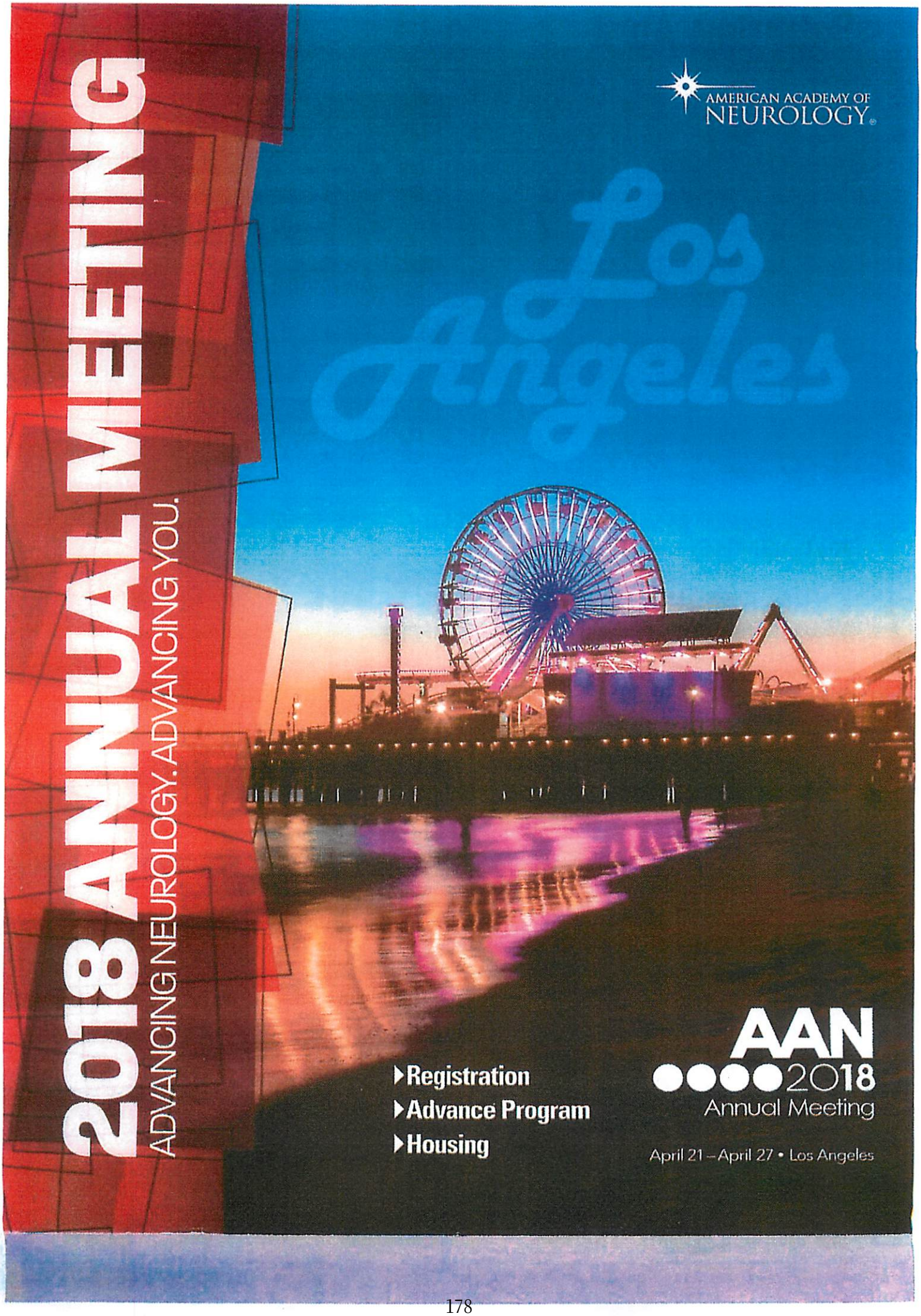
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American Association of Neuropathologists 94TH ANNUAL MEETING

AANP

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS

June 7 - 10, 2018

Hyatt Regency Louisville
Louisville, Kentucky

This activity is provided by the American Association of Neuropathologists.

SATURDAY POSTERS #201-#218

Saturday, June 9, 2018		
Time:	Poster #:	Gulfstream-Hialeah & Keeneland
8:00 am – 5:00 pm	201	**Neuropathological Findings in a Case of Aicardi–Goutières Syndrome with IFIH-1 Mutation** Ahmed Gilani, Kelley Capocelli, Eric Wartchow, Bette Kleinschmidt-DeMasters
	202	**Dual Pathology in Rasmussen Encephalitis** Ahmed Gilani, Eric Prince, Bette Kleinschmidt-DeMasters
	203	**A case report of presumed adult-onset Rasmussen's encephalitis.** Nathan Clement, Matthew Frosch
	204	**Anti-GABA-A receptor antibody-associated encephalitis in an adult and pediatric case: radiologic, biopsy, and CSF findings** Aivi Nguyen, Neena Cherayil, Ana Cristancho, Mariarita Santi, Eric Lancaster, MacLean Nasrallah
	205	**Behcet's Disease of the Central Nervous System (CNS)** Susan de la Monte, Edward Stopa, Galam Khan, Justin Remer, Katarina Dakay
	206	**Fatal Granulomatous Amebic Encephalitis In a Heart Transplant Patient: A Correlation Between Clinical, Radiographic, and Autopsy Findings.** William Harrison, Bruce Leckey, Christine Hulette
	207	**Non-tubercular mycobacterial spinal cord abscesses in an HIV+ male due to *M. Haemophilum*** Bette Kleinschmidt-DeMasters, Kellie Hawkins, Carlos Franco-Paredes
	208	**Congenital rubella syndrome (CRS)--lest we forget** Bette Kleinschmidt-DeMasters
	209	**Pseudorabies Outbreak in Two Catahoula Cur Hunting Dogs in Louisiana** Tiffany Peterson, Fabio Del Piero
	210	**Brainbow labeling in human ex vivo brain slices for high-throughput morphological analysis** Shu-Hsien Sheu, Jonathan Ting, Pichet Adstamongkonkul, Ian Boothby, Leonie Hoyo, Ed Lein, Jeff Lichtman, David Clapham
	211	**Trigeminal Amyloidoma: A Report of Two Cases** Amy Swanson, Rachael Vaubel, Michael Link, Jamie Van Gompel, John Wald, Ellen McPhail, Caterina Giannini
	212	**Validation of THK 5351 PET ligand to detect astrogliosis in vivo** Shigeo Murayama, Renpei Sengoku, Kenji Ishii, Yuko Saito
	213	**A novel in-frame BRAF deletion in a case of central nervous system Rosai-Dorfman disease** Timothy Richardson, Megan Wachsmann, Dwight Oliver, Zahidur Abedin, Dennis Burns, Jack Raisanen, Benjamin Greenberg, Kimmo Hatanpaa
	214	**Histopathology of the Cat Somatosensory Cortex After Chronic Electrical Stimulation** Nishant Tiwari, Ryan Long, Carol Miller, Douglas McCreery
	215	**Relapsing Multifocal Necrotizing Encephalopathy in a 60-year-old Patient** Diana Thomas, Kiruba Dharaneeswaran, Clayton Wiley, Julia Kofler
	216	**Detecting Astrocytopathy with mAb DE-R-11** Diana Thomas, Stephanie Bissel, Geoffrey Murdoch
	217	**Rare/Unsual Pathologies in Epilepsy Surgical Resections, and Their Implications for Genetic Disease Identification in Some Cases.** Meenakshi Bhattacharjee, Gretchen Von Allmen, Manish Shah, David Sandberg, Elliott Friedman, Nitin Tandon
	218	**A novel FIJI workflow demonstrates dynamic changes in postnatal respiratory nuclei innervation by Nkx2.2- and Olig3-derived neurons.** Jillian Liu, Julie Stephens, Catherine Czeisler, Jose Otero

