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End-of-Life Care for the Elderly

Seishi Fukuma*¹

In Japan's aging society, where 19.3% of the total population is aged 65 or over, end-of-life care for the elderly is a key issue. At the Japanese Society for Research on Death and Dying, established in 1977, physicians and nurses have led discussion on the palliative care of terminal patients with malignant tumors, which is the primary cause of death in Japan. In 1981, the Seirei Hospice in Hamamatsu became the first palliative care unit (PCU) to be certified in Japan, paving the way for the establishment of 143 units nationwide. PCU hospitalization costs began being covered by health insurance in 1990, but since only patients with malignant tumors or acquired immunodeficiency syndrome can be admitted to PCUs, many elderly do not qualify for palliative care.

At centers for the elderly (special nursing homes for the elderly, public health centers for the elderly, grooming homes, etc.) used by those incapable of leading an independent life at home and in need of care, many patients have cognitive disorders and are incapable of clearly indicating how they intend the fast approaching last days of their life to be. Those whose condition takes a sudden change for the worse are taken to hospital. Here, their families are asked whether they intend life-prolonging treatment to be administered, but more often than not little consideration is given to the opinions of the elderly persons themselves.

In 2000, Richard Smith, Editor of the British Medical Journal, put forward 12 principles of a good death in a final report on the Future of Health and Care of Older People¹ and, to achieve this, care using an integrated care pathway for the dying patient is offered.² This consists of palliative care respectful of the dignity and privacy of

the individual and considerate of the wishes of the individual in the final stages.

The article, "A qualitative exploration of Japanese elderly patients' preferences for end-of-life care" records the findings of interviews conducted by Ayako Hattori et al. with 17 university hospital in-patients and 13 outpatients of university-affiliated hospitals aged 65 or over to find out their preferences for end-of-life care. Elderly patients' preferences for end-of-life care are influenced by emotional factors, decisions sometimes change and consideration for family members also has an impact. Elderly patients would prefer to spend their last days at home, but out of consideration for the strain on their families they would also consider hospitalization. They would prefer a comparatively quick, peaceful death without long-term care in a bedridden state.

When considering the end-of-life care of elderly patients with cognitive disorders who are no longer able to indicate how they intend to die, carers must consider the wishes and opinions that have been made clear by the elderly patients at that point and ensure that they are able to die with care that they and their families are satisfied with.

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A Qualitative Exploration of Elderly Patients' Preferences for End-of-Life Care

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Abstract

Objectives The objectives of this investigation were to understand, at a broader and deeper level, the wishes of the elderly in Japan concerning their end-of-life care, and to clarify their end-of-life wishes in order that care providers might better understand them.

Design Descriptive study drawing on interview data comprising responses to open and closed-ended questions.

Setting Patients attending a university hospital and a university-affiliated geriatric clinic were interviewed in a private room near their own rooms or the clinic they attended.

Participants Seventeen elderly patients who were hospitalized in a university hospital and 13 elderly patients who received medical services from a university-affiliated outpatient facility.

Measurements An interview was designed to address three major domains: 1) wishes for care at the end of life, 2) patient preferences for information about their illness, and 3) the meaning of death.

Results Wishes for care at the end-of-life were influenced by various factors, namely; family, health condition, personal experience, relationship with physician, and concept of life and death. Wishes expressed in relation to these factors often varied during the interview however, the wish to “die in comfort” remained consistent.

Conclusion Palliative care providers should understand that elderly patients' wishes for end-of-life care may be dependent upon their own ability to make decisions, that their wishes may change during the decision-making process, and that family considerations are a strong influence on decisions, however the desire to die in comfort remains highly stable.

Key words End-of-life care, Patient preference, Elderly patient, Qualitative study

The Background and Purpose

World population projections for the 21st century show that the transition to an aging society is occurring at a rapid pace both in developed and developing countries.¹ Japan is one of the most prominent examples of a nation with a rapidly aging society since the rate of aged death con-

tinues to rise rapidly.² This situation has made end-of-life care for elderly patients an important social and medical issue in Japan and other nations around the world.

Most clinicians and researchers agree that improvement of the patients' quality of life is an important goal in palliative care. One important factor in achieving this goal is “to meet the wishes of the patients.”³ Thus, it is important to know

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Table 1 Characteristics of elderly inpatients

Participants	Gender	Age	Recorded time (min)	Living with his/her family
1	Female	73	60	No
2	Female	74	60	Yes
3	Female	67	50	No
4	Male	76	60	Yes
5	Female	84	50	Yes
6	Male	76	50	Yes
7	Female	80	55	Yes
8	Male	78	45	Yes
9	Female	81	60	Yes
10	Male	81	50	No
11	Female	77	50	Yes
12	Male	73	45	Yes
13	Female	73	50	No
14	Female	78	60	Yes
15	Female	71	55	No
16	Female	81	45	Yes
17	Male	75	45	Yes

Table 2 Characteristics of elderly outpatients

Participants	Gender	Age	Recorded time (min)	Living with his/her family
1	Female	88	50	Yes
2	Female	87	50	Yes
3	Female	82	50	No
4	Female	78	55	Yes
5	Female	88	60	Yes
6	Male	88	70	Yes
7	Female	82	55	Yes
8	Female	79	45	No
9	Female	78	50	No
10	Female	75	65	Yes
11	Female	86	65	Yes
12	Female	85	55	Yes
13	Female	83	45	No

what kind of end-of-life care, elderly people want, yet in Japan, little research has been conducted on this subject. There has been previous work in Japan especially on end-of-life decision-

making with regard to cancer disclosure and euthanasia⁴⁻¹² though these have not primarily focused on elderly patients' preference for end-of-life care. The research that has been done to

date has largely employed quantitative survey methods.^{13,14} These studies have revealed that the most elderly Japanese do not wish for life-sustaining treatments, but desire palliative care if they become terminally ill; approximately 70 percent wish to die in their own homes; and a large number of patients wish to be informed about the nature of their illness, no matter how old they may be. However, in these surveys, the areas investigated were limited to items included in closed-ended questions.

