Fig. 1. (a) Change in total number of medicolegal death and medicolegal deaths of homeless persons during 1999–2010 in the special wards of Tokyo Metropolis. (b) Change in total number of homeless persons and medicolegal deaths of homeless persons during 1999–2010 in the special wards of Tokyo Metropolis.

2. Materials and methods

2.1. Study sample

All medicolegal deaths in the Special wards of Tokyo Metropolis are reported to the Tokyo Medical Examiner's Office. We reviewed the documents concerning medicolegal deaths handled in the Tokyo Medical Examiner's Office during 1999–2010 and selected cases that were considered to be homeless. We considered as homeless those "who, for no reason, occupy city parks, rivers, roads, stations, and other facilities as the living space to lead their daily lives," as defined in the "Law Concerning Special Measures to Support Self-Reliance of the Homeless" [9]. In addition, we also considered persons who stayed for long periods of time in flophouses as homeless for the purposes of this study. Criminal cases are usually transferred to other facilities (Forensic Department of Medical Faculty of Universities) for judicial autopsy, and such cases are excluded from this study. The total number of medicolegal deaths of homeless persons during the study period was 2842 (autopsy rate: 54.8%), and the proportion to total cases handled in the Tokyo Medical Examiner's Office was 2.1%. Men comprised 98.3% of the cases, and age distributed from 23 to 90 (mean age: 61.5). According to the demographic features of the homeless deceased, we selected the non-homeless cases those gender were male (aged 20–90) as a control (n = 83,375, autopsy rate: 24.5%). Age and

manner/cause of death were closely examined in such cases. Data regarding the total number of homeless in the special wards of Tokyo Metropolis in each year was cited from those reported by the Bureau of Social Welfare and Public Health, Tokyo Metropolitan Government [11].

2.2. Comparison of the manners/causes of death

Causes of death were classified according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) [10]. We divided cases into two age groups (i.e., under 60 and above 60 years) when we compared the manners/causes of death between the cases before 2004 and those after 2004. In addition, we divided the cases into four age groups ($\leqslant$49, 50–59, 60–69, $\geqslant$70) when we analyzed the relationship between manner/cause of death and age regarding homeless persons.

2.3. Statistical analysis

We used the chi-squared test for independence for statistical analysis, and values of $P < 0.05$ were considered statistically significant. The chi-square test was performed in two ways (i.e. among total cases, among only autopsied cases) regarding specific causes of death, and we considered each cause of death to be significant when both of the results were significant. The ethical committee
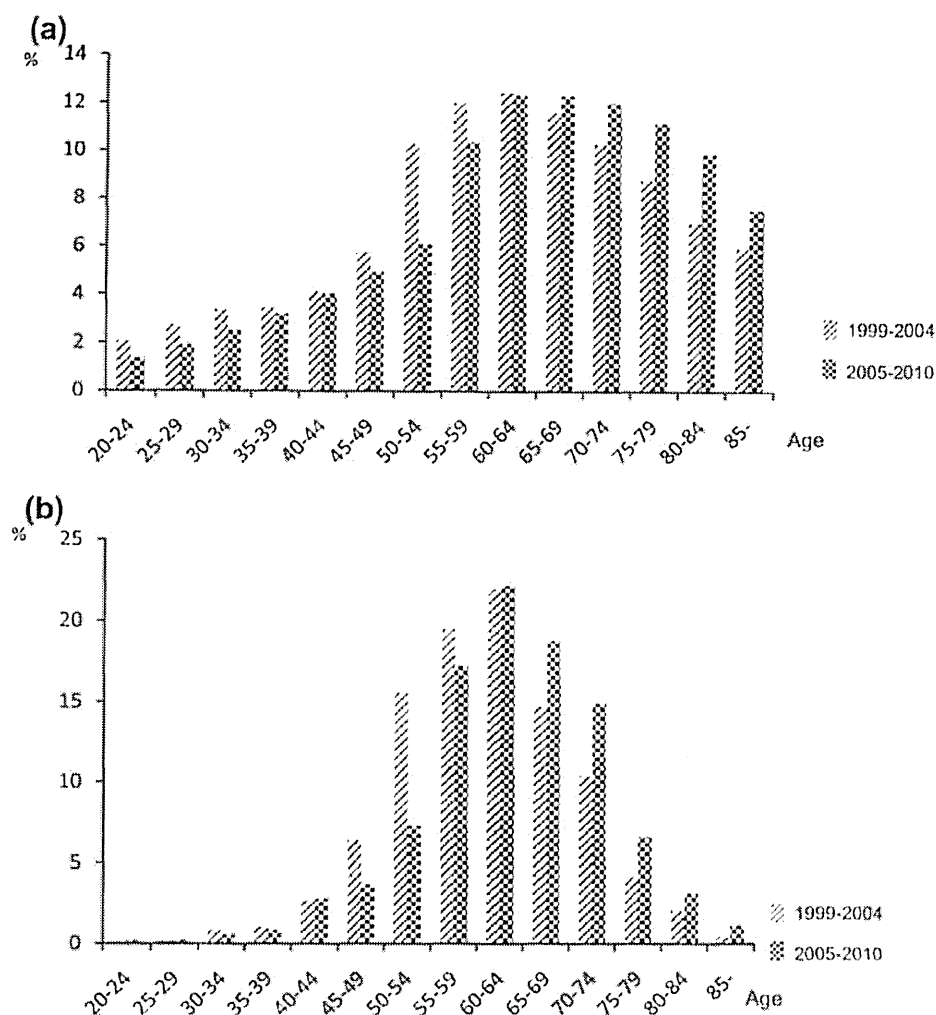
Fig. 2. (a) Age distribution of medicolegal deaths of non-homeless persons during 1999-2004 and 2005-2010 in the special wards of Tokyo Metropolis. (b) Age distribution of medicolegal deaths of homeless persons during 1999-2004 and 2005-2010 in the special wards of Tokyo Metropolis.

Table 1a

Comparison of the manner of death for non-homeless persons between the two groups (cases in 1999-2004 and in 2005-2010) according to age groups.

	Age <60				Age >60			
	1999-2004	%	2005-2010	%	1999-2004	%	2005-2010	%
Disease	7918 (4122)	47.5	7706 (3905)	49.3**	16,436 (3452)	77.0	23,330 (3803)	78.5**
Accident	1924 (582)	11.6	1453 (594)	9.3**	1967 (555)	9.2	2409 (823)	8.1**
Suicide	5754 (162)	34.5	5216 (193)	33.3*	2223 (59)	10.4	2455 (69)	8.3**
Undetermined external cause	494 (326)	3.0	464 (332)	3.0	249 (171)	1.2	275 (207)	0.9**
Unknown	568 (320)	3.4	803 (289)	5.1**	483 (212)	2.3	1248 (288)	4.2**
Total	16,658 (5512)	100	15,642 (5313)	100	21,358 (4449)	100	29,717 (5190)	100

Parentheses indicate the number of autopsied cases.
% Indicate the proportion of each manner of death to the total number of deaths in each group.
* P < 0.05.
** P < 0.01.

of the Tokyo Medical Examiner's Office approved the protocol of this study.

3. Results

3.1. Demographic changes in medicolegal death of homeless persons and non-homeless persons over 12 years

As shown in Fig. 1a, the total number of medicoleal deaths handled in the Tokyo Medical Examiner's Office (and also the number of control case) steadily increased, especially after 2005. On the other hand, the number of medicolegal deaths of homeless persons in each year remained almost the same during the study period, resulting in a lower proportion of medicolegal death of homeless to total medicolegal cases (and control case) after 2005. However, as shown in Fig. 1b, the total number of homeless persons steadily decreased in the special wards of Tokyo Metropolis, especially after 2004, which was similar to the trend in the whole of Japan [1,8]. As a result, proportions of medicolegal death of homeless persons to total numbers of homeless persons became higher after 2004.

Table 1b

Comparison of the manner of death for homeless persons between the two groups (cases in 1999–2004 and in 2005–2010) according to age groups.

	Age <60				Age >60			
	1999–2004	%	2005–2010%	%	1999–2004	%	2005–2010	%
Disease	458 (308)	68.2	292 (202)	63.8	586 (323)	75.0	676 (330)	72.6
Accident	112 (69)	16.7	83 (64)	18.1	130 (80)	16.6	152 (96)	16.3
Suicide	63 (1)	9.4	44 (1)	9.6	29 (0)	3.7	49 (2)	5.3
Undetermined external cause	18 (16)	2.7	8 (6)	1.7	12 (8)	1.5	23 (17)	2.5
Unknown	21 (8)	3.1	31 (6)	6.8*	24 (13)	3.1	31 (8)	3.3
Total	672 (402)	100	458 (279)	100	781 (424)	100	931 (453)	100

Parentheses indicate the number of autopsied cases.

% Indicate the proportion of each manner of death to the total number of deaths in each group.

* $P < 0.05$.

Table 2a

Comparison of the major causes of death for non-homeless persons between the two groups (cases in1999–2004 and in 2005–2010) according to age groups.

