



Nov.23, 2015

# ***HPV vaccination associated with neuro-immunopathic syndrome (HANS)***

**Kusuki Nishioka, MD**

Professor of Medicine,  
Director, Institute of Medical Science,  
Tokyo Medical University



# Relations with our HPV vaccine adverse reaction from when? Why not?

November 2015

November 2013

Patients like to introduce consultation with fibromyalgia specialist foreign to juvenile fibromyalgia (JFM) has increased

March 2014

It was found that there is a HPV vaccination history in juvenile fibromyalgia patients like 20 people

The patients are in addition to the extensive pain had developed symptoms of a variety of central nervous

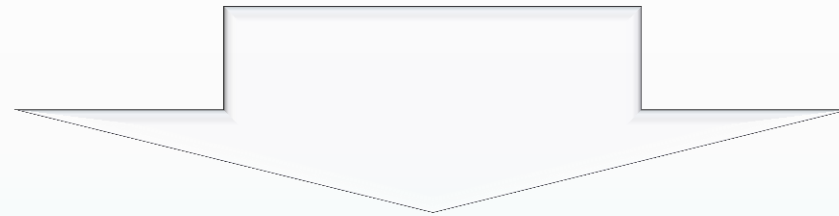
May 2015

**Japan Medical Research Foundation HANS Project Team start**

## — Study contents —

- A Start a study group by expert researchers
- B Start a medical consultation
- C A study of protocol design and the global common protocol
- D Analysis of vaccination age-adverse reaction onset age, time of onset, living area and clinical symptoms
- E Pathological analysis of basic study
- F Construction of medical care network for patients relief
- G Promotion of model hospital expansion of patient relief in the community

**A new syndrome with clinical features of subacute and multilayered manner after HPV vaccination**



**HANS**

**HPV vaccination associated  
with neuro-immunopathic syndrome**



# Proposed Preliminary Diagnostic Criteria for The Diagnosis of “HANS”

Nov.23, 2015

*-According to Clinical Symptoms with HANS Patients-*

Major Criteria : Vaccination of human papillomavirus (HPV)

➤ No abnormality of physical / psychological condition before vaccination of human papillomavirus

➤ The appearance of  
“typical clinical  
manifestations”

• Wide spread pain

• Arthralgia and/or arthritis

• Chronic fatigue, Central nervous system disorder

• Neurological manifestations

(especially associated demyelination, narcolepsy)

• Memory impairment

Minor Criteria

➤ Amenorrhea,

➤ Vagus nerve disease

➤ Spinal fluid abnormality

➤ Involvement of an autoimmune disease (i.e. MS, SSc)



# Number of Multilayered Symptoms in 104 Cases with HANS

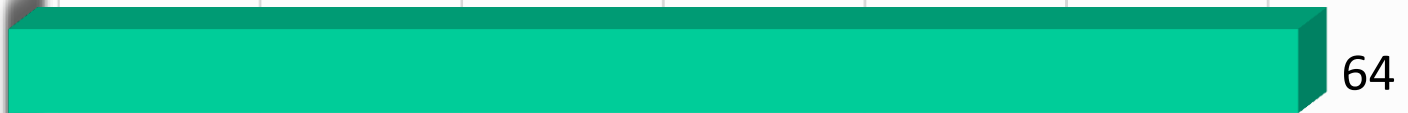
Nov. 2015

2015/11/2  
N=201

2015年後期  
JUL~NOV, 2015



2015年前期  
JAN~JUN, 2015



2014年後期  
JUL~DEC, 2014



2014年前期  
JAN~JUN, 2014



**May-2014 HPV Vaccination Project Term**

2013年



0 10 20 30 40 50 60 70 人



# HPV vaccine adverse reaction is not only in Japan!







Nov 23, 2015





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# Global incidence of HPV vaccine adverse reaction