The objectives of this investigation were to understand, at a broader and deeper level, the wishes of the elderly in Japan concerning their end-of-life care, and to clarify these wishes in order to help care providers understand them. A qualitative design was determined most appropriate for this study in order to elucidate the background and context of elderly patients' wishes, and to understand those wishes through the voices of participants themselves rather than solely in terms pre-defined by a research instrument.²¹

Methods

This investigation employed a qualitative design that generated rich, textual data from personal interviews. This design allowed the research team to investigate the processes and conditions that affect elderly patients at the end of their lives, and to understand their wishes about these factors during this important time. To maximize variation among the sample along the spectrum of acute to chronic health status, we recruited participants from both one inpatient setting and one outpatient setting.

The subjects consisted of 17 elderly patients, age 65 and over, who were hospitalized in a university hospital and 13 elderly patients who received medical services from a university-affiliated outpatient facility between February and July 2000. Only subjects who were not in an acute, life-threatening condition and who could talk for approximately one hour were eligible.

Patients with dementia were excluded from participation. Subjects ranged from 67 to 88 years of age (mean age: 79.2 years); 23 were female and 7 were male. Table 1 and 2 include information regarding age, gender, recorded time, and family status for inpatients and outpatients.

The interviews with the hospitalized patients were conducted by Y.M, and outpatient by A.H.

An interview guide was designed to address three major domains: 1) wishes for care at the end-of-life, 2) preferences for information about the illness, and 3) the meaning of death.

Corresponding questions on the semi-structured interview guide included:

- 1) What wishes do you have for your own end-of-life care? Where would you like to be when you die? Whom would you like to have at your bedside at the time of your death?
- 2) To what degree would you like to have a detailed explanation concerning the selection of treatment? To what extent would you like to be part of the decision-making for your treatment?
- 3) What does death mean to you?

In this paper, we have focused only on the results from the first and third domains.

Participant consent

Procedures for recruiting and obtaining consent differed between the hospitalized and outpatient participants. To reduce stress for the hospitalized participants, a written copy of the interview questions was given to the subjects at the time they consented to being involved. In the process five patients declined to participate further. Interviews were then conducted one to three weeks later. Hospitalized participants received interviews in a private conference room near their own rooms. Each interview lasted about an hour. Since it was not feasible to circulate the questionnaires prior to in the outpatient environment, outpatient participants were interviewed at the point their consent was gained. Thus outpatients were not able to consider the questions in advance nor did they have the time to reassess their desire to participate. However we did consult nurses in advance about suitable patients for this inquiry and after receiving consent from the outpatients that were recommended, we again considered whether or not the interview questions would be acceptable to each individual. Finally, all consenting outpatients were interviewed. We also used a private conference room to interview outpatient subjects. Each interview lasted between 40 and 90 minutes. Interviews were recorded on audiotapes and transcribed verbatim.

Data analysis

We analyzed this qualitative data using the

Table 3 Contents of wishes for the end-of-life

Category of the end-of-life wish	Content of the wish
Wishes for the end-of-life circumstance	
Place of death	Home Hospital Hospice Anywhere
Who is wanted at bedside	Family members One who will listen to one's tale No one; Want to be alone
Treatment and decision-making	Refuse life-sustaining treatment Receive adequate pain and symptom management Entrust others with decision making
State of death	Die easily and without suffering Avoid dependency Avoid being bedridden
Factors influencing wishes for end-of-life care	
	Family Relationship with physician Health condition Personal experience Concept of life and death
Transformation and consistency of wishes for end-of-life care	
Die in comfort	

process of immersion/crystallization.^{22,23} The analysis for this report focused on patients' wishes for end-of-life care and the circumstances prior to their death. We independently identified preliminary categories and emphasized the use of in vivo codes. The coders discussed and resolved any coding discrepancies. The codes and associated passages were then entered into a qualitative analysis database.

Steps were taken to maintain the trustworthiness of the qualitative research.²⁴ These were then iteratively compared in order to refine the categories that ultimately were used to encode the transcripts. Analytical memos from both analysts were used to refine the categories and extract themes. By iteratively refining the codes and categories, the analysts were careful to ground the emergent themes in the data, and interviewing was completed at the point of saturation.

Theoretical saturation was achieved by continuing to interview additional participants until no new themes emerged.²⁵ No new themes

emerged from the interviews with the last four individuals recruited. Theoretical verification of the study results was assessed by asking four individuals who had participated in the study to respond to the results.²⁴ All participants responded that the results accurately represented their and their acquaintances' attitudes.

The methodology of the study was approved by the Ethics Committee of School of Medicine, Nagoya University.

Results

Analysis of the text data yielded four major themes (Table 3): 1) wishes for end-of-life circumstances, 2) factors influencing participants' wishes for end-of-life care, 3) the transformation of wishes for end-of-life care, and 4) the desire to die in comfort. Together, these results guided the development of a conceptual model, the amoeba model of elderly patients' wishes for care at the end of life (Fig. 1).

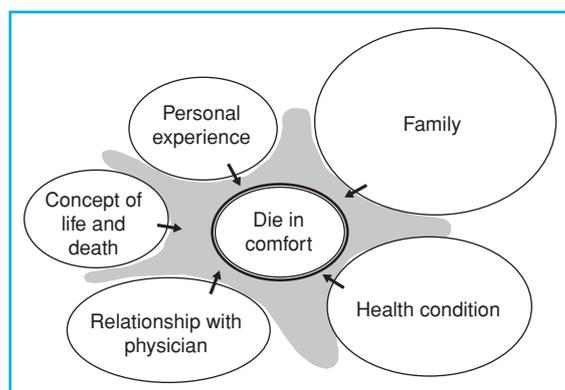


Fig. 1 The amoeba model of elderly patients' wishes for care at the end of life

Wishes for end-of-life circumstances

Wishes for end-of-life circumstances emerged as a theme from the interviews. From among those relevant statements, the wishes were further categorized into two subcategories (see Table 3). The first subcategory involved those wishes concerning the circumstances around the time of death, such as place of death, whom they wanted at their deathbeds, and avoiding extensive life-prolonging treatment. These factors were elucidated by interview questions that addressed the first domain, discussed above. The second subcategory, which related to the state of death, emerged from the data through statements like, "I wish to die easily, without suffering," or "I hope to not be bedridden for a long period of time."

