Table 1. Events

Event	Aged < 75	Aged ≥ 75
Bleeding		
Major		
Rectal bleeding	2	2
Epistaxis	1	2
Bruises	0	1
Hemoptysis	0	1
Hematuria	1	0
Hematemesis	1	0
Minor		
Epistaxis	21	22
Bruises	13	15
Vaginal bleeding	5	4
Hematuria	3	5
Hemoptysis	3	4
Rectal bleeding	2	4
Gum bleeding	3	1
Hemarthrosis	1	0
Conjunctival bleeding	1	0
Thrombotic		
Cerebrovascular accident	5	3
Transient ischemic attack	1	1
Mortality		
Myocardial infarction	2	4
Pneumonia	2	3
Congestive cardiac failure	1	4
Postoperative	2	1
Bowel obstruction	0	1
Carcinoma	0	1
Septicemia	1	0
Withdrawals (discontinued warfarin)		
Bleeding complications	8	10
Successful DC shock	7	4
Medical cardioversion	6	4
General ill health	2	3
Frequent falls	1	2
Chronic anemia	1	2
Carcinoma	1	1
Hair loss	1	0
Jaundice	1	0
Heart transplant	1	0

tients in the older group who developed thromboembolic strokes, one had a subtherapeutic INR of 1.2, whereas the other two were within the target range INR (2.8 and 2.3). There were two cases of transient ischemic attack—one in each group. More subjects in the younger group had DC cardioversion than in the older group (31 (15.3%) vs 7 (3.5%), $P < .001$). Time spent within the target INR was comparable (58 (12.8%) in the younger group; 58 (12.0%) in the older group, $P = .9$). Fourteen (7%) patients in the older group died, compared with eight (3.9%) in the younger group ($P = .10$). There was no bleeding-related death in either group. Twenty-nine (14.3%) patients in the younger group stopped warfarin treatment, compared with 26 (13.1%) in older age group. Thirteen patients were cardioverted to normal sinus rhythm in the younger group (7 electrically and 6 medically), compared with eight in the older group (4 electrically and 4 medically) (Table 1).

In this study, only patients newly started on warfarin were included to ensure that early withdrawals did not bias results in favor of anticoagulation. Advanced age was not a significant risk factor for bleeding. A nonsignificantly higher rate of thromboembolic stroke in the younger group was probably due to subtherapeutic INR in three (60%) of five patients, in comparison with only one (33%) of three patients in the older group. DC cardioversion tended to be attempted significantly more often in younger patients, which could be due to physicians' choice. The findings are consistent with those of investigators who did not detect a significant relationship between age and incidence of bleeding during warfarin treatment.[7,8]

Age alone should not be a major determinant of eligibility for anticoagulation in patients with atrial fibrillation. Clinical emphasis should be on undertaking objective risk–benefit assessment regardless of age to identify patients most likely to derive the greatest benefit from regular warfarin use.

Ahmed H. Abdelhafiz, MBBCh, MSc, MRCP (UK)
Department of Elderly Medicine
Rotherham General Hospital
Rotherham, UK

Nigel M. Wheeldon, MBChB, MD, FRCP (UK), FESC
South Yorkshire Cardiothoracic Center
Northern General Hospital
Sheffield, UK

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OUTBREAK OF HUMAN METAPNEUMOVIRUS INFECTION IN ELDERLY INPATIENTS IN JAPAN

To the Editor: Human metapneumovirus (hMPV), a newly discovered pneumovirus of the *Paramyxoviridae* family,

has been isolated from young children with acute respiratory tract illness (RTI) in the Netherlands.[1] Serological analyses have indicated that the prevalence of hMPV in the Dutch population is high, because virtually all children became seropositive before the age of 6,[1] indicating that hMPV is a common and ubiquitous human pathogen. Subjects aged 65 and older were reported to account for 45.9% of Canadian patients with community-acquired hMPV infection hospitalized for RTI.[2]