	Age <60				Age >60			
	1999–2004	%	2005–2010	%	1999–2004	%	2005–2010	%
Disease								
Circulatory disease	4679 (2716)	28.1	4723 (2535)	30.2	11,561 (2081)	54.1	15,999 (2127)	53.8
Ischemic heart disease	2472 (1295)	14.8	2434 (1136)	15.6	8153 (1260)	38.2	11,222 (1184)	37.8
Cerebrovascular disease	976 (517)	5.9	1044 (535)	6.7	1717 (273)	8.0	2326 (325)	7.8
Other circulatory disease	1231 (904)	7.4	1245 (864)	8.0	1691 (548)	7.9	2451 (618)	8.2
Respiratory disease	415 (282)	2.5	351 (239)	2.2	1335 (408)	6.3	1893 (434)	6.4
Influenza and pneumonia	212 (158)	1.3	205 (152)	1.3	832 (289)	3.9	943 (264)	3.2**
Other respiratory disease	203 (124)	1.2	146 (87)	0.9*	503 (119)	2.4	950 (170)	3.2
Digestive disease	1745 (631)	10.5	1507 (561)	9.6	1634 (474)	7.7	2262 (572)	7.6
Alcohol-related digestive disease	1154 (352)	6.9	1006 (293)	6.4	782 (160)	3.7	1137 (157)	3.8
Gastroduodenal ulcer	140 (109)	0.8	158 (105)	1.0	219 (141)	1.0	438 (198)	1.5
Other digestive disease	451 (170)	2.7	343 (163)	2.2	633 (173)	3.0	687 (217)	2.3
Certain infectious and parasitic diseases	130 (91)	0.8	101 (69)	0.6	212 (85)	1.0	248 (78)	0.8
Tuberculosis	82 (58)	0.5	53 (39)	0.3	142 (59)	0.7	125 (41)	0.4**
Other infectious disease	48 (33)	0.3	48 (30)	0.3	70 (26)	0.3	123 (37)	0.4
Neoplasms	211 (89)	1.3	244 (86)	1.6	709 (204)	3.3	1264 (304)	4.3**
Malnutrition	145 (65)	0.9	111 (60)	0.7	218 (50)	1.0	343 (72)	1.2
Other diseases	593 (248)	3.6	669 (355)	4.3*	767 (150)	3.6	1321 (216)	4.4*
Accident								
Hypothermia	57 (48)	0.3	53 (48)	0.3	71 (61)	0.3	88 (76)	0.3
Blunt force injury	388 (87)	2.3	330 (94)	2.1	512 (136)	2.4	740 (221)	2.5
Traffic injury	897 (71)	5.4	534 (54)	3.4	469 (45)	2.2	359 (43)	1.2
Heatstroke	23 (19)	0.1	51 (38)	0.3**	11 (5)	0.1	112 (45)	0.4**
Other external causes	559 (357)	3.4	485 (360)	3.1	904 (308)	4.2	1110 (438)	3.7**

Parentheses indicate the number of autopsied cases.

% Indicate the proportion of each cause of death to the total number of deaths in Table 1a.

* $P < 0.05$.

** $P < 0.01$ (both among total cases and among autopsied cases).

Age distribution slightly shifted to older cases in 2005–2010 compared to 1999–2004, both in homeless deceased and in non-homeless deceased (Fig. 2a and b).

3.2. Change in the manner and cause of death among homeless persons and non-homeless persons during 1999–2010

Regarding manner of death of non-homeless persons, the proportion of death from disease tended to increase and the proportions of death by accidents and suicide tended to decrease among those in 2005–2010 compared with those in 1999–2004 (Table 1a). Though such tendencies were not observed in homeless persons, the "unknown" category tended to be higher among those in 2005–2010 compared with those in 1999–2004 (especially under 60), similar to non-homeless persons (Table 1b). As most of the deceased certified as having an unknown manner of death showed severe decomposition due to delay of detection, we compared the proportion of the deceased with longer postmortem periods (above 7 days) for all cases between before 2004 and after 2004. Interestingly, a higher proportion of the deceased with longer postmortem periods was observed in 2005–2010, both among

non-homeless and homeless persons (non-homeless: 10.8% in 1999–2004, 12.8% in 2005–2010; $P < 0.01$, homeless: 5.1% in 1999–2004, 7.2% in 2005–2010; $P < 0.05$).

Regarding specific causes of death among non-homeless persons, there were total 9 items (specific causes of death) those were considered to be statistically significant. A higher proportion of death due to heatstroke was observed both under and over 60 years old in 2005–2010 (Table 2a). Regarding homeless persons, there were less items (4 specific causes of death) compared to those among non-homeless persons. Death due to heatstroke tended to be higher among cases in 2005–2010 under 60 years old, similar to non-homeless persons (Table 2b).

3.3. Comparison of manner/cause of death between homeless persons and non-homeless persons

Regarding manner of death, a higher proportion of accidental death and a lower proportion of suicidal death were observed among homeless persons, both in 1999–2004 and 2005–2010 (Table 3a). Regarding specific cause of death from disease, whereas a proportion of death from circulatory disease was lower than

Table 2b

Comparison of the major causes of death for homeless persons between the two groups (cases in 1999-2004 and in 2005-2010) according to age groups.

	Age <60				Age >60			
	1999-2004	%	2005-2010	%	1999-2004	%	2005-2010	%
Disease								
Circulatory disease	150 (100)	22.3	112 (70)	24.5	276 (130)	35.3	332 (129)	35.7
Ischemic heart disease	64 (45)	9.5	52 (31)	11.4	167 (78)	21.4	207 (65)	22.2
Cerebrovascular disease	38 (16)	5.7	36 (21)	7.9	50 (20)	6.4	61 (20)	6.6
Other circulatory disease	48 (39)	7.1	24 (18)	5.2	59 (32)	7.6	64 (44)	6.9
Respiratory disease	63 (50)	9.4	32 (29)	7.0	74 (57)	9.5	80 (48)	8.6
Influenza and pneumonia	53 (42)	7.9	25 (24)	5.5	59 (47)	7.6	60 (40)	6.4
Other respiratory disease	10 (8)	1.5	7 (5)	1.5	15 (10)	1.9	20 (8)	2.1
Digestive disease	157 (103)	23.4	76 (51)	16.6**	115 (70)	14.7	116 (63)	12.5
Alcohol-related digestive disease	88 (57)	13.1	35 (21)	7.6**	40 (18)	5.1	37 (12)	4.0
Gastroduodenal ulcer	37 (33)	5.5	22 (17)	4.8	32 (29)	4.1	47 (39)	5.0
Other digestive disease	32 (13)	4.8	19 (13)	4.1	43 (23)	5.5	32 (12)	3.4*
Certain infectious and parasitic diseases	29 (23)	4.3	23 (20)	5.0	27 (17)	3.5	24 (15)	2.6
Tuberculosis	27 (22)	4.0	20 (18)	4.4	21 (13)	2.7	18 (13)	1.9
Other infectious disease	2 (1)	0.3	3 (2)	0.7	6 (4)	0.8	6 (2)	0.6
Neoplasms	17 (15)	2.5	14 (12)	3.1	41 (24)	5.2	59 (41)	6.3
Malnutrition	29 (12)	4.3	15 (11)	3.3	22 (11)	2.8	28 (16)	3.0
Other diseases	13 (5)	1.9	20 (9)	4.4	31 (14)	4.0	37 (18)	4.0
Accident								
Hypothermia	53 (43)	7.9	47.(43)	10.2	63 (49)	8.1	79 (66)	8.5
Blunt force injury	16 (9)	2.4	7 (3)	1.5	18 (8)	2.3	27 (7)	2.9
Traffic injury	8 (0)	1.2	4 (0)	0.9	16 (3)	2.0	11 (1)	1.2
Heatstroke	1 (1)	0.1	9 (7)	2.0**	6 (3)	0.8	15 (12)	1.6
Other external causes	34 (16)	5.1	16 (11)	3.5	27 (17)	3.5	20 (10)	2.1

Parentheses indicate the number of autopsied cases.
% Indicate the proportion of each cause of death to the total number of deaths in Table 1b.
* P < 0.05.
** P < 0.01 (both among total cases and among autopsied cases).

Table 3a

Comparison of manner of death between homeless persons and non-homeless persons.

	1999-2004				2005-2010			
	Control	%	Homeless	%	Control	%	Homeless	%
Disease	24,354 (7574)	64.1	1044 (631)	71.9**	31,036 (7708)	68.4	968 (532)	69.7
Accident	3891 (1137)	10.2	242 (149)	16.7**	3862 (1417)	8.5	235 (160)	16.9**
Suicide	7977 (221)	21.0	92 (1)	6.3**	7671 (262)	16.9	93 (3)	6.7**
Undetermined external cause	743 (497)	2.0	30 (24)	2.1	739 (539)	1.6	31 (23)	2.2
Unknown	1051 (532)	2.8	45 (21)	3.1	2051 (577)	4.5	62 (14)	4.5
Total	38,016 (9961)	100	1453 (826)	100	45,359 (10,503)	100	1389 (732)	100

Parentheses indicate the number of autopsied case.
% Indicate the proportion of each manner of death to total number of deaths in each group.
** P < 0.01.

non-homeless persons, higher proportions of respiratory disease, digestive disease, infectious disease, neoplasms and malnutrition were observed among homeless persons. Regarding death by accident, whereas death by traffic accident was lower than non-homeless persons, higher proportions of death by hypothermia (in both periods) and heatstroke (in 2005-2010) were observed among homeless persons (Table 3b). When we divided cases into two age groups (under 60 and above 60 years) and compared the manners/causes of death between homeless and non-homeless persons before 2004 and those after 2004, similar results were also observed (data not shown).

3.4. The manner and cause of death among medicolegal deaths of homeless persons during 1999-2010 according to age

We further examined the manner and cause of death of all homeless deceased during the study period according to more detailed age groups (i.e., ≤49, 50-59, 60-69, and ≥70). The proportion of death from disease was higher in older individuals (P < 0.01), whereas the proportion of death by suicide was higher in younger cases (P < 0.01) (Table 4a). Among suicides, we found

that 24 cases (13.0%) had psychiatric disorders, such as depression and schizophrenia, in their past histories.

Subclassification of death from disease showed higher proportions of circulatory diseases and neoplasms in older cases and a higher proportion of digestive diseases and "certain infectious and parasitic diseases" in younger cases (Table 4b). Alcohol-related digestive diseases comprised 66.7% of digestive diseases among cases under 50 years old. The vast majority of death from "certain infectious and parasitic diseases" was comprised of pulmonary tuberculosis cases. Death by hypothermia was a leading cause of accidental death (about 50% of total accidental death). No significant differences according to age were observed in terms of major causes of accidental death, such as hypothermia or blunt force injury.