Factors influencing wishes for end-of-life care

The reasons behind participants' wishes for their end-of-life care were examined in detail, and comments related to factors influencing their wishes were extracted and categorized as: family, relationship with physician, health condition, personal experience, and concept of life and death.

Family: The family factor clearly influenced the place of death and whom they would like to have at their bedsides. Relevant data included statements like: "reservation and consideration toward the family," "expectation," "resignation," and "family background." This factor, in particular, influenced many subjects in their preferences for place of death.

Almost all participants mentioned family members when answering the question, "Whom

would you like to have at your death bed?" The consistency of this response further implicated family as the reason why they originally had wanted to die in their own homes. In contrast, those living alone wished to die in a hospital for fear their conditions might worsen if they were alone at home:

Look, can't you see that dying in a hospital with someone around would be better than dying alone without anyone knowing?

(78-year-old female outpatient)

While family was a prominent theme, participants also struggled with how to balance their desire to have family close with the burden end-of-life care would be on their loved ones. This struggle was revealed through statements such as this one made by a 78-year-old hospitalized female:

I see others being nursed by their families and see how strenuous it is for the younger people to take care of the elderly. It takes time and labor, and it also puts a lot of psychological burden on them. I love my daughter and son, and so that's why I don't want to burden them, if possible.

Relationship with physician: Many of the participants mentioned having faith in and reliance upon their doctors, and this trusting relationship influenced their wishes for their end-of-life care. Their trust was typically directed toward a specific medical institution or doctor. When the hospital was the place of death, they entrusted the appropriate selection of treatment to the doctors.

No matter how much I think about it, there's nothing I can do but to trust the doctor here. I don't know anything (about medicine), so I leave everything to my doctor. If I leave it up to my doctor, I'll have nothing to worry about. (84-year-old hospitalized female)

Health condition: A number of participants wished to be placed in a nursing facility when the time came, assuming their physical functions would deteriorate and they would require nursing care in the future. Again, the family burden factor played a role in their responses. There were also some who wished to be hospitalized for treatment if they were in pain.

Right now, I could be on my own, but I wonder whether my daughter would be able to care for me. So, I think I should be in a place like this so I can be taken care of.

(88-year-old female outpatient)

When the time comes when I can't be on my

own, I guess I'll have to go into the hospital to be taken care of. If I go into a hospital, they'll give me an injection for treatment and take care of me. That would be better, I guess.

(88-year-old female outpatient)

Personal experience: Several of the participants, when speaking of how they wanted to die, gave examples of their experience caring for a family member during that person's end-of-life period. They particularly expressed their desire to die in the same manner as family members or acquaintances who had died within a short period and with little suffering. In contrast, those who had experienced the death of a family member who had been bedridden for a long time without being able to communicate with the family expressed their desire to avoid such a situation. Participants' personal experience clearly influenced their wishes for their end-of-life period.

Both Grandma and Grandpa died of heart attacks while they were walking on the street. I heard my oldest brother died all of a sudden while watching TV. My other older brother died within two or three minutes from choking on mochi (a sticky rice cake). I want to die like them!

(86-year-old female outpatient)

My sister's husband passed away suddenly the other day. He hadn't been ill for long. It was what we consider a good way to die. Everyone envied him because he "died so well." I would like to die like that, too.

(83-year-old female outpatient)

Concept of life and death: Several participants expressed their attitude toward the end of their life by saying they did not care but preferred, instead, to leave the decision up to others. There were also those who had—more or less—abandoned hope, while some had never given any thought to their death. Underlying the latter attitudes seemed to be a concept of life and death, which appeared in statements like: "What will be will be in the end." "Our fate is already set, so there is no sense in thinking about it." In addition, several subjects stated their opinions concerning their life and death philosophically as epitomized by the following statements:

I have lived long enough so I will leave the rest to others. I don't care if I die at home or in a hospital, Do I want someone at my bedside? I don't need anyone. Man is born alone and die alone. No one could do anything

even if there was someone at my deathbed. Wherever I die, that will be the end of me. What's important is how I lived at the prime of my life. (67-year-old hospitalized male) I can't say that I want this or that done for me, because I have left that up to the ones who are nursing me, so I really don't have any wishes. What can I do about it? Even if I said how I wanted to be cared for, there's no guarantee that they'd listen to me. Well, I think whatever happens will be my fate, so I'll have to go along with it.

(74-year-old hospitalized male)

Such concepts of life and death expressed the subjects' interest in or apathy toward their own death, the latter being expressed through giving themselves up to others and/or to what they perceived as their fate.

Transformation and consistency of wishes for end-of-life care

As stated above, wishes concerning end-of-life care are influenced by the respective background of participants, and consideration of family, health condition, relationship with the physician, personal experience of their family members' deaths, or concept of life and death. However, when discussing their care preferences, study participants often seemed to talk themselves from an initial desire into a different conclusion. For example, some participants initially indicated their wish to die in their homes, however, after considering the nursing burden this would place on the family, later changed their minds and concluded that, instead, they would prefer to die in a hospital. Which factors influenced the wishes and the degree of the influence depended on the individual.

If it is possible, I want to die at home with my children around me

Then later:

. . . Even if that doesn't work out, I don't mind because people die anywhere.

(73-year-old hospitalized female)

If possible, I want to die at home

Then later:

. . . I'll go along with my doctor's decision, whatever he decides is best for me, so I won't insist on it dying at home.

(78-year-old hospitalized female)

By contrast, others were interviewed offered consistent responses. Such participants consis-

tently gave either firm wishes concerning their end-of-life environment, from the beginning right the way through to the end of the interview, or did not express any strong wishes. Right from the start of the interview, these patients showed little interest and held no personal hopes for their end-of-life circumstances. Phrases such as “I don’t care” or “I’ll leave it up to others” seemed to indicate they would want their desire to match the intentions of their families and medical practitioners.

Although some patients were consistent either in expressing apathy, or in their expression of a firm wish, the majority of subjects wishes appeared to change during the course of the interview.