		DK 	GB 	AU 	US 	FR 	JP 
Adverse reaction	Number of cases	1,730	8,243	3,530	25,176	2,092	4,267*
	Number of reactions	11,529	19,359	8,815	ND	5,850	14,047*
Vaccination	Number of doses	1,635,768	ND	9,000,000	67,719,000	5,240,000	8,898,150
	Number of people	630,000 <sup>b</sup>	ND	3,460,000	26,050,000	2,020,000	3,380,000
<b>Vaccination / 1,000 adverse reaction number of cases</b>		<b>2.7</b>	<b>ND</b>	<b>1.0</b>	<b>1.0</b>	<b>1.0</b>	<b>1.3</b>

\* : PMDA+ MHLW data

a : ANSM : Estimated from described, b : Estimate value = Doses per 2.6

DK: [DHMA](#), Drug Analysis Print : Data lock 2015/7/31

GB: [MHRA](#), Case Series Drug Analysis Print : Data lock 2015/6/5

AU: [TGA](#), DAEN (Database of Adverse Event Notifications) : Data lock 2015/4/16

US: [CDC](#), MMWR(Morbidity and Mortality Weekly Report), Recommendations and Reports 63(5) : 2014/8/29

FR: [ANSM](#), Suivi National **Gardasil**<sup>®</sup>, 3<sup>ème</sup> rapport Vaccin contre le papillomavirus humain : 2014/2/18

JP: [PMDA](#) Adverse Reaction Database : Data lock 2015/3/31

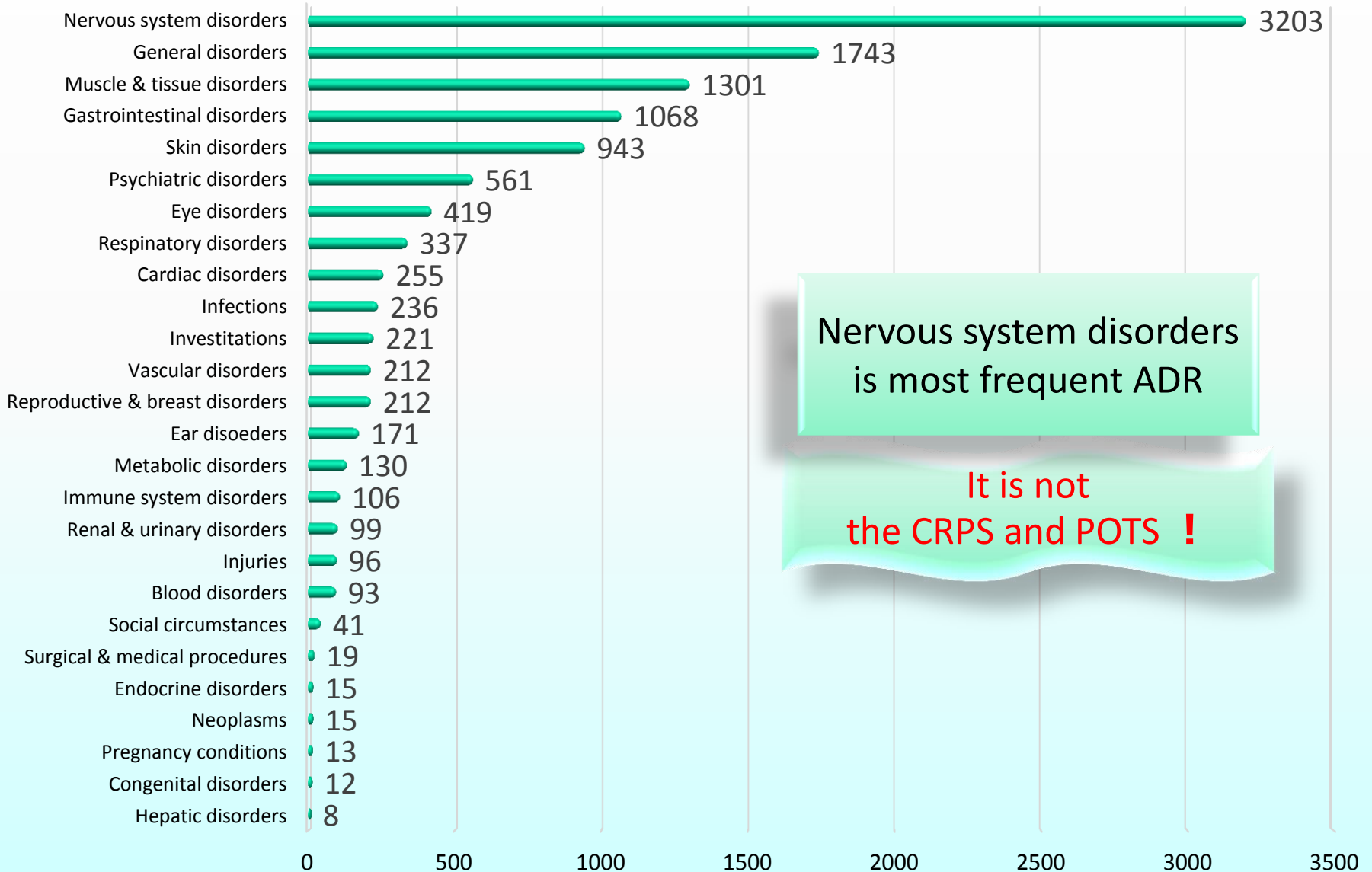
[MHLW](#), 10<sup>th</sup> Examination Meeting for Adverse Reaction of Immunization and Vaccine Subcommittee of MHLW Health Sciences Council, data No.1-8 (Data lock 2014/3) : 2014/7/4