4. Discussion

In 2003 and 2008, the Ministry of Health, Labour and Welfare published "A fundamental policy for supporting self-reliance of the homeless" [7,12]. Those policies mentioned pulmonary tuberculosis should be adequately treated and prevented disease among

Table 3b

Comparison of the major causes of death between homeless persons and non-homeless persons.

	1999–2004				2005–2010			
	Control	%	Homeless	%	Control	%	Homeless	%
Disease								
Circulatory disease	16,240 (4797)	42.7	426 (230)	29.3**	20,722 (4662)	45.7	444 (199)	32.0**
Ischemic heart disease	10,625 (2555)	27.9	231 (123)	15.9**	13,656 (2320)	30.1	259 (96)	18.6**
Cerebrovascular disease	2693 (790)	7.1	88 (36)	6.1	3370 (860)	7.4	97 (41)	7.0
Other circulatory disease	2922 (1452)	7.7	107 (71)	7.4	3696 (1482)	8.1	88 (62)	6.3*
Respiratory disease	1750 (690)	4.6	137 (107)	9.4**	2244 (673)	4.9	112 (77)	8.1**
Influenza and pneumonia	1044 (447)	2.7	112 (89)	7.7**	1148 (416)	2.5	85 (64)	6.1**
Other respiratory disease	706 (243)	1.9	25 (18)	1.7	1096 (257)	2.4	27 (13)	1.9
Digestive disease	3379 (1105)	8.9	272 (173)	18.7**	3769 (1133)	8.3	192 (114)	13.8**
Alcohol-related digestive disease	1936 (512)	5.1	128 (75)	8.8%**	2143 (450)	4.7	72 (33)	5.2
Gastroduodenal ulcer	359 (250)	0.9	69 (62)	4.7**	596 (303)	1.3	69 (56)	5.0**
Other digestive disease	1084 (343)	2.9	75 (36)	5.2	1030 (380)	2.3	51 (25)	3.7
Certain infectious and parasitic diseases	342 (176)	0.9	56 (40)	3.9**	349 (147)	0.8	47 (35)	3.4**
Tuberculosis	224 (117)	0.6	48 (35)	3.3**	178 (80)	0.4	38 (31)	2.7**
Other infectious disease	118 (59)	0.3	8 (5)	0.6	171 (67)	0.4	9 (4)	0.6
Neoplasms	920 (293)	2.4	58 (39)	4.0**	1508 (390)	3.3	73 (53)	5.3**
Malnutrition	363 (115)	1.0	51 (23)	3.5**	454 (132)	1.0	43 (27)	3.1**
Other diseases	1360 (398)	3.6	44 (19)	3.0	1990 (571)	4.4	57 (27)	4.1
Accident								
Hypothermia	128 (109)	0.3	116 (92)	8.0**	141 (124)	0.3	126 (109)	9.1**
Blunt force injury	900 (223)	2.4	34 (17)	2.3	1070 (315)	2.4	34 (10)	2.4
Traffic injury	1366 (116)	3.6	24 (3)	1.7*	893 (97)	2.0	15 (1)	1.1*
Heatstroke	34 (24)	0.1	7 (4)	0.5	163 (83)	0.4	24 (19)	1.7**
Other external causes	1463 (665)	3.8	55 (33)	3.8	1595 (798)	3.5	36 (21)	2.6

Parentheses indicate the number of autopsied case.
% Indicate the proportion of each cause of death to total number of deaths in Table 3a.
** P < 0.01.
* P < 0.05 (both among total cases and among autopsied cases).

Table 4a

Manner of death for all homeless persons (during 1999–2010) according to age groups.

	Total cases	%	Age group							
			<49	%	50–59	%	60–69	%	>70	%
Disease	2012 (1163)	70.8	166 (118)	59.9	584 (392)	68.5	793 (462)	71.3	469 (191)	77.3**
Accident	477 (309)	16.8	35 (29)	12.6	160 (104)	18.8	184 (122)	16.7	98 (54)	16.1
Suicide	185 (4)	6.5	40 (1)	14.4	67 (1)	7.9	62 (1)	5.6	16 (1)	2.6**
Undetermined external cause	61 (47)	2.1	12 (11)	4.3	14 (11)	1.6	24 (16)	2.2	11 (9)	1.8
Unknown	107 (35)	3.8	24 (6)	8.7	28 (8)	3.3	42 (19)	3.8	13 (2)	2.1**
Total	2842 (1558)	100	277 (165)	100	853 (516)	100	1105 (620)	100	607 (257)	100

Parentheses indicate the proportion of each manner of death to the total number of deaths in each group.
** P < 0.01.

homeless persons, which appears to be reasonable because a high prevalence of tuberculosis among homeless people was reported [13]. However, no specific diseases other than tuberculosis were mentioned in those policies. Thus, we designed this study in order to clarify the nature of critical health problems among homeless people by investigating recent trends in medicolegal deaths of homeless persons.

The results of this study showed higher age distribution and higher proportion of deceased persons with longer postmortem intervals in recent years both among non-homeless and homeless deceased. Japan is now facing a rapidly aging society, and the latest national survey also indicated aging among homeless [8]. In addition, a decrease in total number of homeless persons might indicate isolation of residual homeless persons. Aging and isolation might be strongly associated with an increased/unchanged number of medicolegal death of non-homeless/homeless persons in recent years.

From the results of the analysis of manner/causes of death, manner/causes of death of homeless persons in Japan seemed not to change significantly over time. Death from disease constituted 70.8% of all cases of homeless persons, and causes of death from disease were more various than those of non-homeless deceased, which might reflect various background of homeless persons, such as malnutrition, alcohol-dependence, immune-compromised host. Though a proportion of death from circulatory disease was lower among homeless persons than non-homeless persons, analysis of cause of death according to detailed age classification revealed a higher proportion of death from circulatory disease in older cases. During medical checkups organized in 2003 for 917 homeless persons aged 55 years and above in Osaka City, the proportion of persons who were diagnosed as "requiring treatment" or "requiring detailed examination" for blood pressure was 35.2%, about four times higher than in general population [14]. Several factors, such as heavy alcohol intake and chronic psychological stress caused by homeless life, might increase the risk of hypertension, resulting in death from circulatory disease [15,16]. As the aging of the homeless and the longer periods being spent in a homeless state were

Table 4b

Causes of death for homeless persons according to form of disease according to age groups (during 1999–2010).

	Total case	%	Age group								
			≤49	%	50–59	%	60–69	%	≥70	%
Circulatory disease	870 (429)	30.6	48 (32)	17.3	214 (138)	25.1	340 (174)	30.8	268 (85)	44.2**
Ischemic heart disease	490 (219)	17.2	16 (11)	5.8	100 (65)	11.7	195 (94)	17.6	179 (49)	29.5**
Cerebrovascular disease	185 (77)	6.5	16 (9)	5.8	58 (28)	6.8	68 (28)	6.2	43 (12)	7.1
Other circulatory disease	195 (133)	6.9	16 (12)	5.8	56 (45)	6.6	77 (52)	7.0	46 (24)	7.6
Respiratory disease	249 (184)	8.8	17 (16)	6.1	78 (63)	9.1	106 (73)	9.6	48 (32)	7.9
Influenza and pneumonia	197 (153)	6.9	15 (14)	5.4	63 (52)	7.4	83 (62)	7.5	36 (25)	5.9
Other respiratory disease	52 (31)	1.8	2 (2)	0.7	15 (11)	1.8	23 (11)	2.1	12 (7)	2.0
Digestive disease	464 (287)	16.3	57 (39)	20.6	176 (115)	20.6	171 (106)	15.5	60 (27)	9.9**
Alcohol-related digestive disease	200 (108)	7.0	38 (29)	13.7	85 (49)	10.0	62 (29)	5.6	15 (1)	2.5**
Gastroduodenal ulcer	138 (118)	4.9	6 (4)	2.2	53 (46)	6.2	56 (49)	5.1	23 (19)	3.8
Other digestive disease	126 (61)	4.4	13 (6)	4.7	32 (3)	3.8	53 (28)	4.8	22 (7)	3.6
Certain infectious and parasitic diseases	103 (75)	3.6	21 (16)	7.6	31 (27)	3.6	38 (26)	3.4	13 (6)	2.1**
Tuberculosis	87 (66)	3.1	20 (16)	7.2	27 (24)	3.2	28 (20)	2.5	12 (6)	2.0**
Other infectious disease	16 (9)	0.6	1 (0)	0.4	4 (3)	0.5	10 (6)	0.9	1 (0)	0.2
Neoplasms	131 (92)	4.6	3 (2)	1.1	28 (25)	3.3	63 (40)	5.7	37 (25)	6.1**
Malnutrition	94 (50)	3.3	11 (8)	4.0	33 (15)	3.9	31 (19)	2.8	19 (8)	3.1
Others	101 (46)	3.6	9 (5)	3.2	24 (9)	2.8	44 (24)	4.0	24 (8)	4.0
Total death from disease	2012 (1163)	70.8	166 (118)	59.9	584 (392)	68.5	793 (462)	71.8	469 (191)	77.3

Parentheses indicate the number of autopsied cases.

% Indicate the proportion of each cause of death to the total number of deaths in Table 4a.

** P < 0.01 (both among total cases and among autopsied cases).

indicated in the latest national survey [8], much emphasis needs to be placed on measures to address hypertension (circulatory disease), especially for older homeless persons. On the other hand, the proportion of death from digestive disease and infectious disease were higher among younger homeless persons, and alcohol-related digestive disease and tuberculosis constituted a substantial portion of each disease in younger homeless persons. According to these results, measures to address alcohol abuse and tuberculosis require attention, especially for younger homeless persons.