The desire to die in comfort

Though there was a tendency for some of the participants to change their mind showing how their train of thought developed and their wishes for their end-of-life care and circumstances changed, most participants expressed a strong wish to “die in comfort.” While they would entrust end-of-life decisions, such as the place of death or the selection of the treatment, and some also had an “I do not mind either way” attitude, the desire to “die easily, without suffering” was the most prevalent underlying wish, and one which never changed.

I don't want to be bedridden. I tell everyone that I want to die in a situation where everyone realizes that I am dead. I want to be moving around until the very last minute. That way, I won't have to suffer for a long time before I die. But I have to die some day. I've passed my 80th year, so my time is just around the corner, but I'm not afraid to go. I just don't want to die in agony. I want to just drop dead. (88-year-old female outpatient)

Moreover, as expressed by the female outpatient above, most patients wished not to be bedridden for a long time and to die within a short period. Therefore, the desire not to be bedridden for a long period of time is included in the wish for a comfortable death.

There were a few who emphasized the merits of euthanasia. For example, one participant had this to say:

I wish people would let me die in my sleep. You know, there was a doctor in Kyoto who was charged for giving a potassium chloride

injection, but I think that is one possible way to die. Don't you think it would be good to go to the other world in sleep, without any pain or suffering?

(67-year-old male inpatient)

The amoeba model of elderly patients' wishes for care at the end of life

The amoeba model of elderly patients' wishes for care at the end of life is depicted in Figure 1. This conceptual model illustrates a “nucleus wish” for comfortable death surrounded by often-transforming and changing end-of-life wishes. This wish to die in comfort forms the nucleus of the amorphous and ever-changing amoeba. The double-lined border in the middle of the gray amoeba in the model represents the permanence and significance of subjects core desire to die in comfort. While some patients were initially able to articulate their wishes and these remained relatively consistent, it was more commonly seen among the subjects that they changed their wishes. This model illustrates the relationship between the changeable wishes of the subjects, and the factors that change their wishes. The irregularly shaped gray cytoplasm represents patients' changeable wishes concerning end-of-life circumstances, and the various-sized vacuoles surrounding the amoeba-shaped area identify the factors influencing those wishes.

Hence, the wishes for end-of-life care by the subjects are like the vacuoles in an amoeba. While semi-morphous, the size and shape of patients' wishes gradually change and evolve, somewhat like vacuoles inside the cytoplasm of an amoeba. Like vacuoles, these wishes are ultimately incorporated into the nucleus and become an integrated part of the core without changing the fundamental premise of the desire to die in comfort.

Discussion

This qualitative investigation has used the voices of participants to explore issues surrounding the wishes of elderly Japanese patients for their end-of-life care. We have gathered their comments from the interviews and extracted various factors influencing patients' wishes. Although most of their expressed wishes often changed over the course of their respective interviews, the desire to die in comfort remained stable throughout.

These findings are highly consistent with several other qualitative studies that also examined end-of-life issues.^{15–20} Steinhäuser et al. revealed that “to be free from pain” is the most important factor that people considered regarding end-of-life. “To die without pain” may be the final wish for many people.¹⁶ In an anthropological investigation comparing end-of-life care in the United States and Japan, Long also found as a central theme the importance of a peaceful death.⁴

One theme of this analysis that is important for health care providers is the progression of wishes concerning the end-of-life period. In research reported by the International Longevity Center Japan, researchers distributed a survey to examine the self-determination process of elderly patients. Rather than insisting on their own wishes, some of the elderly patients trusted and left decisions to family members and doctors.²⁶ Finally, there were many subjects with “fluid opinions”, hoping to make their own decisions if circumstances allowed. Triangulation of the data from the current study with results from these quantitative studies seem to support a strong case that evolution of wishes may be a consistent pattern among the elderly in Japan. This should be considered when discussing end-of-life care choices with elderly patients.

The transformation of patient wishes described in the amoeba model of elderly patients' wishes for care at the end of life as a process seems unlikely to be particular to the Japanese. In North America, self-determination for medical care, particularly self-determination leading to an advanced directive concerning end-of-life treatment, is considered to be one of the fundamental rights held by human beings.

In contrast to North American thinking, Japanese people's sense of ego—according to one view—has not yet been established.²⁷ Rather, from this perspective, it could be argued that human beings are part of nature, and so should leave their destiny to nature and fate, and that as with other forms of death, human death is to be accepted as a natural part of the life course.²⁸ Such cultural conditioning of elderly Japanese people may be influencing their wishes for the end of their lives. This can, possibly explain—at least to some extent—the nature of the changes and transformations of our interview subjects' wishes.

An investigation conducted in Canada²⁹ reported that there are two types of patients: “activists,” who desire to make their own decisions, and “delegators,” who leave the decision up to nature, fate and God. The study pointed out that the delegators tended to be a less-educated, lower-income group. Many Japanese people, on the other hand, seem to hold a cultural concept of life and death similar to the delegators in the Kelner study, regardless of education or income.²⁸

During this investigation, the family, health condition, trust in the physician, experience, and concept of life and death were all confirmed as factors influencing the wishes of the elderly. Of these factors, consideration of family members was the strongest influence, with most of the subjects feeling burdened by the thought of imposing the provision of nursing care on their family. Subjects expressed the feeling that, in reality, they could not expect too much home care, and would relinquish their original wish to die in their own homes. Previous authors have similarly illustrated the importance of family influence on Japanese decision-making concerning end-of-life context.^{7,8,30,31}

The Family factors also typically arise among qualitative investigations concerning wishes for the end of life in Western countries. Moreover, consideration of the burden of asking family to provide nursing care is common among subjects in both cultures.^{16,32,33,34} A culture in which the decision-making by the family is placed at a higher priority than the wishes of the patients, themselves, is not unique to the Japanese group, but is also reported in other ethnic groups.^{35,36} In the United States there are also many elderly patients who express a desire to respect the decision of the family rather than insisting on their own directive concerning their end-of-life treatment should they lose their decision-making ability.³⁷ This evidence suggests that consideration of the family over individual wishes for end-of-life care may not be culturally distinct, but may not necessarily be an omnipresent, phenomenon either.