# Analysis of 11,529 clinical symptoms associated in Danish 1,730 cases with adverse reactions after HPV vaccination

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## Report of Adverse reaction by Drug Analysis Print 31. JUL. 2015



Nervous system disorders is most frequent ADR

It is not the CRPS and POTS !

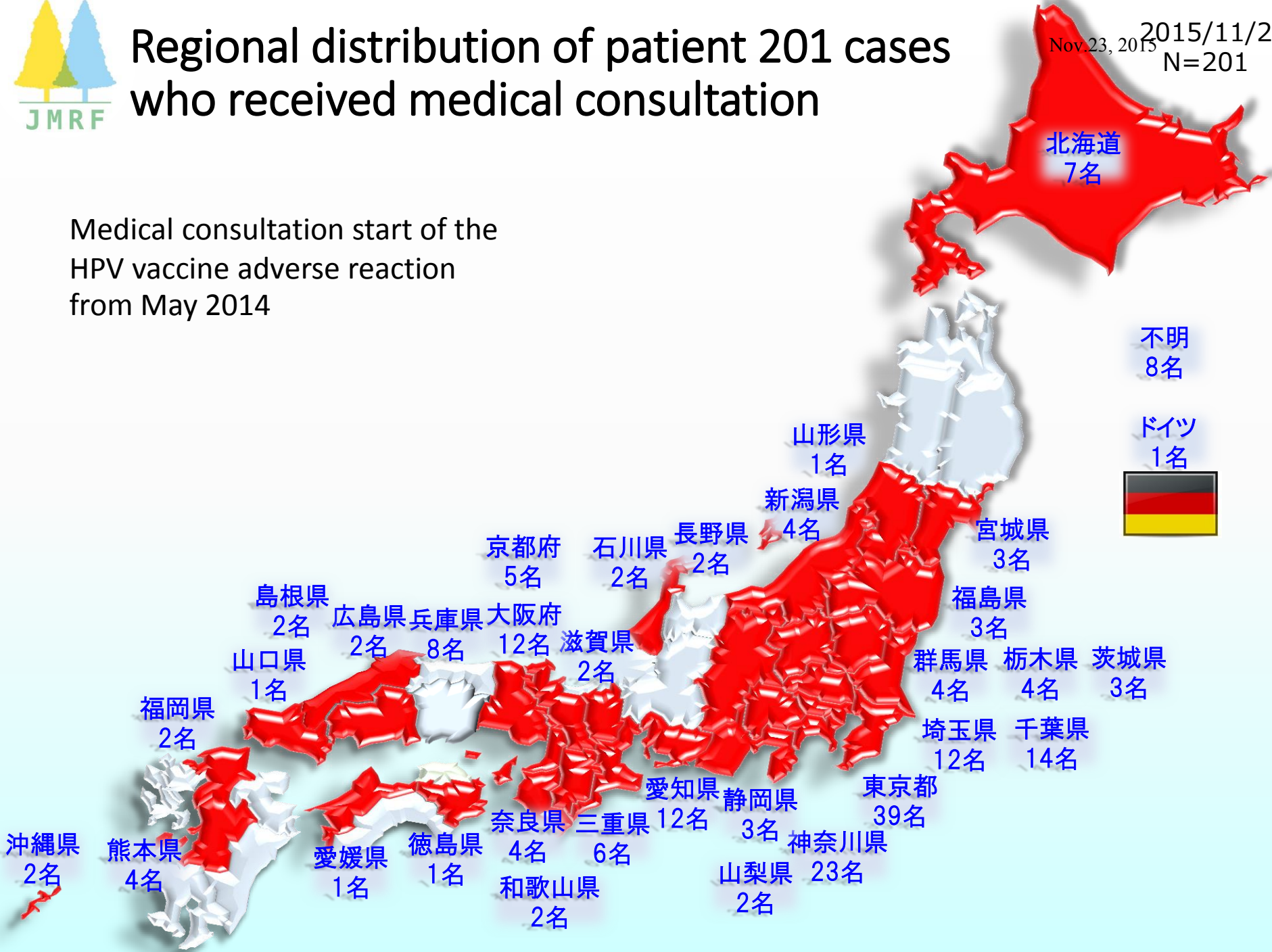




# Regional distribution of patient 201 cases who received medical consultation

Nov. 23, 2015  