Accidental death among homeless persons was more frequent than those of non-homeless persons, and did not decrease among homeless persons in recent years, in contrast to that of non-homeless persons. Hypothermia is a leading cause of accidental death irrespective of age group, and the majority of the cases were found outdoors in the winter season. Our study also showed tendency of recent increase in death by heatstroke among homeless persons. Although the number of temporary shelters for homeless people has increased in Tokyo Metropolis, the latest survey showed that the shelters were not always occupied sufficiently [17]. Thorough spread of information about shelters and patrols for isolated homeless people, not only in the winter season, but in the summer season may be preventive against such deaths.

The proportion of death by suicide among homeless persons was lower than that of non-homeless persons, however, the proportion of suicide slightly increased in recent years, and was significantly higher in younger homeless persons. Homeless people appear to have higher rates of mental illness compared to the domiciled [18,19]. A recent survey conducted in one area of Tokyo showed that 62.5% of homeless persons had psychiatric disorders and 57.0% of homeless persons were at risk of committing suicide [20]. Although our data did not reveal a close relationship between suicide and having a psychiatric disorder, which might be attributable to undiagnosed cases or limited information, further detailed analysis to detect a cause of suicide is needed, especially for younger homeless in the future.

5. Conclusions

Although Japan has succeeded in reducing the total number of homeless persons, aging and isolation among homeless persons in recent years might contribute to an unchanged number of

medicolgal death of them. In addition to measures for frequent causes of death in each age group clarified in this study, better intervention for isolated homeless persons might be a key factor in the future.

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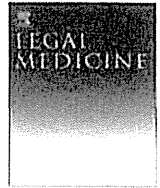
Case Report

An autopsy case of a homeless person with unilateral lower extremity edema

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ABSTRACT

We present an autopsy case of a homeless person showing remarkable unilateral lower extremity edema, which was strongly associated with the cause of death. A 55-year-old homeless man without any past medical history was found dead in a flophouse. External examination showed evidence of malnourishment and remarkable swelling of the right, lower extremity. Putrefactive discoloration in the same area was evident at the time of autopsy (approximately 30 h post-mortem). The autopsy revealed focal pneumonia in the right lower lobe, dehydration and chronic pancreatitis. Dissection of the edematous extremity revealed massive abscess formation in the subcutaneous tissue and superficial fascia around the right knee joint. Histopathological findings were compatible with necrotizing fasciitis and blood chemistry results showed an elevation of HbA1c (6.3%). The cause of death is considered to be necrotizing fasciitis and secondary pneumonia/dehydration. This case suggests that necrotizing fasciitis should be differentiated during post-mortem diagnosis, especially in cases showing lower extremity edema with early putrefactive changes. In addition, forensic pathologists should closely examine a lower extremity of such cases to detect a true cause of death, even if other pathological findings which can be a cause of death, such as pneumonia and dehydration, are observed in major internal organs.

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1. Introduction

Medical examiners often encounter deceased individuals with bilateral lower extremity edema at inquest scenes. Bilateral lower extremity edema, which is usually a manifestation of generalized edema, and failure of vital organs (e.g., heart, liver, kidney) are commonly listed as causes of edema in the whole body [1]. Thus, if a decedent with bilateral, lower extremity edema also shows signs of illness, such as congestive heart failure or liver cirrhosis, medical examiners justifiably suspect that the cause of death may have resulted from the progress of the illness.

A decedent with unilateral, lower extremity edema is, on the other hand, less frequently encountered. Unilateral lower extremity edema is generally caused by regional problems (e.g., regional obstruction of venous or lymphatic flow, trauma) [1]. This increases the difficulty of judging whether the cause of edema was associated with the cause of death, based only on the external investigation. Here, we present an autopsy case showing remarkable unilateral, lower extremity edema and early putrefactive changes. In this case, the autopsy revealed a strong association of the edematous extremity with the cause of death, deep soft tissue infection (necrotizing fasciitis).

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2. Case report

A 55-year-old man was found dead on a bed in a flophouse. He had lived on the streets for a long time, and came to the flophouse 2 weeks before his death. Seven days before his death, he requested a cold patch; however, there was no evidence as to how it was used. The individual complained of appetite loss on the day before his death, but he did not consult a doctor. An external examination performed approximately 12 h after his death, did not reveal any open injuries, but did reveal remarkable right, lower extremity edema with slight purple-green discoloration (Fig. 1a). No past or present diseases were evident that involved right, lower extremity edema, which may have suggested the cause of death.

A forensic autopsy was carried out about 30 h after his death. The decedent was 160 cm tall and weighed 41 kg (body mass index of 16.0). Upon autopsy, greenish, putrefactive discoloration was prominent in the right, lower extremity (Fig. 1b). Upon dissection of the body, moistness in the serous membrane of the thoracic/abdominal cavity was disappeared, and right lower lung was slightly indurated. Other macroscopic findings of internal organs included an atrophic, indurated pancreas and a muddy discoloration in the red pulp of the spleen. Dissection of the discolored skin of right lower extremity disclosed the absence of a fracture, but did reveal the presence of a massive abscess in the subcutaneous tissue and superficial fascia, mainly around the right knee joint (Fig. 2). The underlying muscle did not appear to be extensively involved. Abscess formation was not observed in the
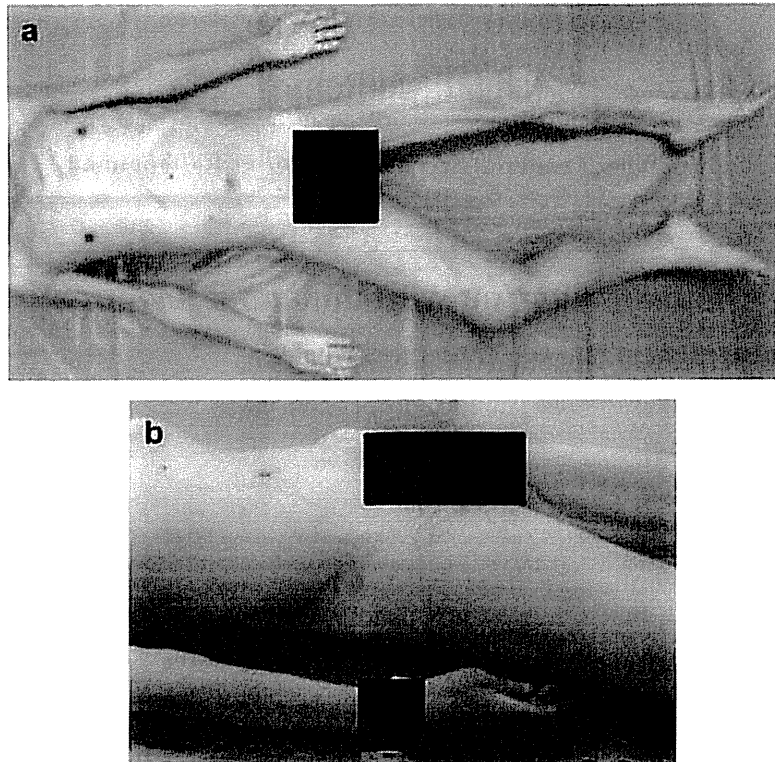
Fig. 1. Appearance of the decedent. (a) Remarkable right, lower extremity edema with slight purple-green discoloration (approximately 12 h after death). (b) Putrefactive change was prominent in the right lower extremity at autopsy (approximately 30 h after death).

Fig. 2. Macroscopic findings of the right lower extremity. Dissection of the skin of the right lower extremity disclosed massive abscess formation in the subcutaneous tissue and superficial fascia, mainly around the knee joint.

pelvic space or around the rectum, and thrombi were not observed in the right external iliac artery or vein. Microscopic examination showed plentiful neutrophil infiltration in the subcutaneous tissue around the right knee and the perimysium of the right vastus lateralis muscle (Fig. 3a and b); some of the muscle cells were necrotic (Fig. 3b). Thrombi were seen in several micro-vessels in the subcutaneous tissue. Acinar atrophy, dilation of ducts and fibrosis were observed in the pancreas. Other findings included

patchy neutrophil infiltrations in the right, lower lung, acute tubular necrosis in the kidney and an increased number of plasma cells and macrophages in the red pulp of the spleen. No pathological findings relevant to cause of death were observed in other internal organs. Blood chemistry results showed an elevation of acetone (5.7 μg/mL) and HbA1c (6.3%) levels. Escherichia coli were cultured from the abscess. Any drugs were not detected from blood and gastric content by toxicological analysis. From the autopsy findings, the
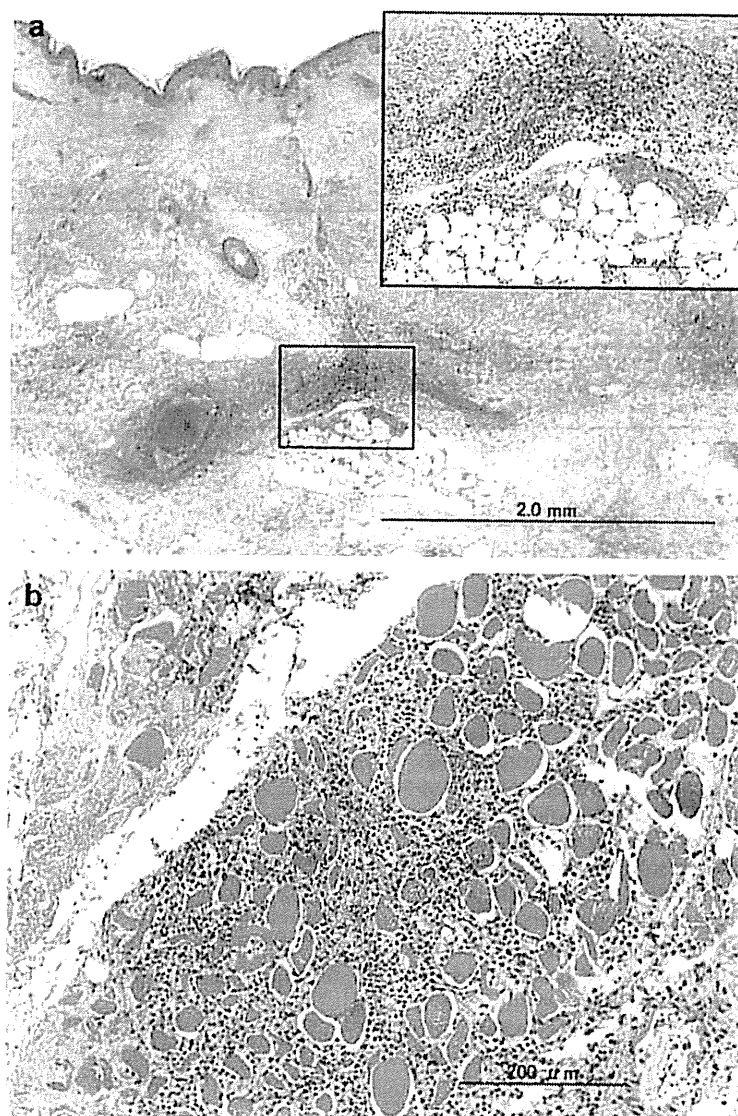
Fig. 3. Microscopic findings of the skin and muscle of the right lower extremity. (a) Plentiful neutrophil infiltration in the subcutaneous tissue. Inset: high magnification of the indicated space. (b) Neutrophil infiltration in the perimysium of the right vastus lateralis muscle. Some of the muscle cells were necrotic.