Between January 18 and 31, 2005, a cluster of eight inpatients (mean age 79; range 65–89; 6 male, 2 female) developed RTI in a 23-bed ward in a hospital for older people in Japan. The clinical features and outcomes of the subjects are shown in Table 1. All individuals were sharing the same day-care room on the ward. Two patients had bronchiolitis (Cases 1 and 7), five bronchitis (Cases 2–5 and 8), and one upper RTI (Case 6) based on the clinical symptoms and chest roentgenograms. Mean duration of exothermic reaction ($>37.0^{\circ}$C) was 4 days (range 0–6). Wheezing and dyspnea were observed in only two subjects; coryza and productive cough were observed in all. White blood cell count (mean 4.1×10^9 cells/L, range 2.3–6.5×10^9), and C-reactive protein blood levels (25.7 mg/L, range 1.7–52.9) remained low. Treatment for RTI included aminophylline, oxygen supplementation, antibiotics, and acetaminophen. All subjects showed recovery from acute RTI, although two patients newly developed asthma and secondary pneumonia (*Klebsiella pneumoniae* identified in sputum).

hMPV fusion gene was detected using reverse-transcription polymerase chain reaction (RT-PCR)[3] in nasal swabs from all subjects at onset. The genotype of the amplified products from every specimen was identical to that of the prototype strain (designated NL/1/99, Gene Bank accession no. AY525843), which belongs to genetic lineage B1.[4] The results of other viral cultures, antigen tests (influenza virus A/B, adenovirus, and respiratory syncytial virus (RSV)), and RT-PCR (RSV, parainfluenza virus (types 1–4), coronavirus, and rhinovirus) were all negative. hMPV was not found in swabs from other inpatients without RTI (n = 6) in the same ward or the care workers (n = 4).

Immunoglobulin (Ig) G antibody to hMPV with indirect immunofluorescence assay[1,5,6] was already present in serum from eight hMPV-infected patients and 10 control individuals in the acute phase. The IgG titers in six hMPV-infected subjects except Cases 4 and 7 were more than four times as high in the convalescent phase, and the titers in one of the controls were more than four times as high as in the convalescent phase. Two months after recovery of the final patient, purified protein derivative (PPD) reaction was retrospectively investigated in the hMPV-infected subjects (n = 8), the controls (n = 8), and the care workers (n = 9). Seven individuals (87.5%) (all except Case 4) showed a negative reaction, whereas the controls and the workers showed negative rates of 37.5% and 22.2%, respectively.

The clinical symptoms induced by hMPV infection in children are similar to those caused by RSV infection, ranging from mild respiratory problems to severe cough, bronchiolitis, and pneumonia.[1] hMPV ribonucleic acid was detected in respiratory samples from hospitalized patients aged 65 and older with RTI, whereas RSV was not found in the same elderly group.[7] A cluster of eight hMPV-infected cases with RTI was found in a hospital for older people. Thus, hMPV rather than RSV should be considered as a causative pathogen in elderly subjects with RTI.

One study[8] has reported detection of hMPV antigens in nasal secretions obtained from 48 hospitalized children with RTIs using an immunofluorescent-antibody test (IFA). IFA is a rapid and useful test for the diagnosis of hMPV infections in children, although the sensitivity of IFA (73.3%) is lower than that of RT-PCR. It is important to establish rapid virus detection assays, including RT-PCR or antigen tests, especially for older people, as are currently applied for diagnosing infections with other viral pathogens, because older people with pneumonia who are infected with hMPV are at risk of death due to respiratory failure.[2]

In addition, a difference was found in the PPD reaction between the hMPV-infected patients and control subjects or care workers, although the reaction was checked retrospectively. This observation suggests that a negative PPD reaction, reflecting reduced cellular immunity, is a potential risk factor for hMPV infection, as well as tuberculosis and shingles, in older people. It is necessary to conduct a wide-ranging prospective study to better evaluate risk factors that may be associated with hMPV infection.