2015/11/2  
N=201

Medical consultation start of the HPV vaccine adverse reaction from May 2014

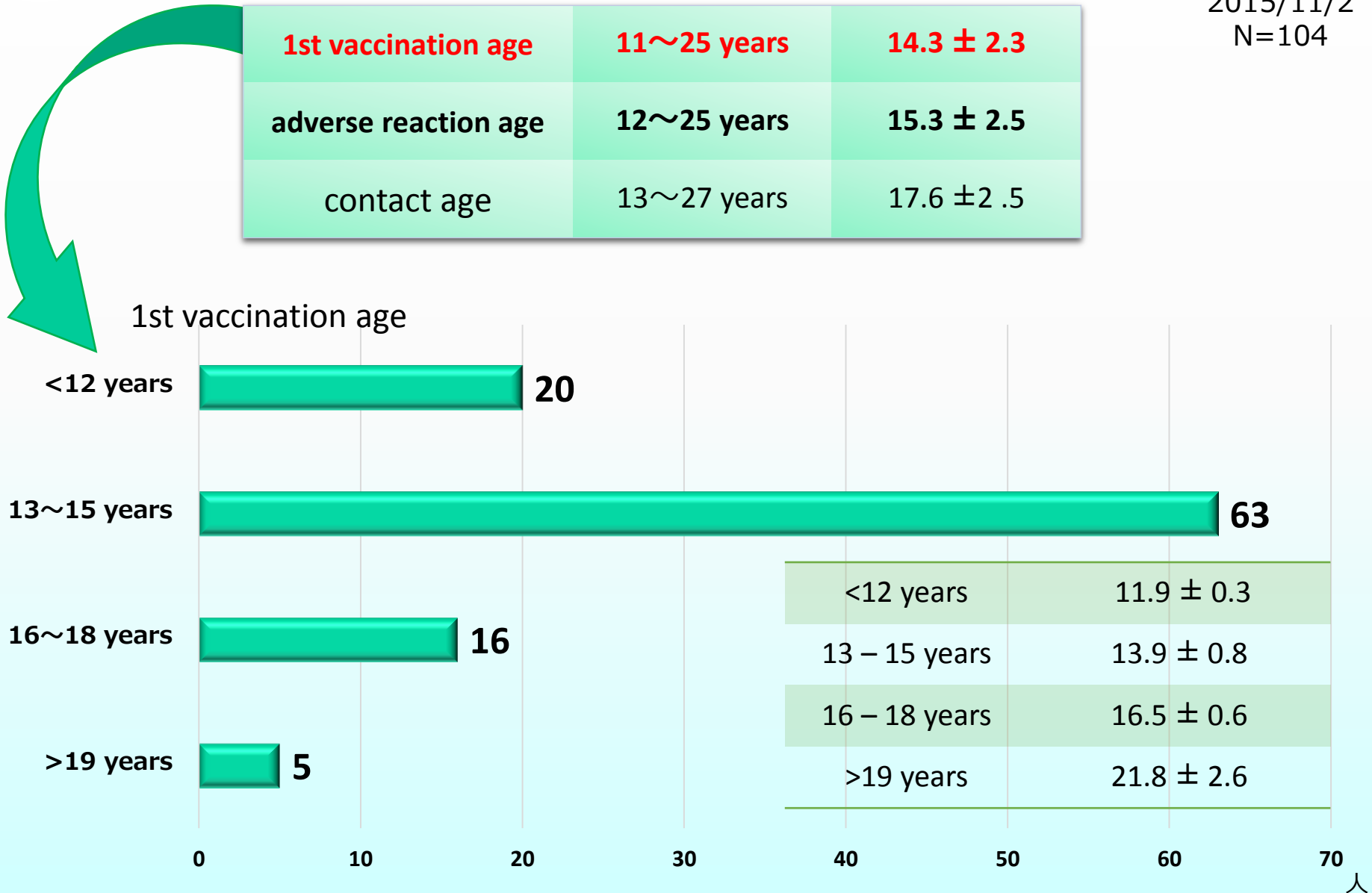




# Vaccination age and adverse reaction age at onset of the 104 cases of patients who are diagnosed with HANS

2015/11/2  
N=104

<b>1st vaccination age</b>	<b>11~25 years</b>	<b>14.3 ± 2.3</b>
adverse reaction age	12~25 years	15.3 ± 2.5
contact age	13~27 years	17.6 ± 2.5