cause of death in the present case was thought to be necrotizing fasciitis, and secondary dehydration and pneumonia.

3. Discussion

Necrotizing fasciitis is a rare, soft tissue infection characterized by widespread fascial necrosis with relative sparing of the underlying muscle [2]. It involves the subcutaneous tissue and superficial fascia in a dissecting suppurative process [3]. In 1979 six diagnostic criteria were presented by Fisher [4] (Table 1), and the differential diagnosis of necrotizing fasciitis include bacterial synergistic gangrene, erysipelas and gas gangrene [3] (Table 2). Though several ante-mortem clinical information (e.g., reduced mental status) were unknown, the pathological findings of this case, particularly the site of inflammation/necrosis (subcutaneous tissue and superficial fascia), are compatible with necrotizing fasciitis. The other diseases differentiated can be ruled out by lack of wounds, bordered erythematous lesion and deep muscular lesion.

Necrotizing fasciitis is frequently associated with severe systemic toxicity. As a result, this type of tissue infection is usually rapidly fatal, unless recognized quickly and treated aggressively [2,3]. Host factors, such as diabetes mellitus (DM), protein-calorie malnutrition, hypoglobulinemia, and intravenous drug use are reported to be risk factors associated with necrotizing fasciitis [3]. DM impairs immune functions, such as phagocytosis, cell chemotaxis, delayed hypersensitivity skin tests, and lymphoproliferative response to mitogens [5–7]. Protein energy malnutrition is a common cause of secondary immune deficiency and susceptibility to infections [8]. DM resulting from chronic pancreatitis and malnutrition in this case is likely to have played crucial roles in the decedent's susceptibility to this infection.

The initiating factor for necrotizing fasciitis has been reported to be skin trauma (sometimes trivial) or an occult, enteric source of bacteria, such as a diverticular or an appendiceal abscess, but the initiating event often remains obscure [9,10]. Although the initiating factor in the present case was not evident, the lower extremities and perineal areas of homeless persons are generally not sanitary because of long periods of street life. In addition,

Table 1
Diagnostic criteria for necrotizing fasciitis (Fisher [4]).

1. Extensive necrosis of the fascia with extension to the overlying skin
2. Moderate to severe systemic intoxication with reduced mental status
3. Lack of primary muscle involvement
4. No evidence of clostridial infection in microbiological culture
5. No evidence of large vessel occlusion as the causative mechanism
6. Infiltration of leucocytes, local necrosis of the fascia and the surrounding tissue as well as microvascular thrombosis on histological examination

Table 2
Differential diagnosis of necrotizing fasciitis (Ref. [3]).

1. *Bacterial synergistic gangrene (Meleney's ulcer)*: Usually seen postoperatively and located around drains or retention sutures
2. *Erysipelas*: Characterized by an erythematous area with sharply defined borders, induration, and marked pain
3. *Gas gangrene*: A deep infection usually found in contaminated wounds. It involves muscle as well as subcutaneous tissue

various factors common among homeless persons, such as alcohol abuse [11,12] and poverty may lead to alcohol-related liver and pancreatic diseases as well as malnutrition, all of which may result in compromised immunity, as was observed in this case. Thus, physicians should be aware of this disease in daily practice, especially when they see lower extremity edema in a homeless person.

An early putrefactive change, affecting the lower extremity, was a characteristic finding in this case. Massive numbers of bacteria at the affected site may have promoted the early, postmortem putrefactive changes. Though several potential causes, such as deep venous thrombosis or thrombophlebitis, cancer, cellulitis, and a fractured femur, should be differentiated in cases involving unilateral lower extremity edema [1], this case suggests that necrotizing fasciitis should also receive more attention as a possible cause of edema when an edematous extremity is accompanied by an early putrefactive change. In addition, forensic pathologists should closely examine a lower extremity of such cases to detect a true cause of death, even if other pathological findings which can be a cause of death, such as pneumonia and dehydration in this case, are observed in major internal organs before dissection of an extremity.

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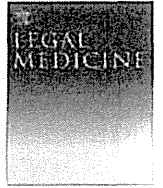
Case Report

Accidental death of elderly persons under the influence of chlorpheniramine

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ABSTRACT

Older individuals are susceptible to accident, such as falls, some of which are fatal. In such cases, autopsies and toxicological analysis may be deemed unnecessary, especially if the critical injuries and manner of death can be determined conclusively based on information at the scene and an external investigation. Here, we report the results of two autopsies performed on elderly individuals who died accidentally under the influence of chlorpheniramine. These autopsies revealed valuable additional information.

Case 1: A woman in her 70s, who was living alone, was found dead under the stairs in her house. She had no history of a condition that could have led to sudden death. The autopsy revealed a neck fracture, multiple rib fractures, and a coccyx fracture. The histopathological findings showed fat embolisms in numerous small vessels of the interalveolar septum. Toxicological analysis of blood samples revealed the presence of chlorpheniramine (0.41 μg/ml).

Case 2: A woman in her 70s, who was living alone, was found dead in the bathtub in her house. There was no past medical history other than diabetes mellitus and vertigo. The autopsy revealed hyper-inflated lungs and brown–red fluids in the trachea, but there was no evidence of a pathology or injury that could have induced a loss of consciousness. Toxicological analysis of the fluids in the right thoracic cavity revealed the presence of chlorpheniramine (0.57 μg/ml).

In both cases, re-examination of the scene after the autopsy revealed the presence of common cold medicine containing chlorpheniramine. The victim may have accidentally overdosed on common cold medicine. This overdose would have been compounded by anti-histamine-induced drowsiness. The present cases suggest that forensic pathologists should always notify physicians/pharmacists of findings pertaining to unexpected drug side effects. Such intervention would prevent many accidental deaths. In addition, each autopsy must be performed in conjunction with a detailed postmortem investigation. Such efforts would also increase the accuracy of the public health record's mortality statistics.

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1. Introduction

Older persons are susceptible to accidental deaths such as falls [1] and motor-vehicle-related injuries [2]. Among patients with stroke or Parkinson disease, health-related problems can further undermine a vestibular system that has already been weakened by age-related changes [1]. If the external investigation identifies a likely cause of death, the autopsy and toxicological analysis may be foregone for such cases. This is the case in countries such as Japan, where the death inquiry system is still in a developmental stage [3]. If an autopsy and toxicological analysis is not performed, the potential contribution of unexpected factors is ignored (e.g., alcohol intake or the recent onset of disease). Here, we report the results revealed by two autopsies performed after accidental fatalities. In combination with toxicological analysis, the information

obtained suggests that both individuals died under the influence of a chlorpheniramine overdose.

2. Case report

2.1. Case 1

A woman in her 70s, who was living alone, was found dead under the stairs in her house. She had undergone operations for bilateral femoral neck fractures and walked with difficulty, but there was no history of a condition that could have led to sudden death (e.g., ischemic heart disease). External examination of the deceased revealed bilateral bruises in the orbital area as well as bruises on the right cheek, the right shoulder, the right forearm, the upper back of the trunk, and the backs of both hip joints (Fig. 1a). A contusion was noted on the right forearm.

A forensic autopsy was carried out approximately 48 h after her death. The deceased was 147 cm tall and weighed 30 kg. The autopsy revealed a neck fracture (C7) (Fig. 1b), multiple rib fractures (right ribs 4–7, in the anterior axillary line), and a coccyx fracture.

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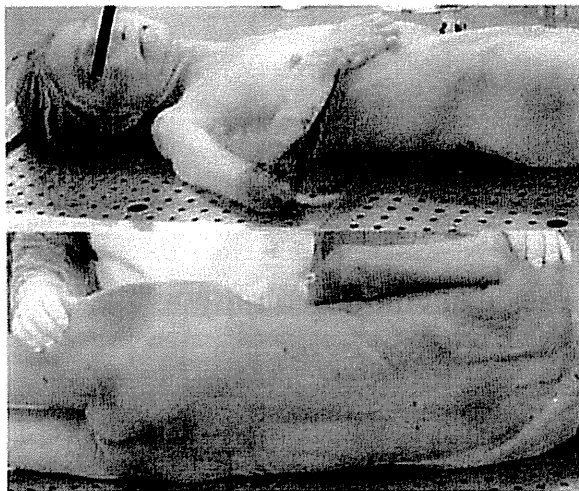E-mail address: hideto-@qk9.so-net.ne.jp (H. Suzuki).