These data illustrate that patients worry about becoming ill and bedridden and that such health conditions influence their wishes for end-of-life care. Long has demonstrated that conflict between self-reliance and being a burden is an important factor in the Japanese context vis-à-vis attitudes toward euthanasia or suicide.¹¹

This investigation found that some subjects have considerable confidence and reliance in their doctors and toward the medical institutions from which they receive outpatient treatment. This, in turn, tended to influence their wishes concerning their end of life, such as the place of death and selection of treatment. This fact is important for medical practitioners. All medical practitioners must take into account the great extent to which confidence and reliance is placed in them and on their decision making. Among the patients who had an ongoing relationship with the medical profession and source of care, many reported feeling confident that they had a reliable doctor (or medical institution) to whom they could leave their end-of-life treatment decisions.

Limitations

The participants in this investigation were elderly patients who were either hospitalized or who had been receiving medical treatment for a number of years as outpatients of a university hospital. It

is assumed that they actively chose these facilities based on the expertise of the professionals practicing there. This might result in a biased group of patients compared with the elderly population in Japan who have no links with specific hospitals whether as in- or outpatients. Therefore, the data obtained may not represent Japanese elderly people as a whole. While we are confident that we have accurately depicted the views of these participants, and that these depictions likely hold for many elderly Japanese patients, we cannot be certain how common these views are and whether they represent the spectrum of views.

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Prevention of Morning Surge of Hypertension by the Evening Administration of Carvedilol

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Abstract

Object To test the clinical usefulness of chronotherapy with a β -blocker, evening carvedilol administration was added to first-line antihypertensive therapy in patients with essential hypertension showing a morning blood pressure surge.

Methods Patients with hypertension (12 men and 5 women) were treated with first-line antihypertensive drugs for 4 weeks and then underwent 24-hr ambulatory blood pressure monitoring. Patients (6 men and 3 women) who still had high blood pressure exceeding 140/90mmHg in the morning were given carvedilol (10mg/day) as a single dose in the morning or evening in a randomized, crossover open-label protocol. After 4 weeks, ambulatory systolic blood pressure, diastolic blood pressure, and pulse rate were reassessed by 24-hr monitoring.

Results Evening carvedilol administration significantly suppressed the morning surge, while morning administration lacked an significant anti-surge effect. The 24-hr mean systolic pressure was also significantly reduced by evening carvedilol administration. Evening administration significantly decreased the early morning, but not the nocturnal, pulse rate.

Conclusions Evening carvedilol administration significantly suppressed the morning increases in systolic pressure and pulse rate. The addition of chronotherapy with carvedilol may be an effective way to suppress morning surges of hypertension.

Key words Hypertension, β -blocker, Chronotherapy, Circadian rhythm, Morning surge, Carvedilol

Introduction

Since ambulatory blood pressure monitoring has become common, certain patterns of circadian variation in blood pressure have been closely linked with the risk of hypertensive organ damage.¹⁻³ In particular, an early morning blood pressure surge appears to be associated with an increased risk of cerebrovascular and cardiovascular events.⁴⁻⁵ Controlling 24-hr variation in blood pressure as well as pressure measured casually at office visits has become an important aim of antihypertensive therapy. Pharmacotherapy that targets such specific circadian blood pressure changes is increasingly recognized as an impor-

tant strategy. Clinical research concerning the management of hypertension has traditionally focused on the choice of antihypertensive drugs, while more recently, chronotherapy — timing of administration based on a chronobiologic approach — has attracted attention.⁶ Incorporating the concept of chronotherapy into routine antihypertensive strategies will be a major challenge for clinicians.

Newly introduced antihypertensive drugs with differing mechanisms of action have greatly facilitated blood pressure control in patients with hypertension. The choice of first-line antihypertensive treatment is not usually difficult, being based on national and international guidelines.^{7,8} However, more variability is introduced upon

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selecting a second-line antihypertensive drug when the first-line drug has failed to achieve good 24-hr blood pressure control. When first-line therapy fails to prevent a morning surge in blood pressure, the dose of the first-line drug can be increased; the drug can be replaced by a mechanically similar drug with a longer half-life; or the first drug can be combined with another drug having a different mechanism of action.⁹ The greatest advantage of adding another drug with a different mechanism of action is the likelihood of antihypertensive synergism between the two treatments without an increase in toxicity such as might occur after simply increasing the dose of the original drug. However, little has been determined about the optimum timing of second-line treatment to suppress a morning surge after the failure of the first-line drug to do so.

For the management of hypertension, β -blockers have been recommended by various national and international guidelines¹⁰; unless contraindicated, they are considered the drugs of first choice for lowering high blood pressure in patients with increased sympathetic tone. Since β -blockers specifically block the sympathetic drive, they may be particularly effective for suppressing the morning blood pressure surge, which occurs when sympathetic activity exceeds parasympathetic activity in the course of the circadian rhythm of autonomic regulation. However, adequate evidence of the effectiveness of this strategy has not been obtained.

In the present study, patients with essential hypertension who still showed a morning blood pressure surge despite first-line therapy were additionally given carvedilol, a long-acting β -blocker, as second-line therapy to determine whether this addition could suppress the morning surge. The antihypertensive effect of carvedilol was compared between two different once-daily dosing schedules: adding morning administration at the same time as the first-line drug, and adding evening administration instead, to clarify the chronopharmacodynamic profile of the drug.

Methods

Seventeen untreated patients (12 men and 5 women) initiating ambulatory treatment at our University Hospital for moderate essential hypertension diagnosed according to the criteria specified in the sixth report of the Joint National

Committee⁷ gave informed consent to participate in the study. They received first-line treatment with a long-acting calcium antagonist ($n=9$) or an angiotensin-converting enzyme inhibitor ($n=8$) once in the morning every day. Patients with heart failure, asthma, arteriosclerosis obliterans, severe bradycardia, severe hepatic dysfunction, and severe diabetes mellitus were excluded from the study.