# 104 analysis of the overlapping symptoms of 4,455 clinical symptoms associated with the example of HANS

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2015.11.2

N=104

101-110

91-100

81-90

71-80

61-70

51-60

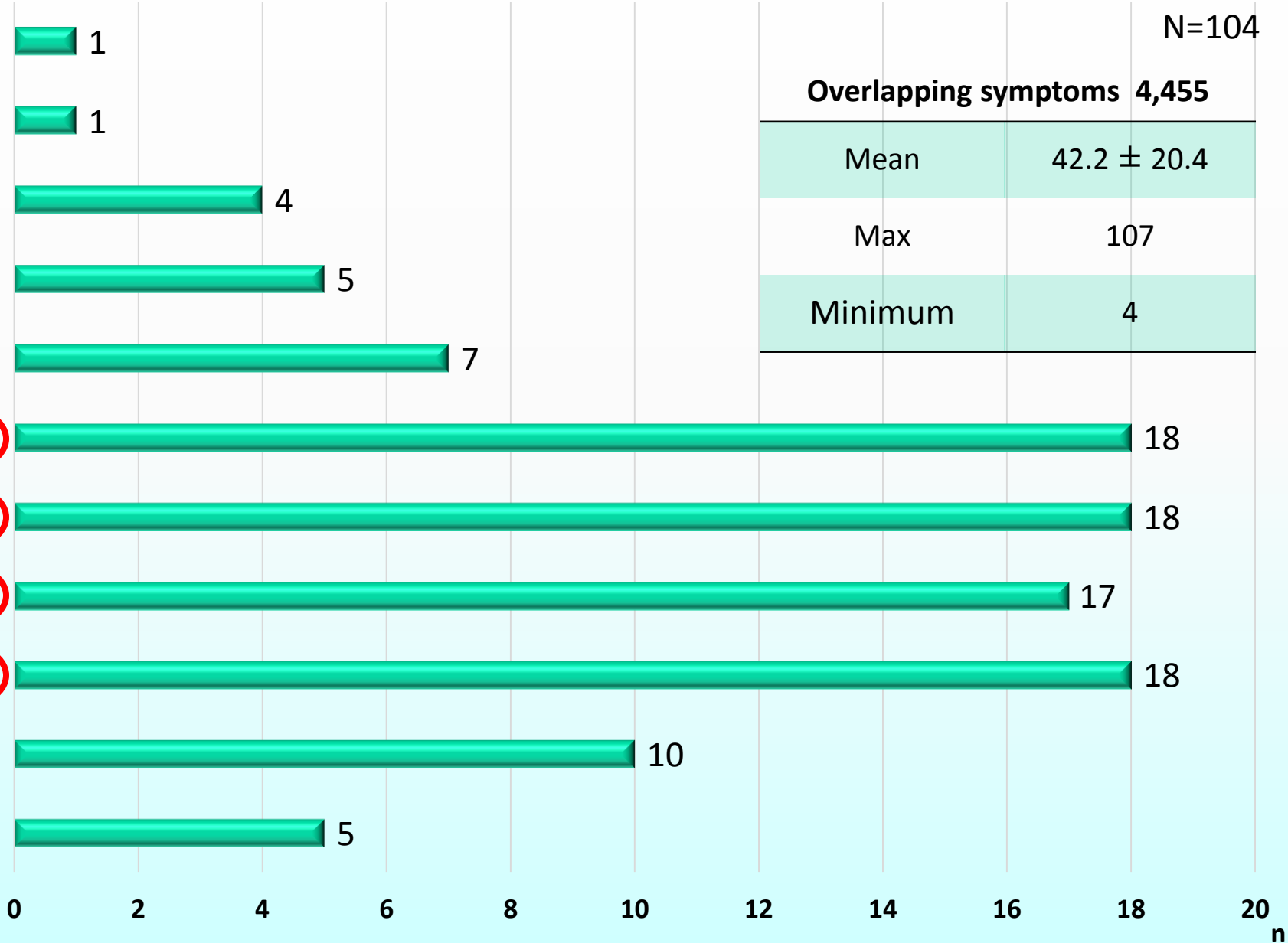
41-50

31-40

21-30

11-20

1-10



**Overlapping symptoms 4,455**

Mean	42.2 ± 20.4
Max	107
Minimum	4

# Characteristic of time-series change of symptoms in HANS patients

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HPV vaccination



Fatigue, Sluggishness,  
Malaise

Consecutive involuntary movement  
of whole body

Locomotive disorders  
(Gait disturbance)  
→ Wheelchair,  
Bedridden

Widespread pain,  
Numbness

Brainstem  
abnormality

The symptoms  
gradually became  
multilayered as time  
from vaccination  
increased, and their  
severity varied from  
day to day