Fig. 1a. Appearance of the decedent (case 1). External investigation revealed bruises around the face, the right upper extremity, the upper back of the trunk, and the back of the bilateral hip joints.

Fig. 1b. Macroscopic examination of the frontal side of the cervical spine in case 1. A neck fracture (C7) was observed in association with hemorrhage.
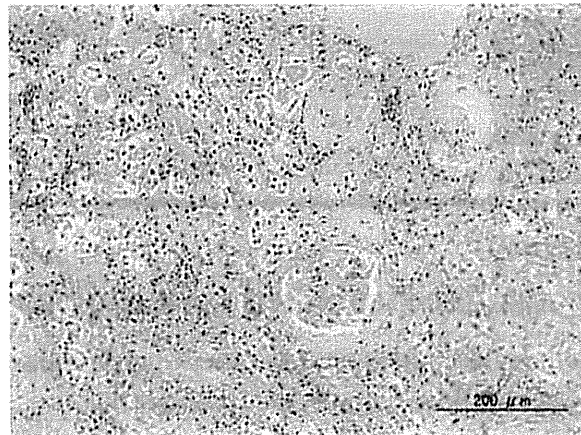

Fig. 1c. Microscopic findings of the lung and the kidney in case 1. Sclerotic glomeruli, dilated uriniferous tubules with casts, and lymphocyte infiltration were observed in the kidneys.
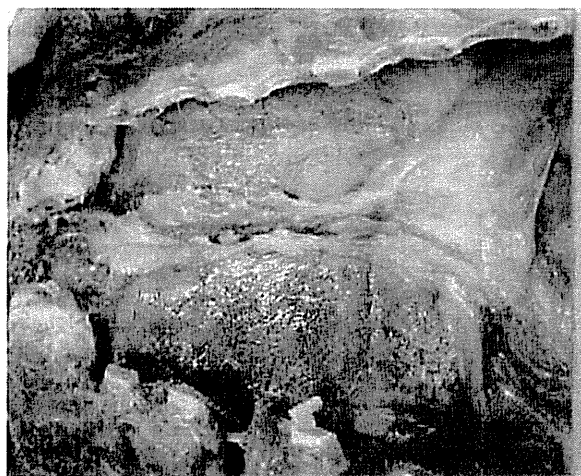

Fig. 2. Thoracotomy: macroscopic findings (case 2). Hyper-inflated lungs (emphysema aquosum) revealed by the thoracotomy.

Other macroscopic autopsy findings included bilateral atrophic kidneys with superficial granularity (right, 50 g; left, 55 g). The microscopic examination revealed fat embolisms in numerous small vessels of the interalveolar septum. Other microscopic findings included sclerotic glomeruli, a dilated uriniferous tubule with casts, and renal lymphocyte infiltration (Fig. 1c). The toxicological analysis of posthumous blood samples revealed the presence of chlorpheniramine at a concentration of 0.41 µg/ml (therapeutic, 0.003–0.017 µg/ml; comatose-fatal, from 1.1 µg/ml [4]; therapeutic, 0.01–0.017 µg/ml; lethal, 0.5–1.1 µg/ml [5]). The autopsy findings show that in case 1, the cause of death was respiratory distress due to a neck fracture incurred during a fall while under the influence of chlorpheniramine.

2.2. Case 2

A woman in her 70s, who was living alone, was found dead in the bathtub in her home. She was found with the right side of her face and body submerged. A family member reported that the deceased had been forgetful during the period preceding her death, but there was no past medical history other than diabetes mellitus and vertigo. The external examination revealed prominent putrefactive marbling on the trunk and maceration throughout the body. No foam had issued from the nose or mouth, and no injury was noted.

A forensic autopsy was carried out approximately 4 days after the patient's death. The deceased was 153 cm tall and weighed 57 kg. The autopsy revealed hyper-inflated lungs (emphysema aquosum; Fig. 2) and brown–red fluids in the trachea. The blood in the cardiac cavity had disappeared post-mortem, but red fluid was observed in the right thoracic cavity (80 ml). Although the organs were malacic because of post-mortem decomposition, there was no pathological finding or evidence of an injury that could have rendered this woman unconscious. The fluid in the thoracic cavity was subjected to toxicological analysis, which revealed the presence of chlorpheniramine (0.57 µg/ml). The autopsy findings showed that the cause of death was drowning while under the influence of chlorpheniramine.

3. Discussion

First-generation H1-receptor antagonists are popularly used for alleviating symptoms of allergy and common cold, but these antihistamines also cause drowsiness and sedation. Such side effects impair performance and thereby increase the likelihood of dangerous accidents. Indeed, the use of antihistamines by pilots was determined to be the cause or a contributing factor in 63 of the 338 aviation accidents [6].

In both cases presented here, secondary police investigation of the scene revealed common cold medicine containing chlorpheniramine. It is suspected that both deceased may have overdosed on that medicine by accident. Because the elimination half-life of chlorpheniramine is greatly prolonged in patients with chronic renal disease [7,8], nephrosclerosis may have contributed to the increased serum levels observed, especially in case 1. Dementia undetected while alive may have concerned with the overdose in case 2.

Although the influence of psychotropic drugs on the incidence of injury is well documented [9], the findings in the present cases suggest that patients and caregivers should pay special attention to drug side effects, even for some commonly used drugs. Forensic pathologists should always notify physicians and pharmacists of any findings regarding drug side effects, which could potentially lead to the modification of medication regimens. This type of educated approach will help to prevent unexpected accidental deaths related to medication use. In addition, each case requires a detailed post-mortem investigation. This will help to increase the precision of the mortality statistics in the public health database.

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Case report

Acute fatal poisoning with Tolfenpyrad

CrossMark

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ARTICLE INFO

ABSTRACT

The authors present a fatal case of poisoning with Tolfenpyrad (TFP), a pesticide first approved in Japan in 2002. A man in his fifties was found dead in the supine position at his son's home and the small towel with a smell of naphthalene was found nearby. Forensic autopsy was unremarkable, except for a very small amount of light pink fluid in the stomach, with naphthalene odour. The toxicological analyses revealed the presence of TFP and its major metabolite PTCA (4-[4-[(4-chloro-3-ethyl-1-methylpyrazol-5-yl)carbonylaminomethyl]phenoxy]benzoic acid), together with naphthalene and methyl naphthalenes in the post-mortem sample, with liquid chromatography—mass spectrometry (LC—MS) and gas chromatography—mass spectrometry (GC—MS) respectively. The plasma concentrations of each substance were quantified as 1.97 μg/ml (TFP), 2.88 μg/ml (PTCA), 1.70 μg/ml (naphthalene), 0.67 μg/ml (1-methyl naphthalene) and 1.44 μg/ml (2-methyl naphthalene). According to these results together with autopsy findings, the cause of his death was determined to be acute Tolfenpyrad poisoning. This is the first case report of fatal poisoning attributable to an intake of TFP product.

1. Introduction

Tolfenpyrad (TFP) is a pesticide developed in Japan and was first approved in 2002. It possesses a pyrazole—carboxamide structure, as shown in Fig. 1. The mechanism of cytotoxicity is brought by the inhibition of Complex I in the respiratory electron-transfer chain of mitochondria, which makes it effective against the pests resistant to pre-existing insecticides with other modes of action.[1] It has been registered for commercial use in several countries other than Japan to date, including the Dominican Republic, Thailand, the United Arab Emirates, Indonesia and the United States of America.

Ten fatal TFP poisoning cases were reported in Japan between 2003 and 2010.[2,3] Another published report showed ten TFP poisoning cases in Japan up to 2009, consisting of 1 fatal and 1 non-fatal cases, with the outcome of 8 remaining cases unknown.[4] Despite these statistical data, no case report on this new pesticide

has been published to date. In this paper, a fatal case of poisoning of TFP in an adult male is presented, with a literature review.

2. Case history

A man in his fifties without any significant medical history was found in the supine position at his son's home in a state of cardiac pulmonary arrest and was pronounced dead on arrival at hospital. He had no regular medication and no history of attempted suicide. There was no distinct evidence of drug intake at the scene, but the small towel beside him had a chemical smell according to his son, the first discoverer of the corpse. As the cause of death could not be ascertained at the inquest, a forensic autopsy was carried out approximately 23 h after his death. The decedent was 164 cm in height and weighed 61 kg. The external and internal examination, both gross and microscopic findings, revealed no remarkable pathomorphological changes, except for the prominent postmortem lividity. There was no distinct evidence of intake of toxicological agents, such as erosion or discolouration of upper respiratory and gastric tracts. All organs were strongly congested. The weights of lungs were 514 g left and 600 g right, both strongly

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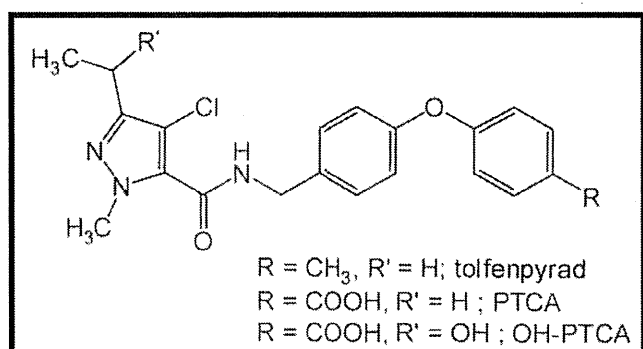
Fig. 1. Molecular structures of Tolfenpyrad (TFP), 4-[4-[(4-chloro-3-ethyl-1-methylpyrazol-5-yl)carbonylaminomethyl]phenoxy]benzoic acid (PTCA) and OH-PTCA.

oedematous. The heart was of normal size, weighing 366 g, and the coronary arteries were free of atherosclerosis. No clots were found in the heart blood. A small amount of light pink liquid material was found in the stomach, with naphthalene odour. Intracardiac blood was reserved for further toxicological analyses but a substantial amount of peripheral blood, gastric contents and urine could not be obtained. The sample was stored at 4 °C until analyses and the routine toxicological study was carried out using the gas chromatography—mass spectrometry (GC—MS).