After 4 weeks of first-line treatment, each patient underwent monitoring of blood pressure for 25 hr using an ambulatory blood pressure monitor (ES-H-531; Terumo, Tokyo). Systolic blood pressure, diastolic blood pressure, pulse pressure, and pulse rate was measured at hourly intervals. The data obtained from the second hour onward were processed by a specifically configured analyzer (ES-A531; Terumo, Tokyo). The 24-hr mean value was calculated, as well as the mean values for early morning (6 to 10 AM), waking hours (6 AM to 10 PM), and nighttime (10 PM to 6 AM).

After 4 weeks of first-line treatment, nine patients (five treated with a calcium antagonist, four treated with an angiotensin-converting enzyme inhibitor) showed an early morning (6 to 10 AM) mean systolic pressure over 140 mmHg or a diastolic pressure over 90 mmHg. The nine patients were then treated further with the addition of carvedilol (10 mg once daily). This group included six men and three women; their ages ranged from 51 to 78 years (65 ± 3). They were assigned randomly to one of two groups. Five took the additional drug in the morning for 4 weeks, followed by 25-hr ambulatory blood pressure monitoring, and then in the evening for 4 weeks followed by monitoring (Group I). The two treatments were given in reverse order in Group II ($n=4$). This crossover design was used to compare the two dosing schedules.

For each hemodynamic parameter, changes at the end of the morning or evening administration of carvedilol from the values observed at various times of day at the end of the first-line treatment were tested for significance using multivariate analysis of variance. For the same parameters, differences in mean values in early morning, waking hours, nighttime, and 24-hr periods between the first-line and post-supplemental treatment were tested for significance using a paired t-test. In all analyses, significance was defined as a P value below 0.05.

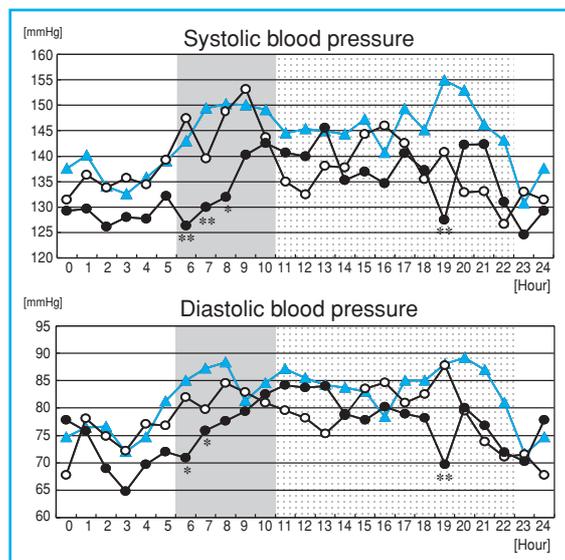


Fig. 1 Circadian rhythms of blood pressure at the end of each treatment period (closed triangles, first-line treatment; open circles, morning carvedilol administration; filled circles, evening carvedilol administration)

Asterisks; first-line treatment vs. morning or evening carvedilol addition (*: $P < 0.05$, **: $P < 0.01$).

Results

The concomitant morning administration of carvedilol did not alter the circadian rhythms of systolic and diastolic pressure from those observed during first-line antihypertensive treatment alone. In contrast, the administration of carvedilol at the same daily dose in the evening accomplished a significant reduction in systolic pressure at 6:00, 7:00, and 8:00 the next morning. The evening administration of carvedilol also caused a significant reduction in diastolic pressure at 6:00 and 7:00 the next morning compared with the values recorded at the end of the first-line treatment period (Fig. 1). Irrespective of the timing of administration, carvedilol caused no significant changes in pulse pressure or its circadian rhythm.

The evening administration of carvedilol caused the mean systolic pressure in early morning (6 to 10 AM) to decrease significantly, from 148 ± 17 to 134 ± 14 mmHg ($P < 0.01$). After the morning administration of carvedilol, the early morning mean systolic pressure was 147 ± 17 mmHg, which remained similar to the value observed at the end of the first-line

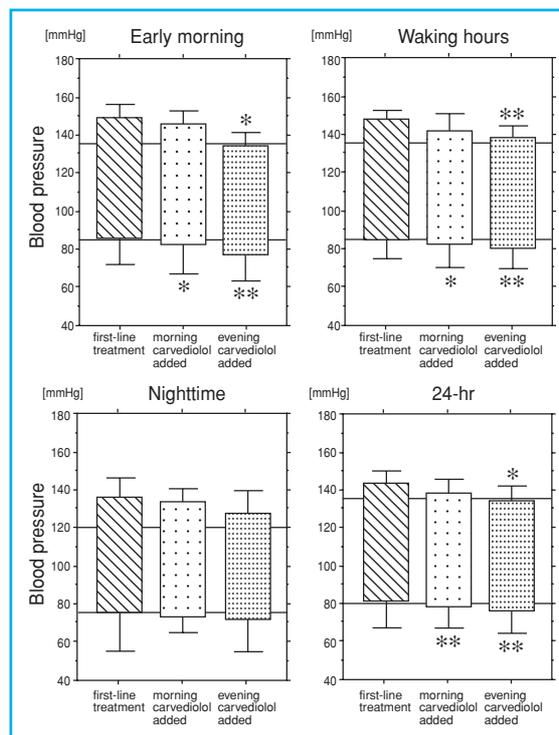


Fig. 2 Changes in mean systolic and diastolic blood pressure at the end of each treatment period

The asterisks indicate significant differences in blood pressure with first-line treatment vs. the addition of carvedilol in the morning or evening (*: $P < 0.05$, **: $P < 0.01$).

treatment. Compared with the first-line value (85 ± 9 mmHg), the early morning mean diastolic pressure was significantly reduced to 82 ± 8 mmHg ($P < 0.05$) by the morning administration of carvedilol, and to 77 ± 8 mmHg ($P < 0.01$) by the evening administration. The 24-hr mean systolic pressure was significantly reduced from 144 ± 14 mmHg at initial measurement to 134 ± 12 mmHg ($P < 0.05$) by the evening administration of carvedilol. Both the morning and evening administration of carvedilol significantly reduced the 24-hr mean diastolic pressure, from 82 ± 7 mmHg at initial measurement to 78 ± 9 and 76 ± 9 mmHg, respectively ($P < 0.01$; Fig. 2).