Posters are not offered for CME credit

Validation of THK 5351 PET ligand to detect astrogliosis in vivo

Shigeo Murayama[1], Renpei Sengoku[1], Kenji Ishii[2] & Yuko Saito[3]

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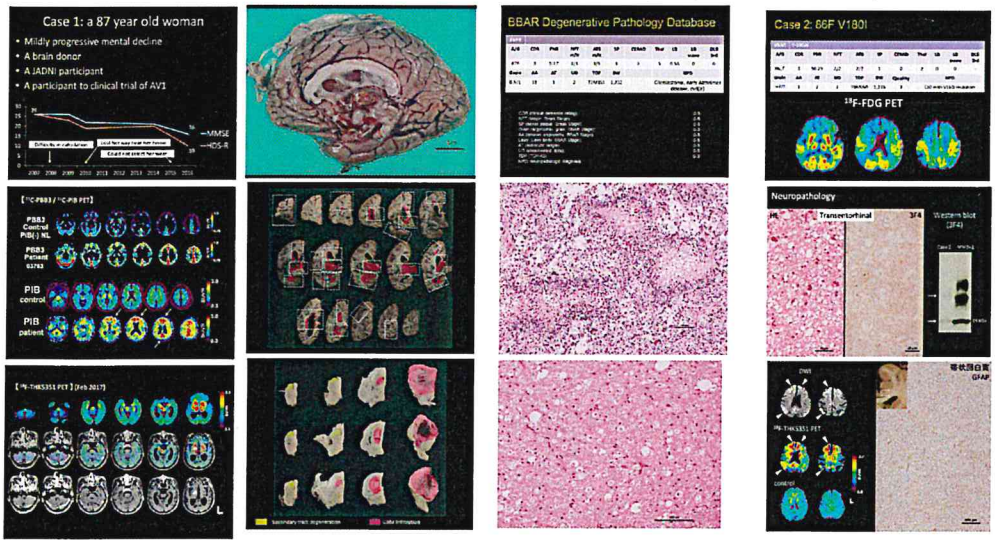
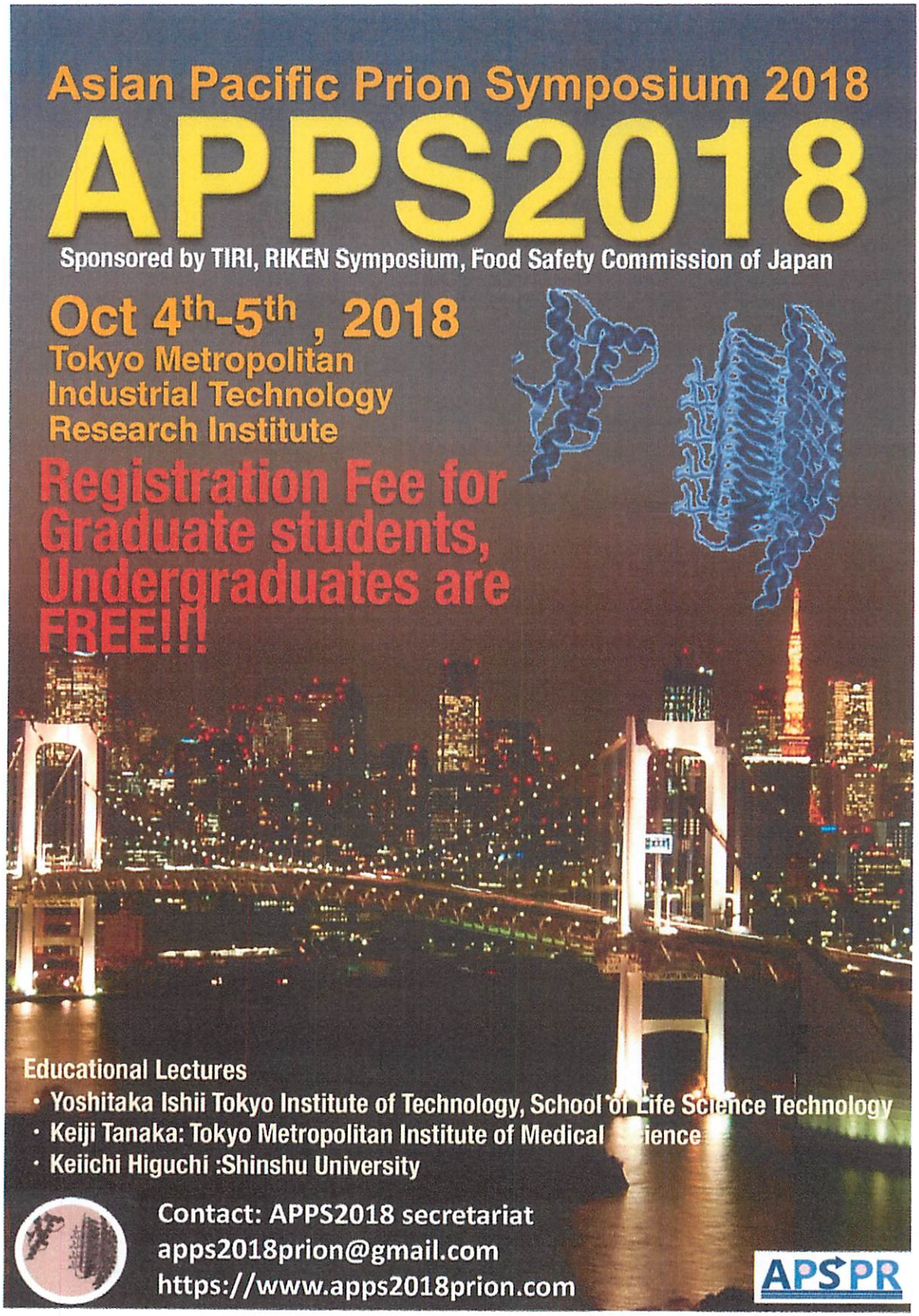
3. Department of Pathology and Laboratory Medicine, National Center of Neurology and Psychiatry Hopsial, Kodiara, Japan