3. Results and discussion

Although the initial drug screening for acids and bases using the intracardiac blood by GC—MS was negative, the drug profiling system detected a pronounced peak. However, a compatible drug was not registered in the drug library released in 1992 and could not be identified. Additional toxicological analyses performed at forensic laboratories in Nippon Medical School and the University of Tokyo confirmed the presence of TFP, its major metabolite PTCA (4-[4-[(4-chloro-3-ethyl-1-methylpyrazol-5-yl)carbonylaminomethyl]phenoxy]benzoic acid) as well as naphthalene and methyl naphthalenes in plasma. TFP and PTCA were both identified by retention time and mass spectrum acquired in scan mode using liquid chromatography—mass spectrometry (LC—MS), whereas GC—MS was used for the analyses of naphthalene and methyl naphthalenes. The detailed analytical methods have been described in the previously published paper.[5] Post-mortem toxicology did not reveal any other toxic substances. Table 1 shows the plasma concentration of TFP, PTCA, naphthalene, 1-methyl naphthalene and 2-methyl naphthalene in the presented case.

The number of fatal intoxications with pesticides has been declining in developed countries due to laws restricting the distribution of highly toxic chemicals.[6] Nevertheless, forensic scientists and clinicians must be aware of the fact that there are fatal cases being reported constantly worldwide and new products with significant morbidity and mortality keep being released and distributed, which include TFP.

TFP is commercially available in form of water dispersible powder or emulsifiable concentrate (EC), and either product can be purchased without any special license or proof of ID in Japan. Both naphthalene and methyl naphthalenes are the ingredients of TFP EC product, which probably accounted for the odour of the gastric content and those detected in plasma in the presented case.

It is predicted that the unique mechanism of cytotoxicity of TFP, the inhibition of Complex I in the respiratory electron-transfer chain in mitochondria, brings rapid effects to pests, and if used inappropriately, to other organisms. The documented symptoms of TFP intoxication in humans include impaired consciousness, respiratory depression, mydriasis, blood pressure reduction, metabolic acidosis, vomiting and mucosal erosions of alimentary tracts.[4] The actual symptoms remain unknown in the presented case as the man was already in a state of cardiac pulmonary arrest when found. However, there was no evidence of vomiting or incontinence at the scene. On the other hand, the autopsy findings, such as the prominent formation of postmortem lividity and the absence of clots in cardiac blood are compatible with the characteristics of sudden death, which are in accordance with TFP intoxication.

The tabulated reference range for TFP is not well established as with other newly developed chemicals, where a sufficient number of clinical case reports is yet to be published. The only comparable study is an oral administration experiment of rats conducted by the manufacturer, although it needs an assumption that the bioavailability of TFP in rats and in humans correlates with each other. In this experiment, the radioactivity of the samples was measured and expressed in terms of TFP concentration, after ingesting ^{14}C labelled TFP to rats at a dose of 320 mg/kg, which was close to LD_{50} in male rats. The TFP concentration at 6 h after ingestion were 5.18—6.97 μg/ml (one fatal individual was excluded). The sum of the concentrations of TFP and PTCA in the presented case is of the same magnitude (4.85 μg/ml) to the results obtained from the animal experiment study. It is therefore predicted that the presented case is clearly consistent with an overdose, but furthermore, lethal intoxication.[1]

Tebufenpyrad is another pesticide with a pyrazole—carboxamide structure, and was approved and commercialized in 1993 in Japan. It is considered to bring toxicity to pests by the same mechanism of action as TFP. Although there are a number of reported poisoning cases, only 1 human lethal case report in the Japanese language can be found to date. The blood concentration of tebufenpyrad in this published case was 1.6 μg/ml.[7] It is predicted that 1.97 μg/ml, the TFP concentration in the presented case is within the lethal level, as the LD_{50} value of tebufenpyrad is reported to be higher than that of TFP based on the animal experiments.[1,4]

As previously stated, naphthalene and methyl naphthalenes were also detected in plasma of the presented case. The clinical consequences of naphthalene ingestion may include headache, vomiting, diarrhoea, abdominal pain, fever, altered mental status and a decrease in urine output, which may persist up to 48 h.[8] It has also been pointed out that oxidative stress from the hepatic metabolites of naphthalene causes haemolysis and methaemoglobinaemia.[9] It is predicted that naphthalene and their metabolites had a little toxicological relevance in relation to the cause of death of the presented case, as there were no evident morphological changes found in organs including liver or kidneys. There is a report stating that TFP plays the main role in poisonings after ingestion of the EC form of TFP, as the effects are seen very rapidly and the symptoms observed are not typical to those of naphthalene poisonings.[4] The authors therefore predicted that, on the basis of case history, external and internal autopsy findings, microscopic examination and analytical data, the death of the present case is attributable to an acute TFP poisoning.

Table 1
The plasma concentrations of Tolfenpyrad (TFP), 4-[4-[(4-chloro-3-ethyl-1-methylpyrazol-5-yl)carbonylaminomethyl]phenoxy]benzoic acid (PTCA), Naphthalene, 1-methyl naphthalene and 2-methyl naphthalene (μg/ml) detected in this case.

	TFP	PTCA	Naphthalene	1-Methyl naphthalene	2-Methyl naphthalene
Plasma concentration (μg/ml)	1.97	2.88	1.7	0.67	1.44

Apart from TFP and tebufenpyrad, pesticides such as fenazaquin, fenpyroximate, pyridaben, pyrimidifen and rotenone are also believed to bring toxicity by the inhibition of Complex I in the respiratory electron-transfer chain in mitochondria.[10] There are a number of experimental reports on these chemicals but only 1 fatal case report on pyrimidifen and 3 on rotenone can be found on human poisoning in the English literature out of those mentioned above.[11–14] The abuse potential and forensic importance of these substances are also in need to be established.

The presented case is the first reported fatal poisoning attributable to TFP. Forensic autopsy with detailed toxicological studies were essential to clarify the cause of death, as there were a very few hints of TFP ingestion at the point of inquest. However, whether a family member of the deceased attempted to conceal the evidence of TFP ingestion or not remained unknown.

The amount of TFP production has been steadily increasing in Japan according to the statistics by the Japan Plant Protection Association.[15] There is a strong and urgent need to accumulate human poisoning cases, regardless of whether they are lethal or non-lethal, to spread the awareness and to share the information on this new pesticide and its related chemicals among professionals.

Ethical approval
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Conflict of interest
The authors have no conflict of interest.

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Original communication

Suicide of physicians in the special wards of Tokyo Metropolitan area

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ABSTRACT

Numerous studies on physician suicide in various countries have been reported but no data from Japan on the issue can be found to date. In this study, physician suicides in the special wards of Tokyo Metropolitan area in 1996–2010 were investigated retrospectively. A total of 87 cases were enrolled. The results suggested that physician suicide has been linked to pre-existing psychiatric illnesses and occupational problems, and that psychiatrists have a relatively higher suicide risk compared to those majoring in other specialities of medicine. A distinctive feature was that 19 cases had used either drugs or devices which were accessible due to their profession some time during the process of committing suicide. Another notable feature was that 4 out of 5 anaesthesiologists enrolled in the study had chosen poisoning for their suicide method, with the drugs frequently used in their speciality. The findings advocate strongly for efficient suicide prevention measures for physicians including an early detection and treatment of psychiatric illnesses, as well as an urgent need for a more effective pharmacy management in applicable institutions together with the implementation of self discipline on each physician. This is the first broad academic study on physician suicide in Japan.

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1. Introduction

Suicides numbered 32,863 in Japan in 1998 and have exceeded 30,000 in every subsequent year, which accounts for the highest rate in the world.[1] Various analyses, researches and measures have been taken by professionals in various fields to stop such a long lasting trend of a complex public health problem. However, an absence of central institution to manage the detailed data on suicide has been making it difficult to grasp the actual condition through a large scale epidemiological study nationwide.

On the other hand, the shortage of physicians in Japan has become a serious social problem in recent years.[2,3] It is a great loss for the whole society to lose a physician by suicide, even though the number of cases is expected to be relatively small. It should be an issue to be dealt with not only by the professionals of forensic science or epidemiology, but by those from a variety of academic fields. No broad academic study on physician suicide from Japan can be found to date, due to the lack of academic epidemiological data.

The main objective of the present study was to examine the characteristics of physician suicide cases in the special wards of Tokyo Metropolitan area in 1996–2010, as the first broad academic study on the issue in Japan.

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2. Methods

Data on suicides of physicians and non-physicians handled in the Tokyo Medical Examiner's Office during 1996–2010 were extracted for descriptive analysis retrospectively. The Tokyo Medical Examiner's Office is an institution in which all unnatural deaths, including suicide, occurring in the special wards of Tokyo Metropolitan area are reported and the inquests are performed. This therefore provides that all suicide cases occurring in the area are processed by this institution. Death certificates and supplementary documents were examined which included age, gender, professional speciality, past and present illness/es, device/s used, proposed motive and other relevant information of each case. The ethical committee of the Tokyo Medical Examiner's Office approved the protocol of this study.