Haruhito Honda, MD
Jun Iwahashi, MD
Takahito Kashiwagi, MD
Yoshihiro Imamura, MD
Nobuyuki Hamada, MD
Department of Virology
Kurume University School of Medicine
Kurume, Fukuoka, Japan

Takehiko Anraku, MD
Seiichiro Ueda, MD
Ueda Hospital
Chikugo, Fukuoka, Japan

Tsugiyasu Kanda, MD
Takashi Takahashi, MD
Department of General Medicine
Shigeto Morimoto, MD
Department of Geriatric Medicine
Kanazawa Medical University, Kahoku, Ishikawa, Japan

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Table 1. Clinical Features and Outcome for a Cluster of Eight Elderly Inpatients in Japan Infected with Human Metapneumovirus

No.	Age	Sex	Main Cause of Admission	Date of Onset (January 2005)	Highest Body Temperature (°C)	Exothermic Duration (>37.0°C) (Days)	Coryza	Sore Throat	Hoarseness	Cough	Sputum	Wheezing	Chest X-Ray	Dyspnea	Minimum Oxygen Saturation in Arterial Blood (%)	Cyanosis	White Blood Cell Count ($\times 10^9$ cells/L)	C-Reactive Protein (mg/L)	Treatment	Outcome
1	84	F	Cyclothymic disorder	18	38.9	6	(+)	(+)	(−)	Productive	White viscous	(+)	Hyperinflation, patchy and linear shadows in left lower field	(+)	88	(+)	3	52.9	APAP, aminophylline, O_2 (1 L/min), CTRX	BA and secondary pneumonia (*Klebsiella pneumoniae*)
2	71	M	Senile depression	24	38.8	5	(+)	(+)	(+)	Productive	White viscous	(−)	Patchy and linear shadows in right hilar and lower fields	(−)	NT	(−)	5	41.2	APAP, CTRX	Recovered
3	65	M	MCLI	24	38.5	5	(+)	(+)	(−)	Productive	White or yellow viscous	(−)	No change	(−)	NT	(−)	2.3	39.4	APAP, CTRX	Recovered
4	74	M	Schizophrenia	24	38.1	4	(+)	(+)	(+)	Productive	White viscous	(−)	NT	(−)	NT	(−)	2.3	1.7	APAP, RXM	Recovered
5	81	F	MCLI	27	38.6	4	(+)	(+)	(+)	Productive	White viscous	(−)	NT	(−)	NT	(−)	3.3	9.1	APAP, RXM	Recovered
6	86	M	MCLI	27	38.5	4	(+)	(+)	(−)	Productive	(−)	(−)	No change	(−)	NT	(−)	5.3	45	APAP, RXM	Recovered
7	89	M	MCLI	31	37.8	4	(+)	(+)	(+)	Productive	White viscous	(+)	Hyperinflation	(+)	91	(−)	6.5	13.7	APAP, aminophylline, O_2 (1 L/min), CTRX	BA and secondary pneumonia (*K. pneumoniae*)
8	86	M	MCLI	31	36.8	0	(+)	(+)	(−)	Productive	White viscous	(−)	Linear shadows in bilateral lower fields	(−)	NT	(−)	5.4	3.1	APAP, RXM	Recovered

M = male; F = female; − = negative; + = positive; APAP = acetaminophen; O_2 = oxygen; CTRX = ceftriaxone; BA = bronchial asthma; NT = not tested; MCLI = multiple cerebral lacunar infarction; RXM = roxithromycin.