Abstract

THK 5351 PET ligand was originally developed to detect tau in Alzheimer disease (AD) but now proved to bind MAOB receptor, which is abundant in astroglias. We conducted correlative study of THk5351 Image and postmortem neuropathology in case of glioblastoma complicated by AD and a case of familial Creutzfeldt Jakob disease (fCJD) with V180I mutation. Each case received THK 5351 PET scan to evaluate AD tau and astroglial pathology. MRI of the first case presented right thalamic enhanced mass, infiltrating to corpus callosum in addition to mesial temporal atrophy. Diffusion weighted image (DWI) of the second case showed high signal involving swollen cortical ribbons. THK 5351 PET scan detected strong positive signal in the enhanced mass as well as ipsilateral pyramidal tracts. The scan of the second case detected high signal in subcortical white matter adjacent to the cortex which presented high signal with DWI. Neuropathological examination of the first case showed typical glioblastoma without IHD mutation. The tumor involved pyramidal tracts caudally to pons followed by secondary degeneration to medullary pyramis. The second case showed typical diffuse cortical spongiformic changes with severe subcrotical astrogliosis. The western blot of the affected cortex with 3F4 antibody showed typical band pattern of V180I fCJD. 80% of autoradiographic binding of THK 5351 of the first case was blocked by a MAOB inhibitor. Our study confirmed that THK 5351 PET scan could detect astroglioma and astrogliosis in vivo and may be useful for dynamic neuropathology.

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Oct. 4th Day1			
Time	**Location**	**Sessions**	
11:30	1F Hall (Center)	Reception Desk Open	
	Mazzanime	Poster Posting	
12:50-13:00	5F Lecture Hall	Opening Remarks	
13:00-13:30	5F Lecture Hall	Keynote Lecture : Motomasa Tanaka (RIKEN CBS)	
13:30-14:35	5F Lecture Hall	Session 1: Cell and Molecular Biology of Prion Research	
		13:30-13:50	Invited Speaker Presentaion: Jiyan Ma (Van Andel Institute)
		13:50-14:05	Selected Presentation from Poster Presentaion
		14:05-14:20	Selected Presentation from Poster Presentaion
		14:20-14:35	Selected Presentation from Poster Presentaion
14:35-15:00	Mazzanime	Poster Viewing, Exhibition, Coffee Break	
15:00-16:05	5F Lecture Hall	Session 2: Pathological Science of Prion Research	
		15:00-15:20	Invited Speaker Presentaion: Steven J Collins (University of Melbourne)
		15:20-15:35	Selected Presentation from Poster Presentaion
		15:35-15:50	Selected Presentation from Poster Presentaion
		15:50-16:05	Selected Presentation from Poster Presentaion
16:10-17:40	5F Lecture Hall	Educational Lectures	
		16:10-16:40	Yoshitaka Ishii (Tokyo Institute of Technology School of Life Science and Technology)
		16:40-17:10	Keiji Tanaka (Tokyo Metropolitan Institute of Medical Science)
		17:10-17:40	Keiichi Higuchi (Department of Biological Science for Intractable Neurological Disease, Shinshu University)
17:40-18:25	Mazzanime	Poster Viewing, Exhibition	
(17:40-)	(5F Room531)	(APSPR Board Meeting)	
18:25	1F Hall (North)	Departure by Bus (or 10~min by Yurikamome-train, 20 min by walk)	
19:00-21:00	Hilton Daiba	Night Event@Hilton Daiba Presented by"Science Bar Incubator" Special Lecture:Suzanne Solvyns	

Oct. 5th Day2			
Time	**Location**	**Sessions**	
9:30-10:20	5F Lecture Hall	Session 3: Animal Science of Prion Research	
		9:30-9:50	Invited Speaker Presentaion: Takateru Daikai (Food Safty Commision of Japan)
		9:50-10:05	Selected Presentation from Poster Presentaion
		10:05-10:20	Selected Presentation from Poster Presentaion
10:20-11:00	Mazzanime	Poster Viewing, Exhibition, Coffee Break with a small meals	
11:00-11:50	5F Lecture Hall	Session 4: Sturucrul Science of Prion Research;Protein folding/misfolding (non-prion)/;Amyloid	
		11:00-11:20	Invited Speaker Presentaion: Masayuki Yamasaki (Ryukoku University)
		11:20-11:35	Selected Presentation from Poster Presentaion
		11:35-11:50	Selected Presentation from Poster Presentaion
11:50-12:50	5F Lecture Hall	Session 5: Clinical Science of Prion Research	
		11:50-12:10	Invited Speaker Presentaion: Takehiro Nakagaki (Nagasaki University)
		12:10-12:25	Selected Presentation from Poster Presentaion
		12:25-12:50	Selected Presentation from Poster Presentaion
12:50-13:10	5F Lecture Hall	General Assambly of APSPR	
13:10-13:15	5F Lecture Hall	Award Ceremony	
13:15-13:20	5F Lecture Hall	Announcement of APPS2019	
13:20-13:25	5F Lecture Hall	Closing Remarks	