3. Results

The total number of suicides handled in the Tokyo Medical Examiner's Office during the study period was 28248 and 87 were physicians (0.31%). Of these 87 cases, the age varied from 25 to 82 (mean = 47.97, median = 47.00) and the male to female ratio was 68:19 (the percentage of female physicians = 21.84%). The suicide methods consisted of 49 hanging, 14 poisoning, 12 jumping, 3 diving, 3 hypoxia, 3 cutting, 1 hydrogen sulfide intoxication, 1 carbon monoxide intoxication and 1 drowning. The percentage of

methods chosen by physicians and non-physicians are shown in Fig. 1. Regardless to the suicide method, 19 physicians (21.84%) were found to have used either drugs or devices which were accessible due to their profession at some time during the process of committing suicide. Forty five cases (51.72%) had been diagnosed with a psychiatric illness, and the main motives of suicide of each case were psychiatric illnesses, occupational problems and non-psychiatric illnesses. The area of speciality of physicians consisted of 21 internists, 16 psychiatrists, 6 paediatritians, 5 anaesthesiologists, 4 dermatologists, 3 otolaryngologists, 2 radiologists, 2 surgeons, 2 obstetricians/gynaecologists, 1 orthopaedist, 1 plastic surgeon, 1 ophthalmologist, 1 pathologist, 1 researcher, 1 freelance, 1 industrial physician and 4 unknown, while 6 were junior residents (Table 1). Out of 5 anaesthesiologists, only 1 had chosen hanging as a suicide method but the remaining 4 had chosen poisoning with anaesthetics, using the devices most likely to have been taken out from their workplace (Table 2).

4. Discussion

Several studies have been carried out on the issue of suicide of physicians in various countries,[4–10] presenting notable findings in the distribution of suicidal methods and specialities in medicine. The present study revealed numerous noteworthy findings on the issue, some of which were unique in characteristics.

The mean and median age of physician suicides enrolled in the present study, 47.97 and 47.00 respectively, had no statistical difference compared to those of non-physician suicides in the equivalent period (mean = 49.69, median = 51.00, $p > 0.05$). The

Table 1
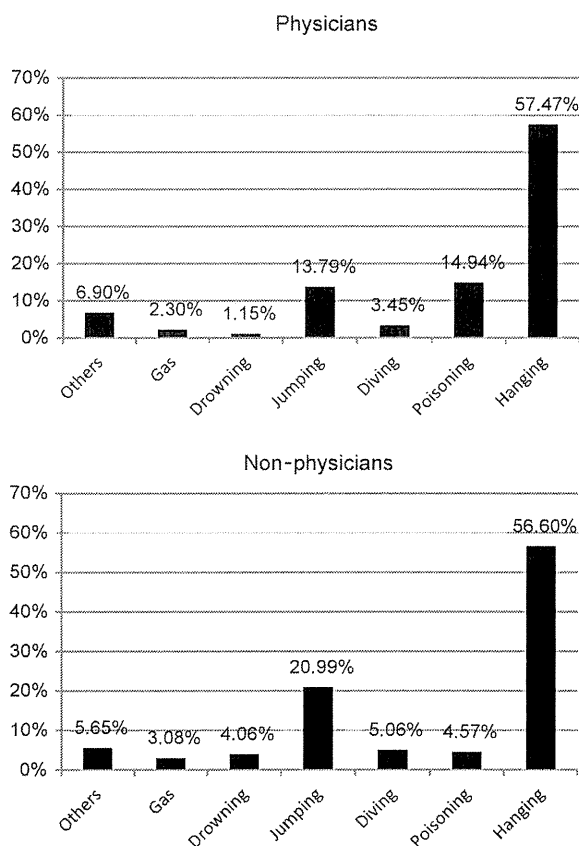The speciality of physicians on the national registry and those in the present study.

	Percentage in physicians over 15 years	Number of physician suicide	%
Internists	37.15–40.65%	21	24.14
Dermatologists	2.95–3.06%	4	4.60
Paediatritians	5.58–5.98%	6	6.90
Psychiatrists	4.64–5.06%	16	18.39
Surgeons	9.54–12.03%	2	2.30
Orthopaedists	7.09–7.44%	1	1.15
Plastic surgeons	0.57–0.78%	1	1.15
Ophthalmologists	4.56–4.99%	1	1.15
Otolaryngologists	3.22–3.84%	3	3.45
Obstetricians/ gynaecologists	4.40–5.39%	2	2.30
Radiologists	1.82–2.00%	2	2.30
Anaesthesiologists	2.19–2.75%	5	5.75
Unknown	0.47–0.77%	13	16.09
Others	7.32–13.96%	10	11.49

percentage of female physicians enrolled in the study (21.84%) was slightly higher compared to the percentage of females accounting for whole physicians; which increased from 13.39% in 1996 and 18.94% in 2010.[11,12]

It was found that 45 out of 87 cases had been diagnosed and received some kind of treatment for a psychiatric illness. Furthermore, a closer examination of supplementary documents revealed that the most common motives of suicide were pre-existing psychiatric illnesses, mostly depression, followed by occupational problems and non-psychiatric illnesses. There has been some evidence that depression, drug abuse, and alcoholism are often associated with suicides of physicians according to the studies conducted in other countries,[8,9] which is in accordance with the results of present study. The most common motive among non-physician suicides during the equivalent period was also psychiatric illnesses [data not shown], which indicates that an early detection and an appropriate treatment of psychiatric illnesses would be a key factor in the prevention of suicides, regardless of the occupational background.

It has been pointed out that psychiatrists and anaesthesiologists have a relatively higher risk of suicide compared to physicians majoring in other specialities.[10,13,14] According to the biennial reports released by the Ministry of Health, Labour and Welfare of Japan in 1996–2010, psychiatrists accounted for 4.64–5.06% of the whole registered physicians respectively.[11,15–21] On the other hand, there were 16 psychiatrists (18.39%) enrolled in the present study, which accounted for a distinctly higher percentage compared to the proportion of physicians in the national registry over the equivalent period; the assumption that the speciality distribution is the same in the Tokyo Metropolitan area. It is unknown whether there are occupational stresses particular to the psychiatric fields of medicine, or if the choice of speciality is influenced by factors that might differentially influence risk. However, there is a study reporting high levels of stress and dissatisfaction for psychiatrists.[22]

The present study revealed that the most common suicide method was hanging for physicians. Although the percentage of suicidal poisoning for physicians was relatively high compared to that of non-physicians, it only accounted for about a quarter of that of hanging (Fig. 1). On the other hand, poisoning was found to be the most common suicide method among physicians in some previous studies.[4,7] Some authors suggested that this phenomenon is due to physicians being rich in knowledge on lethal drugs and doses, as well as accessibility to them. While these factors may have had effects to the results, another factor

Physicians

Non-physicians

Fig. 1. The suicide method of physicians and non-physicians in 1996–2010 in the Tokyo Metropolitan area.

Table 2
The method of suicide by the speciality of physicians.

Speciality/ method of suicide	Internists	Dermatologists	Paediatritians	Psychiatrists	Surgeons	Orthopaedists	Plastic surgeons	Ophthalmologists	Otolaryngologists	Obstetricians/ gynaecologists	Radiologists	Anaesthesiologists	Unknown	Others	Total
Hanging	14	2	4	12			1	1		2	1	1	6	4	49
Poisoning	3	1		3								4	1	2	14
Diving	1												1	1	3
Jumping	1		2		2				1				3	3	12
Drowning	1	1							1						1
Gas				1							1		2		2
Others	1					1			1						6
Total	21	4	6	16	2	1	1	1	3	2	2	5	13	10	87

for consideration was established through the cases noted in the present study.

Physicians generally have more knowledge of effective suicide methods than those with less medical knowledge. It is notable that either drugs or devices only accessible to medical professionals had been used during the process of committing suicide in 19 out of 87 cases (21.84%). Furthermore, it is concerning to note that 4 out of 5 anaethesiologists had chosen poisoning for their method of suicide, using anaesthetics; droperidol, vecuronium bromide, midazolam, barbiturate and propofol. This is a distinct contrast to internists, with only 4 out of 21 using accessible medical drugs or devises during the suicidal process. Anyhow, these results indicate that an easy access to and a substantial knowledge of potentially dangerous drugs may lead to an inappropriate usage. For example, it is well known to medical professionals that propofol has sedative and relaxing properties, and brings euphoric feelings.[23] Quite a number of lethal cases have been reported on those dying from the misuse of propofol on themselves.[24–27] Medical institutions are responsible in managing potentially dangerous drugs and devices appropriately, but it also strongly depends on the moral of each professional involved. Every member of staff, not only those with management responsibilities, should be aware that there is a possibility that they might be used for unintended purposes other than suicide, such as addiction and homicide. There are case reports in which anaesthetics were suspected of having been accessories in homicides.[28,29]

It is clear that measures need to be taken to address the current problem of drug and device misuse by physicians. With the availability and ease of obtaining them along with the difficulty of detection, the use of prescribed drugs for wrong purposes, including suicide, will probably continue in the future. However, the best solution may not be to place restrictions on their circulation as the majority would be used for their intended purpose. Instead, a more strict pharmacy accounting of potentially dangerous drugs and devices in applicable institutions, together with the implementation of self-discipline on physicians should be encouraged to prevent their illicit diversion.

There are a number of limitations to this study. Due to the extremely small number of cases covered despite 15 years of study period, it is impossible to draw a reliable conclusion on the trends on physician suicide by age and period. A new distinctive characteristic may be revealed by continuous research on the issue and the accumulation of further cases of this nature. Furthermore, the study is based only on the physician suicides occurred in the Tokyo Metropolitan area. A different trend, such as the distribution in the speciality of medicine, may be observed in the other areas of the nation, particularly in the rural area.

5. Conclusion

Although the number of physician suicide accounted for less than 1% of whole suicides in the Tokyo Metropolitan area, numerous distinctive features were observed by background analyses. The results of the present study should encourage physicians and all physician associated co-workers to pay attention to the need for early intervention for psychiatric illness among themselves, and also to review of pharmacological management in their workplace and their morals as professionals handling potentially dangerous drugs and devices.

Conflict of interest

The authors have no conflict of interest.