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MILD BEHAVIORAL IMPAIRMENT: A PRODROMAL STAGE OF FRONTOTEMPORAL LOBAR DEGENERATION

To the Editor: Frontotemporal lobar degeneration (FTLD) is the third most common type of dementia after Alzheimer's disease (AD) and dementia with Lewy bodies. FTLD is a disorder of behavior, social conduct, and executive function and starts between the ages of 40 and 60. The Neary research criteria define three clinical FTLD syndromes.[1]

The hypothesis that mild cognitive impairment (MCI) represents a transitional state between normal cognitive aging and dementia is widely accepted. Three types are defined (Table 1): MCI-amnestic; MCI-multiple domains, slightly impaired (for example, vascular cognitive impairment); and MCI-single nonmemory domain.[2] The last presents as impairment in a single cognitive domain other than memory, such as a dysexecutive syndrome. This condition was described as mild behavioral impairment (MBI) and as MCI of the frontotemporal type.[3,4]

Three patients referred to the memory clinic are described. A 56-year-old man had conflicts at work due to poor judgment. He became gradually more aggressive and showed signs of hyperorality and disinhibition. His score was 36 of 72 (cutoff = 27) on the Frontal Behavioral Inventory (FBI)[5] and 24 of 42 (cutoff = 14) on the Apathy Scale of Starkstein.[6] Cerebral single photon emission computed tomography (SPECT) scanning revealed left frontotemporal hypoperfusion. Neuropsychological testing showed impairment on frontal executive tests, but he did not meet the criteria for FTLD, and his wife reported normal activities of daily living (ADLs), instrumental activities of daily living (IADLs), and general functioning. A diagnosis of MBI was made. He was treated with citalopram, a serotonin-selective reuptake inhibitor (SSRI), and became less disinhibited. A year later, his memory had deteriorated. A 62-year-old male teacher presented with changes in behavior. He had always been aggressive, but during the previous 2 years showed loss of empathy, impulsivity, hyperorality, inflexibility, and repetitive behavior. He had a high score on the FBI (54). SPECT scanning showed left temporal hypoperfusion. Neuropsychological evaluation revealed some repetitive behavior, loss of insight, and mildly decreased verbal fluency, but he did not meet the criteria for FTLD, and his wife reported normal IADLs/ADLs and general functioning. Because of persistent behavioral changes, mild psychiatric symptoms, no memory complaints, and normal functioning, he was diagnosed with MBI. Citalopram improved his aggression slightly. A 57-year-old man developed apathy, aspontaneity, and behavioral changes with emotional unconcern and inflexibility. He made repetitive noises, lacked initiative, and showed inappropriate behavior and disinhibition in eating. His FBI score was 43. SPECT scanning demonstrated bilateral frontal hypoperfusion. Neuropsychological examination revealed general slowing, intact memory and orientation, diminished flexibility and self-inhibition, decreased verbal fluency, and mild executive problems, but he did not meet the criteria for FTLD, and his wife reported normal IADLs/ADLs. A diagnosis of MBI was made. A year later, he had developed FTLD.

By separating clinical and preclinical stages, the importance of disease course is emphasized, which makes it possible to describe various stages of the same disease or, alternatively, to describe one disease-related syndrome that changes its features over time as the disease process continues. Dementia presents with psychiatric symptoms in about 50% of cases. Diagnosis is difficult when symptoms are still mild and atypical. A prospective cohort study of nondemented patients at risk of FTLD was performed;[3] after 3 years 77% had developed into dementia: 7% dementia with Lewy bodies, 25% AD, and 45% FTLD; six of seven patients diagnosed with MCI of the frontotemporal type developed FTLD within a mean $\pm$ standard deviation of 1.8 ± 1.0 years.[4] In the case with disinhibition as an early symptom, the risk of dementia was more than two and a half times as high. In the case with a frontotemporal SPECT pattern, the risk of FTLD was three and a half times as high. A normal SPECT decreased the risk of dementia 93%, so functional imaging is a valuable tool.[3]

If a normally functioning person presents with persistent mild psychiatric symptoms, especially disinhibition, MBI should be considered. SPECT scanning is recommended. In populations without dementia, behavioral symptoms often improve with medications that increase serotonin activity. Low serotonin-receptor binding has been reported in FTLD. Treatment with SSRIs improved behavioral symptoms in at least half of FTLD patients.[7] It has been reported that paroxetine addressed anxiety and repetitive, ritualistic behaviors.[8] In FTLD, treatment with SSRIs is considered of interest when the target symptoms are disinhibition,