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No.	Speaker/Chair	Full name	Country
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3	Speaker	Craig Anderson	Australia
4	Speaker	Messoud Ashina	Denmark
5	Speaker	Iwata Atsushi	Japan
6	Speaker&Chair	Hee-Joon Bae	Republic of Korea
7	Speaker	Jae-sung Bae	Republic of Korea
8	Speaker	Jong Seok Bae	Republic of Korea
9	Speaker	Oh Young Bang	Republic of Korea
10	Chair	Hamidon Basri	Malaysia
11	Speaker	Mohit Bhatt	India
12	Speaker	Andrew Bleasel	Australia
13	Chair	Saeed Boholega	Saudi Arabia
14	Speaker&Chair	Natan Bornstein	Israel
15	Speaker&Chair	Bruce Campbell	Australia
16	Speaker&Chair	William Carroll	Australia
17	Chair	Jae-Kwan Cha	Republic of Korea
18	Chair	Dae-Il Chang	Republic of Korea
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20	Speaker	Luke Chen	Australia
21	Speaker	Shih-Pin Chen	Taiwan
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23	Speaker&Chair	Jinwhan Cho	Republic of Korea
24	Chair	SooJin Cho	Republic of Korea
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28	Speaker	Jeong-Yoon Choi	Republic of Korea
29	Speaker	Jung-Ah Choi	Republic of Korea
30	Speaker	Kyomin Choi	Republic of Korea
31	Speaker	Seung-Hong Choi	Republic of Korea
32	Chair	Young-Chul Choi	Republic of Korea
33	Speaker	Seong Hye Choi	Republic of Korea
34	Chair	Min Kyung Chu	Republic of Korea
35	Chair	Chin-Sang Chung	Republic of Korea
36	Chair	Kyung-Cheon Chung	Republic of Korea
37	Speaker&Chair	Sun Ju Chung	Republic of Korea
38	Speaker	Patricia K. Coyle	USA

132	Chair	Hyung Lee	Republic of Korea
133	Chair	Jae-Hong Lee	Republic of Korea
134	Chair	Jun Lee	Republic of Korea
135	Chair	Kwang Ho Lee	Republic of Korea
136	Chair	Kwang Soo Lee	Republic of Korea
137	Chair	Kwang-Woo Lee	Republic of Korea
138	Speaker	Meng Lee	Taiwan
139	Speaker	Sang Ahm Lee	Republic of Korea
140	Speaker	Sang Kun Lee	Republic of Korea
141	Speaker	Seung-Han Lee	Republic of Korea
142	Speaker	Seung-Hoon Lee	Republic of Korea
143	Speaker&Chair	Seung-Koo Lee	Republic of Korea
144	Speaker	Soon-Tae Lee	Republic of Korea
145	Chair	Tae-Kyeong Lee	Republic of Korea
146	Speaker	Tsong-Hai Lee	Taiwan
147	Speaker	Yi-Chung Lee	Taiwan
148	Speaker&Chair	Yong-Seok Lee	Republic of Korea
149	Speaker	Shen Yang Lim	Malaysia
150	Speaker&Chair	Shih-Hui Lim	Singapore
151	Speaker&Chair	Tchoyoson Lim	Singapore
152	Speaker&Chair	Wei-Che Lin	Taiwan
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173	Speaker&Chair	Mariko Okubo	Japan
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175	Speaker&Chair	Lekha Pandit	India
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177	Speaker	Jong-Moo Park	Republic of Korea

225	Speaker	Takao Takeshima	Japan
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242	Speaker&Chair	Shuu-Jiun Wang	Taiwan
243	Speaker	Yen-Feng Wang	Taiwan
244	Speaker	Yongxiang Wang	China
245	Speaker	Mohammad Wasay	Pakistan
246	Speaker&Chair	Hirohisa Watanabe	Japan
247	Speaker	Tissa Wijeratne	Australia
248	Speaker&Chair	Lawrence Wong	Hong Kong
249	Speaker&Chair	Chueh-Hung Wu	Taiwan
250	Chair	Shey-Lin Wu	Taiwan
251	Speaker&Chair	Yih-Ru Wu	Taiwan
252	Speaker&Chair	Kei Yamada	Japan
253	Speaker	Masahito Yamada	Japan
254	Speaker	Bernard Yan	Australia
255	Speaker&Chair	Dong Won Yang	Republic of Korea
256	Speaker&Chair	Lo Yew Long	Singapore
257	Chair	Byung-Woo Yoon	Republic of Korea
258	Chair	Shengyuan Yu	China
259	Speaker	Sungwook Yu	Republic of Korea
260	Speaker&Chair	Chang-Ho Yun	Republic of Korea
261	Speaker	Alessandro Zagami	Australia

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Poster Session

The poster number is assigned to each abstract on Day 2(Nov 9) and Day 3(Nov 10), and you can find your abstract by searching Presenter's name, Abstract's subject and Abstract Number for the abstract

Poster Presentation 1
Day 2 - Nov 9 (Fri.)

Poster Presentation 2
Day 3 - Nov 10 (Sat.)