The first-line 24-hr mean pulse rate was 67 ± 11 /min; this was significantly reduced to 63 ± 12 /min by morning carvedilol and to 64 ± 11 /min by evening carvedilol. The decrease in pulse rate induced by carvedilol was significant during waking hours, but not at night. The mean pulse rate in the early morning was significantly

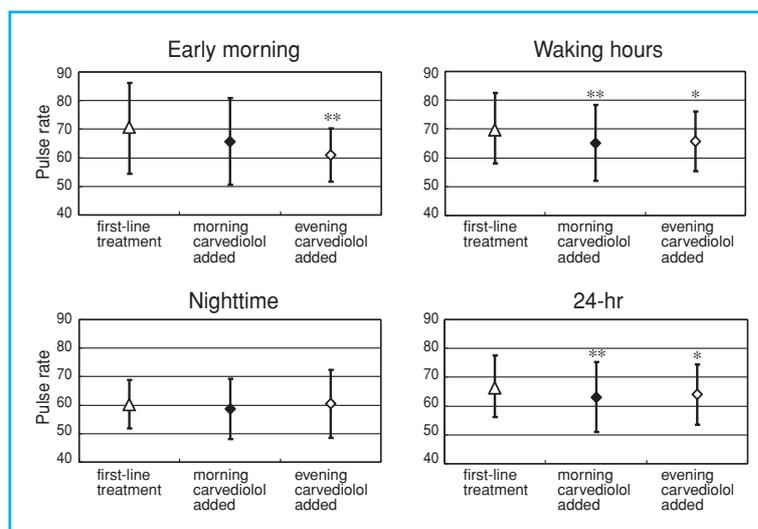


Fig. 3 Changes in mean pulse rate at different intervals during the day
The asterisks indicate significant differences in pulse rate with first-line treatment vs. carvedilol added in the morning or evening (*: $P < 0.05$, **: $P < 0.01$).

reduced by the evening but not the morning administration of carvedilol (Fig. 3).

Discussion

Cardiovascular events in patients with hypertension, including myocardial infarction and stroke, are well known to occur predominantly during the morning.^{11,12} Data concerning circadian variation in blood pressure indicate that a morning blood pressure surge is involved in the etiology of these cardiovascular events.¹³ Hemorheologic studies have also shown that a morning increase in platelet aggregability may trigger ischemic events.¹⁴ The increase in both blood pressure and platelet aggregability has been linked to a morning increase in sympathetic tone.^{15,16} We demonstrated that the evening administration of a β -blocker, carvedilol, significantly suppressed the morning blood pressure surge. Suppression of sympathetic hypertonia might therefore be effective in suppressing the surge.

A number of biologic functions maintain their individual circadian rhythms. Data obtained by ambulatory monitoring have elucidated the circadian rhythm of blood pressure.^{17–20} Patients with hypertension show various patterns classified as “nondipper,” “dipper,” and “extreme-

dipper,” defined by the extent of the nocturnal fall in blood pressure compared with daytime pressure, specifically as less than 10%, 10% to 20%, and more than 20% for these respective groups of patients.²¹ A study of hypertensive patients with coronary disease showed that anti-hypertensive therapy led to an increase in the risk of nocturnal myocardial ischemia in subjects showing an extremedipper pattern.^{22–25} Therefore, the risk of an excessive fall in nocturnal blood pressure should be avoided. In the present study, no excessive decrease in nocturnal blood pressure occurred after the evening administration of carvedilol, while the morning surge was suppressed effectively. Since nocturnal autonomic regulation is characterized by the predominance of parasympathetic activity, sympathetic blockade by carvedilol might be less effective at that time.

The negative chronotropic effect of β -blockers is another concern with evening administration, considering the reported risk of an excessive decrease in nocturnal pulse rate.²⁶ We actually found less reduction in nocturnal pulse rate with the evening than the morning dosage. The negative chronotropic effect of carvedilol appeared to be weak, although the reliability of this finding was limited by the small sample size.

The benefit of chronotherapy in suppressing

the morning blood pressure surge has been investigated by the nighttime administration of doxazosin, an α_1 -blocker,^{27,28} but few studies have assessed the benefit of chronotherapy with a β -blocker.²⁹ Carvedilol has some α_1 -blocking activity, but this is far less potent than its β -blocking activity (about one-eighth). Suppression of the morning surge by carvedilol was considered to have resulted from β -blocking activity.

Chronotherapy is an approach to treatment based on the observed circadian rhythms of various parameters.³⁰ The development of long-acting antihypertensive drugs ordinarily permits the maintenance of normal blood pressure by taking the drug(s) once in the morning.^{31,32} When the morning surge can be controlled by a single dose of an antihypertensive drug in first-line treatment, there may be little benefit from additional consideration of chronotherapy, which instead appears to be an effective option in patients who need second-line antihypertensive therapy. Our findings indicate that the morning and evening addition of carvedilol to a first-line antihypertensive drug has different effects upon

the circadian rhythm of blood pressure. This suggests that adding a second-line drug at a different time may yield an adequate response with no change in the dose of the first drug, avoiding dose-related adverse reactions.

The 24-hr mean blood pressure profile has been reported to show good correlation with the severity of hypertensive organ damage and to predict the prevention or reversal of hypertensive damage by long-term treatment. Our data indicate that the addition of chronotherapy with carvedilol where needed may also help to prevent or reverse hypertensive organ damage by improved management of the 24-hr mean blood pressure. However, further studies are needed to evaluate the long-term efficacy of chronotherapy with carvedilol in a larger patient population showing a morning surge after first-line therapy with morning drug administration.

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Recent Trend for Integrated Management of Childhood Illness

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Abstract

The health problems of the children who will lead the next generation are a matter of global importance. In the Western Pacific Region alone, as many as 3,000 children die every day. The causes of these deaths are mostly preventable or easily treated illnesses. UNICEF and WHO have long since established preventative measures against every illness, and have eradicated or brought under control diseases like smallpox and polio. Subsequently, under the slogan "Health for All by the Year 2000", a general primary health care initiative known as the Primary Health Care Program was developed, and the UN set the Millennium Development Goals, the fourth of which was to reduce the 1990 mortality rate among children under five by at least two thirds by 2015. Integrated Management of Childhood Illness is an integrated strategy designed to secure child health, and it is expected to produce results.