Autonomic nerve system disorders

Consciousness disorders

Recent memory  
impairment,  
Epileptic seizure

3 years after HPV vaccination

1<sup>st</sup> stage

2<sup>nd</sup> stage

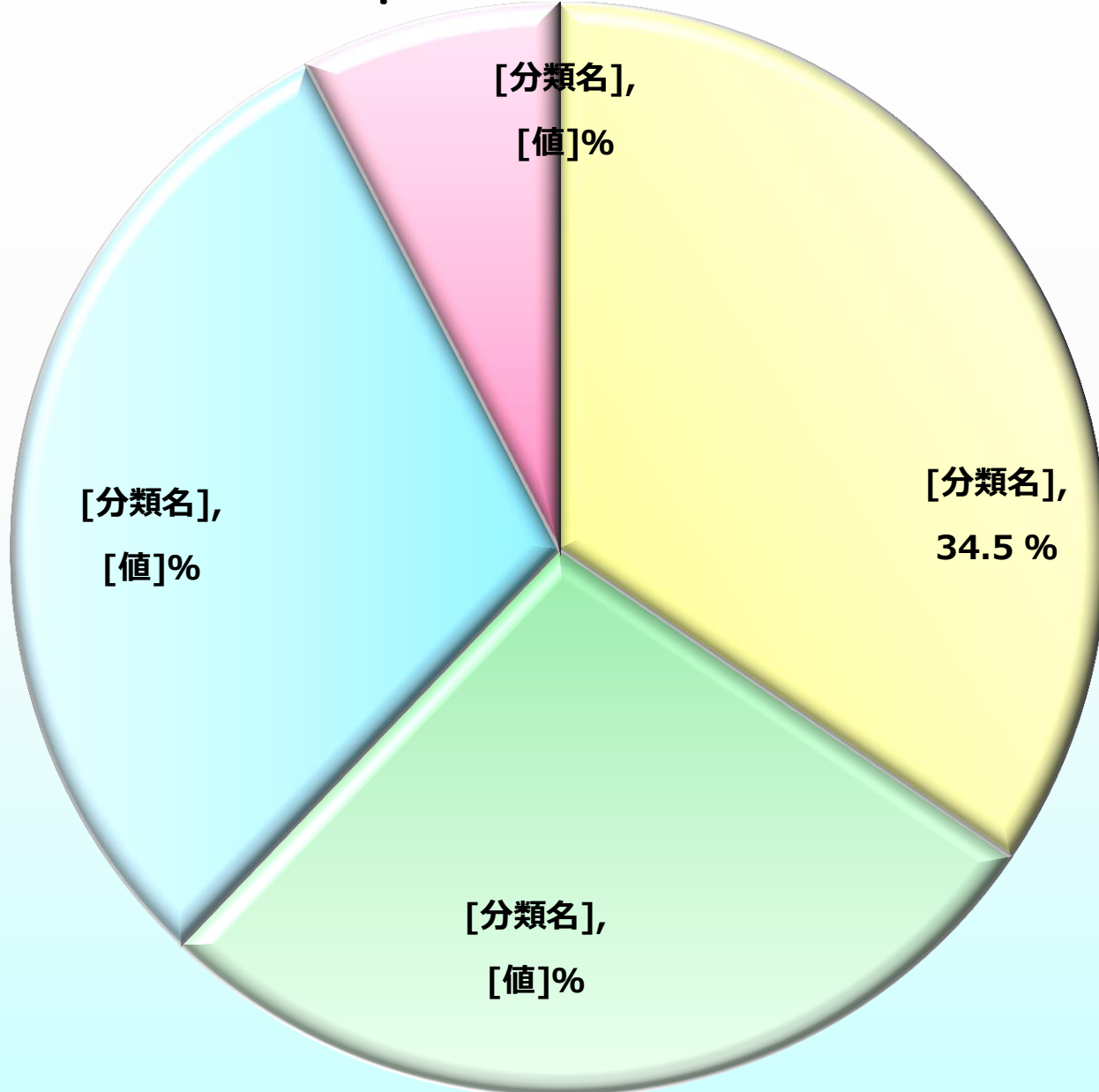
3<sup>rd</sup> stage

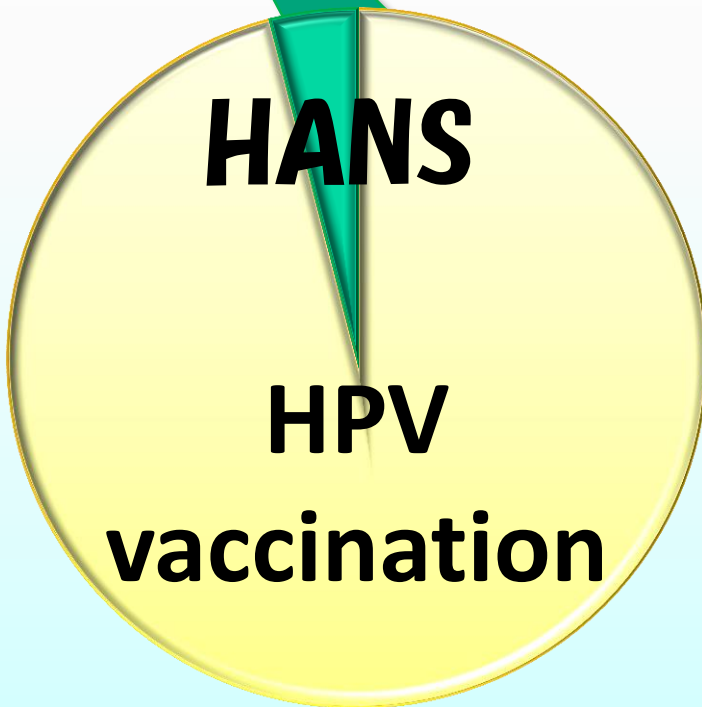


# Symptomatic another adverse reaction incidence of HANS patient 104 cases

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2015/11/2現在  
N=104

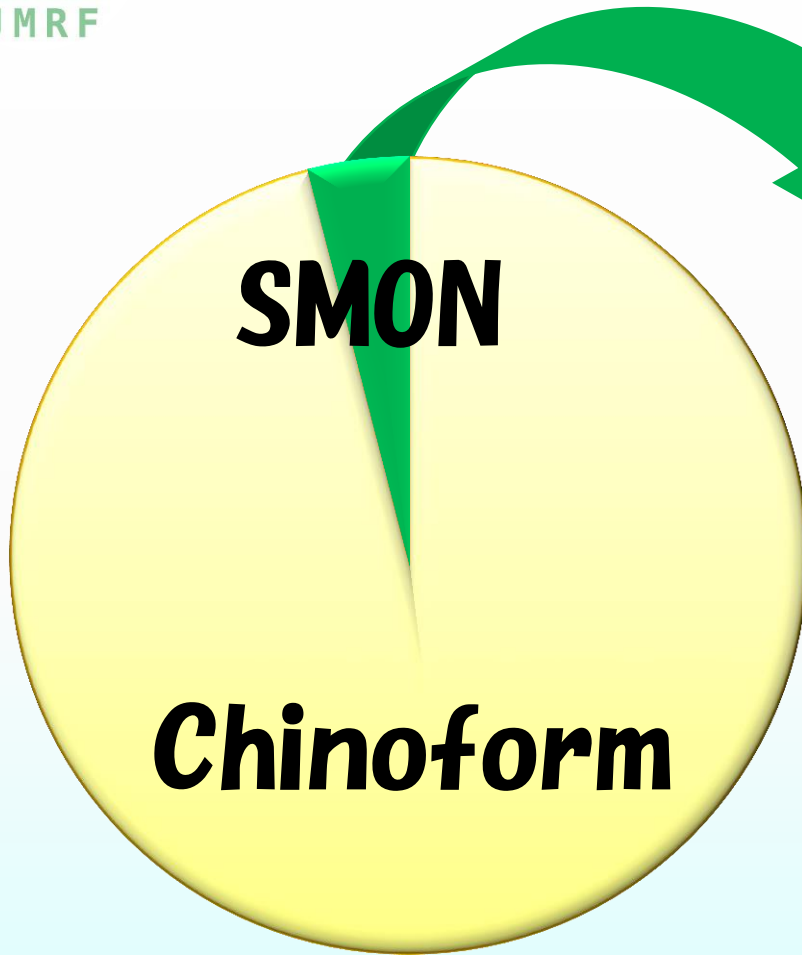




<p>pain in extremity, widespread pain, photosensitivity reaction, hyperesthesia, acoustic hyperesthesia, hypersomnia, severe menstrual pain</p>	<p>➔ Sensory system disorders</p>
<p>irritable bowel syndrome, bulimia, hyperventilation, asthma, fever, hypothermia, hyperhidrosis, circadian rhythm disorder (sleep disorder), orthostatic syncope, menstruation irregularity, narcolepsy,</p>	<p>➔ Autonomic nerve and endocrine system disorders</p>
<p>posture abnormal, dysstasia, gate disturbance, involuntary movement, convulsion</p>	<p>➔ Locomotor system disorders</p>
<p>apathy, fatigue, irritability, visual hallucination, auditory hallucination, delusion, abusive speech, refusal to attend school, panic attack, prosopagnosia, dyscalculia, poor concentration, decline in academic performance</p>	<p>➔ Cognitive dysfunction and emotional disorders</p>

# SMON : The drug induced damage affair

Nov. 25, 2015



onset in dysesthesia
dysesthesia of bilaterality
Locomotor system disorders
pyramidal sign
visual disorder of bilaterality
brain inflammation
psychiatric symptom
bladder and rectal disturbance
nervous system • sensory system • locomotor system , etc

1950	Symptom finding
1958	The first case was reported from Wakayama Medical University
1964	<b>The proposal the SMON (Prof. Tsubaki • Prof. Toyokura, et al.)</b>