Presenter's name | tsukamoto

Poster Presentation 1 (Day 2, 13:00-14:00, Nov 9)

Poster No.	Abs No.	Title	Presenter	Country
P-1039	FP-0315	Epidemiological features of Prion diseases in Japan - Is the Incidence Increasing? -	Tadashi Tsukamoto	Japan

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Abstract

Presentation Type	Poster
Poster Type	General
Topic	Dementia
Abstract No.	FP-0315
Abstract Title	Epidemiological features of Prion diseases in Japan - Is the Incidence Increasing? -
Abstract	**Purpose** To clarify the epidemiology of prion diseases in Japan using the data of the Prion disease Surveillance Committee in Japan. **Methods** We had developed a nation-wide surveillance system by the Prion disease Surveillance Committee in the Research Group on Surveillance and Control of Prion diseases, Ministry of Health, Welfare and Labor since 1999 in Japan. Statistical analyses were performed using the data of the Surveillance Committee. **Results** As of February, 2018, the cumulative number of Prion disease patients were 3,287 out of 6,458 investigated. They were composed of sporadic CJD (sCJD) (77%), familial Prion (fCJD) disease (20%), and acquired Prion disease (3%) including a case of variant CJD. Compared with the first half of the 2000s, after 2016, the increase in the number of patients was observed in all age groups over 60 years old. When examining by gender and age, in both gender, the number of onset cases was largest in their 70's. Excluding those under 39 and over 80, the number of cases per population was higher for female patients than for males. Regarding the period from onset to death, the mean value of sCJD is 16.9 months, the average value of dCJD (CJD after dural transplantation) and fCJD is somewhat longer, and in GSS it is even longer. The autopsy rate is 14%. Ninety-one cases of dCJD have been reported so far. Including cases before surveillance studies, the total number of cases of d CJD is 154 cases. The average period from dura mater transplant to disease onset was 164 months (SD: 81 months). Recently, a natural history project was started, and more than 400 cases were registered. **Conclusions** In order to raise the accuracy of diagnosis of prion diseases in Japan, it is necessary to increase the autopsy rate and follow up surveys of individual cases, and it is thought that natural history research would provide some solution to this issue. The prion diseases in Japan have been characterized by some features including apparently increasing incidence. The natural history project would be very helpful for clinical trials in near future.
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I confirm that this submission has been approved by all authors.
Signature (Name) : **Tadashi Tsukamoto** / Date: **2018-09-09**

Close

The Asian and Oceanian Association of Neurology

16th Asian Oceanian Congress of Neurology*(AOCN 2018)*

COEX Convention and Exhibition Center , Seoul, South Korea
November 8-11

Invited Chair & Speaker : Hidehiro Mizusawa

Speaker : Masahito Yamada

Poster Presentation 1: (Day 2, 13:00-14:00, Nov 9)

Presenter: Tadashi Tsukamoto
Title: Epidemiological features of Prion diseases in Japan
- Is the Incidence Increasing? -

Update: Dura Mater Graft–Associated Creutzfeldt-Jakob Disease — Japan, 1975–2017

Ryusuke Ae, MD, PhD[1]; Tsuyoshi Hamaguchi, MD, PhD[2]; Yosikazu Nakamura, MD[1]; Masahito Yamada, MD, PhD[2]; Tadashi Tsukamoto, MD, PhD[3]; Hidehiro Mizusawa, MD, PhD[3]; Ermias D. Belay, MD[4]; Lawrence B. Schonberger, MD[4]

Creutzfeldt-Jakob disease (CJD) is a fatal neurodegenerative disorder that, according to the most well-accepted hypothesis (*1*), is caused by replicating, transmissible, abnormal forms of a host-encoded prion protein (prions). Most CJD cases occur spontaneously (sporadic CJD) or are inherited (genetic CJD). Iatrogenic CJD can occur after exposure to prion-contaminated instruments or products in medical/surgical settings. Cadaveric dura mater graft–associated CJD (dCJD) accounts for a common form of iatrogenic CJD. This report summarizes the epidemiologic features of 154 cases of dCJD identified in Japan during 1975–2017; these cases account for >60% of dCJD cases reported worldwide (*1*,*2*). The unusually high prevalence of dCJD in Japan was first reported in 1997 (*3*). In 2008, a single brand of graft (Lyodura [B. Braun Melsungen AG, Melsungen, Germany]), frequently used as a patch in neurosurgical procedures, was identified as the probable vehicle of transmission (*4*). No international recall of the implicated Lyodura occurred, the product had a relatively long shelf life, and the grafts were used frequently in Japanese patients with non–life-threatening conditions (*4*,*5*). Since 2008, additional cases have been ascertained, reflecting the identification of previously missed cases and the occurrence of new cases with longer latency periods (interval from exposure to symptom onset) for dCJD (up to 30 years), underscoring the importance of maintaining surveillance for dCJD.

In 1996, after the first report of variant CJD (the human prion disease caused by the agent of bovine spongiform encephalopathy ["mad cow disease"]) in the United Kingdom (*6*), the nongovernmental Japanese CJD Surveillance Committee (J-CJDSC), with support from the Japanese Ministry of Health, Labour, and Welfare, conducted a preliminary nationwide mail survey to identify cases of human prion disease in Japan; since 1999, J-CJDSC has maintained a national CJD registry (*7*). J-CJDSC members investigate each reported suspected CJD case in cooperation with CJD specialists in each prefecture. The methods for identifying dCJD cases in Japan have been described previously (*5*,*7*,*8*). All identified CJD cases, including cases of dCJD, are entered into the J-CJDSC database, which contains demographic and clinical information, including a detailed history of any surgical procedures and international travel and CJD laboratory test results (including cerebrospinal fluid analyses and genetic testing) (*7*).

Among 829 identified physician-diagnosed cases of CJD during 1979–May 1996, a total of 43 (5%) patients had received a dura mater graft as part of a surgical procedure (typically a patch during neurosurgery); 41 (95%) of these dCJD patients had received a Lyodura graft (*3*). A 1987 U.S. investigation of a dCJD case found that Lyodura produced before May 1987 carried an unusually high risk for dCJD because of the contamination-prone method of production (*9*,*10*); after that report, the manufacturer reported revising its collection and processing procedures to reduce the CJD transmission risk.

By 2008, a total of 132 dCJD cases had been reported in Japan, and among 120 (91%), Lyodura was identified as the probable vehicle of transmission; the graft brand for the other 12 dCJD patients was unknown (*4*). By the end of 2017, the J-CJDSC database included 154 patients with dCJD, including an additional 22 patients identified since the last report (*4*).

Among 154 dCJD patients, receipt of a Lyodura graft was documented in 140 (91%); the brand of dural graft received by 14 patients was not identified. The most common medical conditions for which patients received the cadaveric dura mater grafts were brain tumors (including meningioma) (69; 45%), facial palsy or trigeminal neuralgia (26; 17%), and brain hemorrhage (25; 16%). Less common conditions included intracranial aneurysm (10; 6%), unspecified anomalies (eight; 5%), intracranial hematoma (seven; 5%), trauma (seven; 5%), and other (two; 1%). The median age at symptom onset among dCJD patients was 58 years (range = 15–81 years; mean = 56 years); 89 (58%) patients were female. All patients had received their dura mater graft during 1975–1993 (Figure 1) (Figure 2), and dates of illness onset ranged from 1985 to 2016.

Although the shelf life of Lyodura established by the manufacturer was 5 years, three dCJD patients had surgical procedures in 1993, at least 6 years after the company had changed their collection and processing procedures. J-CJDSC determined that all three patients had received a Lyodura graft, and that at least one of the grafts was processed before 1987, and had therefore expired (the processing date of the second and third patients' grafts are unknown). Eleven (7%) dCJD patients identified by J-CJDSC received grafts during 1988–1993 (Figure 2), including eight during 1988–1991,

FIGURE 1. Number of cases (N = 154) of dura mater graft–associated Creutzfeldt-Jakob disease (dCJD), by year of neurosurgical procedure and year of symptom onset — Japan, 1975–2017

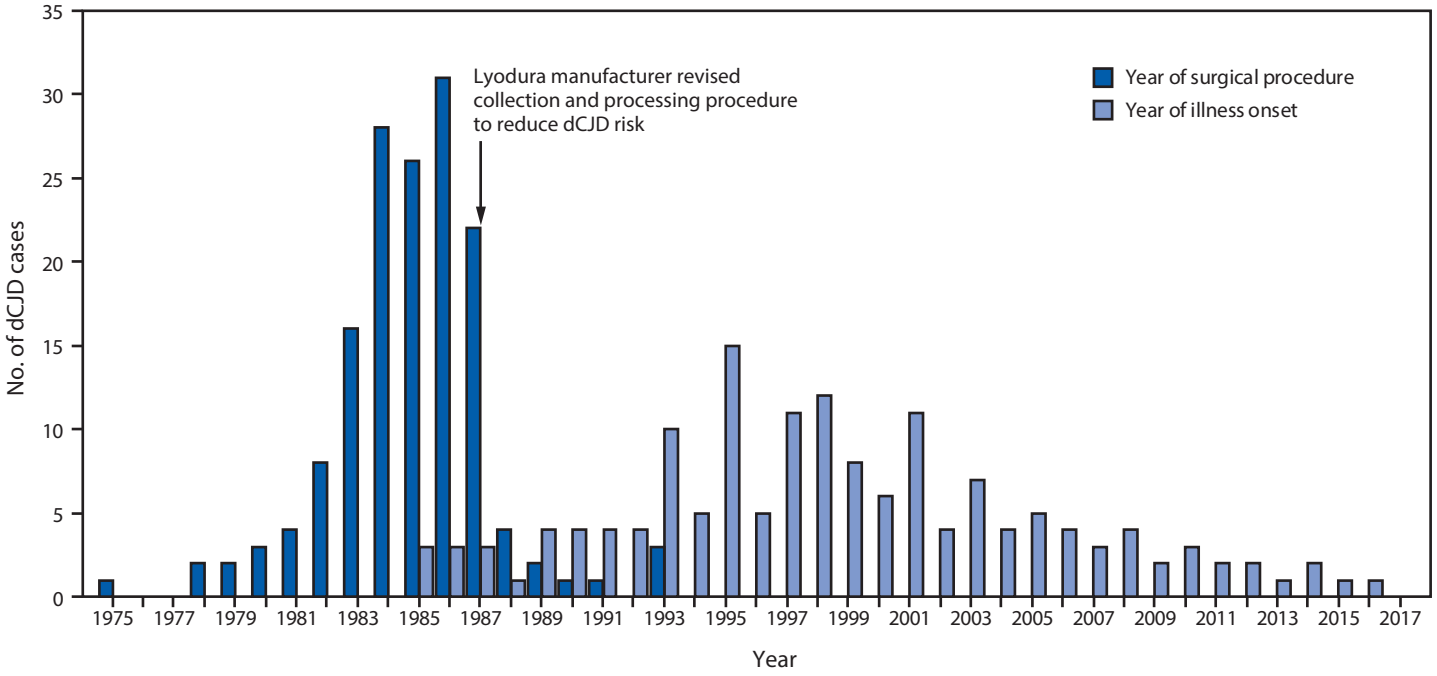
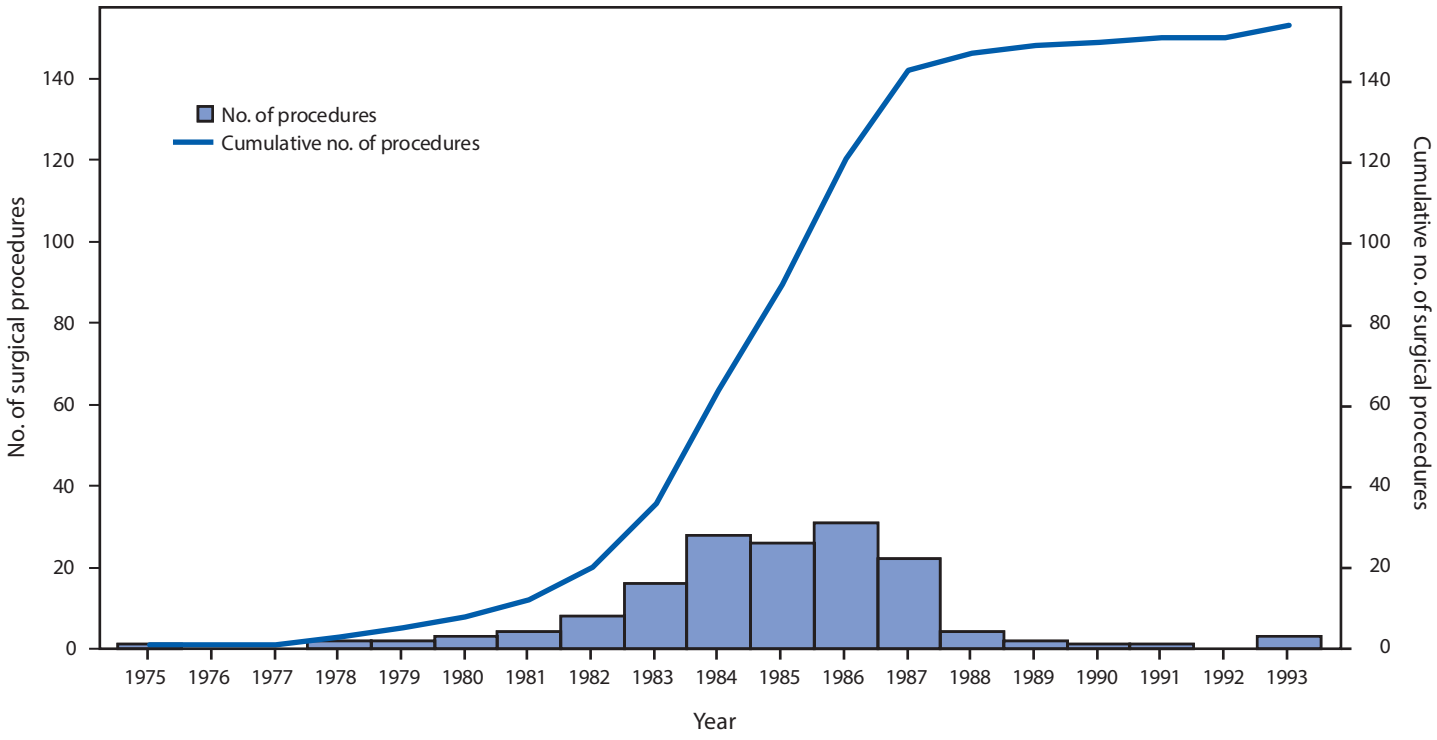


FIGURE 2. Number of surgical procedures linked to cases of dura mater graft–associated Creutzfeldt-Jakob Disease (dCJD),* by year of surgical procedure — Japan, 1975–1993†



* Among 154 dura mater graft procedures, the brand was documented as Lyodura in 140 (91%).
† The manufacturer of Lyodura reported that it revised its collection and processing procedures in May 1987 to reduce the risk for CJD contamination; the recommended shelf life for Lyodura was 5 years.

indicating that they might have received unexpired Lyodura produced before the company changed its processing procedures in 1987. In 1997, a case occurred in a patient with a history of two neurosurgical procedures in 1991. Investigation by J-CJDSC revealed that the patient had received a graft produced before 1987 during the first procedure. None of the dCJD cases identified to date received a dural graft after 1993.

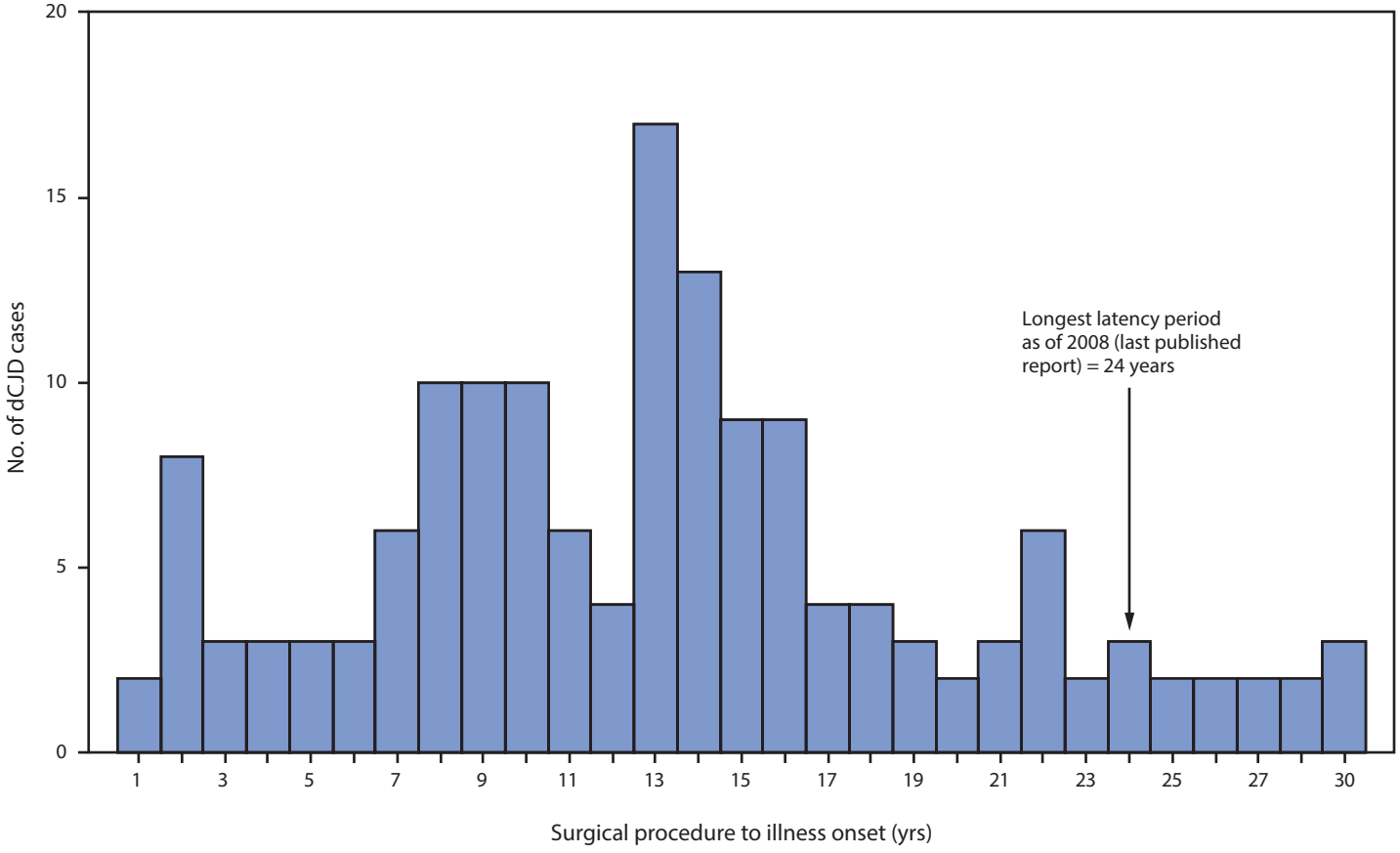
In Japan, it is estimated that 20,000 persons received a Lyodura graft each year during 1983–1987, approximately 50 times more than the estimated number of U.S. recipients (*4*). During this period, 123 Japanese patients who subsequently developed dCJD had surgical procedures, including 114 (93%) who had documentation of receipt of a Lyodura graft (the graft brand of the other nine patients was unknown), indicating that the risk for developing dCJD within 30 years of receiving a Lyodura graft in Japan was at least one per 877 (i.e., 114 dCJD cases per 100,000 Lyodura graft recipients). In this analysis, both the median and mean intervals from receipt of dural graft to illness onset (latency period) were 13 years (range = 1–30 years) (Figure 3). Since the update in 2008, 11 of the 22 newly reported dCJD cases have had latency periods exceeding 24 years, the longest interval reported in 2008 (*4*) (Figure 3). In three of these 11 cases, the latency period was 30 years, the longest reported to date.

Discussion

A comprehensive 2012 global summary of dCJD cases by country (*2*) reported that 142 (62%) of 228 cases of dCJD described worldwide occurred in Japan, and that at least one dCJD case was reported from 20 other countries. In the United States, four cases attributed to dura mater grafts have been identified; three were linked to a Lyodura graft produced before 1987, and one to a different commercially produced cadaveric dura mater graft. Lyodura grafts produced before 1987 were widely distributed to many countries, but most frequently to Japan.

During the U.S. investigation of the first Lyodura-associated CJD case in 1987 (*9*,*10*), investigators learned that the company mixed dura from multiple donors during batch processing of single lots and sterilized the grafts with gamma irradiation,

FIGURE 3. Interval from surgical procedure to illness onset* among 154 cases of dura mater graft–associated Creutzfeldt-Jakob disease (dCJD) — Japan, 1975–2017



* Median = 13 years; range = 1–30 years.

a procedure that does not inactivate prions (*10*). A Lyodura representative also reported that the company did not maintain records identifying donors, so they could not be traced. Lyodura was only available to U.S. hospitals by mail if ordered from a non-U.S. distributor because the manufacturer did not produce the product for distribution in the United States.

Owing to Lyodura's 5-year shelf life, it is likely that the eight dCJD patients in Japan who received Lyodura during 1988–1991 received grafts produced before the company changed its processing procedures in 1987. In addition, the three patients who received a graft in 1993 all received Lyodura grafts, one of which was documented to be an expired graft processed before 1987.

Age at onset of dCJD depends on the patient's age at receipt of a dural graft and the latency period. Although the latency period varies among patients, currently available data indicate that the upper limit is at least 30 years, which is longer than has been reported previously (*4*). The most recently diagnosed case, for example, occurred in a patient who received Lyodura during surgery for a craniopharyngioma in 1985 at age 27 years and developed dCJD 30 years later in 2015.

The findings in this report are subject to at least four limitations related to ascertainment of dCJD cases. First, because it is possible that dCJD patients with an unknown brand of dural graft did, in fact, receive Lyodura, it is likely that one dCJD case per 877 Lyodura recipients is an underestimate of the proportion of dCJD patients with Lyodura-related CJD. Second, the risk for a Lyodura-related CJD infection among dural graft recipients is unknown because many infected patients likely died from other causes before developing CJD. Third, additional dCJD cases related to receipt of Lyodura might still occur. The increased use of Lyodura in Japan is the most likely reason for the unusually high number of dCJD cases in Japan (*4*), although only estimates of the numbers of recipients in Japan and other countries, including the United States, are available. Finally, the medical conditions for which dura mater grafts were used in Japan differed from those in other countries (*5*): patients with dCJD in Japan more frequently received dura mater grafts for non–life-threatening conditions than did patients in other countries (*5*).

The cases described in this report indicate that recipients of prion-contaminated grafts could remain at risk for CJD for at least 30 years after receiving grafts. Given the known potential for even longer latency periods for prion diseases, this outbreak is expected to continue. The dCJD cases underscore the importance of establishing measures to eliminate or greatly reduce the possibility of CJD transmissions (e.g., strict donor screening, appropriate record keeping, prevention of cross-contaminations, and ideally, the use of validated sterilization methods) whenever human tissues, particularly of cadaveric origin, might be used to treat other patients. In addition, a system of human disease surveillance to detect the possible emergence of new sources of prion disease transmissions is needed. Furthermore, physicians maintaining a high index of suspicion for unusual prion disease cases, as well as a system of human disease surveillance to detect the emergence of new sources of prion disease transmissions, is needed to enable the prevention of infections Finally, maintaining surveillance for CJD in Japan is important to better assess the impact of the outbreak of dCJD and to identify additional cases.

Summary

What is already known about this topic?

During 1975–2008, a total of 132 cases of dura mater graft-associated Creutzfeldt-Jakob disease (dCJD), a fatal neurodegenerative disease caused by replicating, transmissible prion proteins, had been identified in Japan and accounted for >60% of patients worldwide with dCJD. This relatively high number of cases was most likely related to the increased use in Japan of the primary vehicle of transmission, Lyodura brand cadaveric grafts produced before May 1987, when the manufacturer changed its production process to reduce the risk for prion transmission.

What is added by this report?

During 2008–2017, an additional 22 dCJD patients, with onset from 1985 through 2016, were identified in Japan, resulting in 154 dCJD patients in Japan. No new dCJD patient whose surgery occurred after 1993 has been identified. However, the latency period is now known to be at least 30 years and because of the known potential for even longer latency periods for prion diseases, this outbreak is likely to continue.

What are the implications for public health practice?

The dCJD outbreak underscores the importance of strict screening of donors, appropriate record keeping, avoidance of comingling of grafts, and ideally, the use of validated sterilization procedures whenever dura mater grafts are manufactured. The long latency (decades) of human prion diseases can pose challenges to the detection of new sources of infection and highlights the need to recognize prion disease outbreaks and implement preventive measures as early as possible.

Acknowledgments

Ministry of Health, Labour and Welfare, Japan.

Conflict of Interest

No conflicts of interest were reported.

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