Key words Primary health care, Integrated management of childhood illness, Child health, Safe motherhood, Child survival, Millennium development goals

Introduction

In Japan, the total fertility rate is falling year after year, and, according to a recent report, stood at 1.29. As a result of the progress of medical care and improvement in sanitary environments, life expectancy is also growing longer every year, and Japan boasts the longest life expectancy in the world. The socioeconomic consequences of a society with a falling birth rate and aging population are, therefore, seen as a problem, and measures are being taken to address this problem.

On the other hand, other parts of the world, particularly Asia and Africa, which account for the majority of the world population, have a high fertility rate and a high mortality rate, and due to economic factors and political factors the gap between regions is growing wider and wider. The health of the children who will lead the next generation serves as an indicator of the welfare and development of a particular country, and

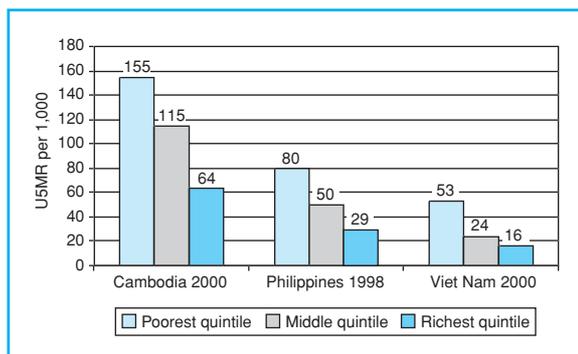
UNICEF has made the Under-5 mortality rate (U5MR) an indicator of the degree of development of a country's health situation. Improvement of U5MR is also stated as the fourth goal (MDG 4) of the UN Millennium Development Goals, and securing child health has become a matter of global importance.

Meanwhile, in November 1989 the UN adopted the Convention on the Rights of the Child, and proclaimed the Declaration of the Rights of the Child, saying that the health of a child must be secured not as something passive safeguarded by the state, but as the basic right of a child. To this end the global strategy of Integrated Management of Childhood Illness (IMCI) has been adopted since 1997.

Income Disparities, Regional Disparities and Health Disparities

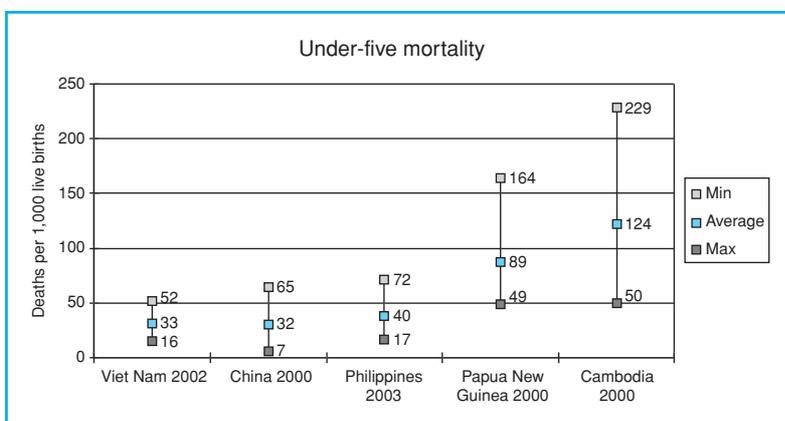
Health problems are inversely proportional to the economic conditions of a particular country,

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(UNICEF/WHO, 2005)

Fig. 1 Disparities in U5MR by difference in income



(UNICEF/WHO, 2005)

Fig. 2 Regional disparities in U5MR

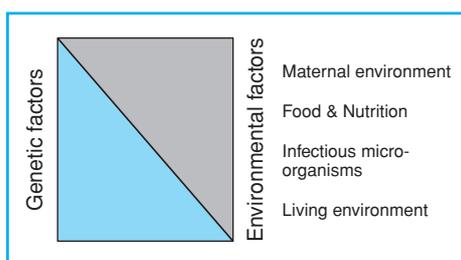


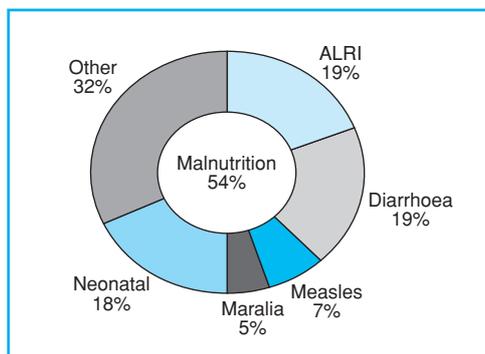
Fig. 3 Onset of illness

and are greatly influenced by the political situation and degree of priority given to health policy in a country. This is something that can also be said in the context of one country, and, as shown in Fig. 1, for example, if we compare the U5MRs by income of Cambodia, the Philippines and Vietnam, we see that the lower the income bracket children are in, the higher the mortality rate, and in the high income bracket, even Cambodia registers a figure of 64 per 1,000 births,

which puts it among the middle-ranking countries. This is a reflection of the fact that a difference in food & nutrition and living environment, and income disparities in terms of usage of primary health care facilities affect the mortality rate of children.

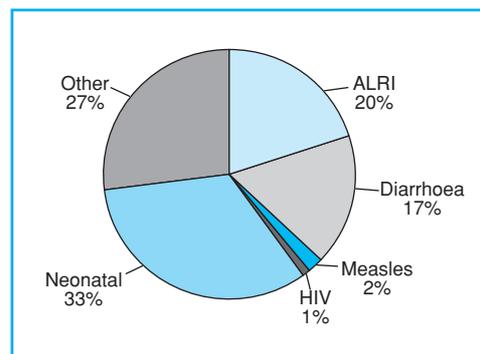
Similarly regional differences in a country are also a factor affecting the mortality rate (See Fig. 2). This is attributable not only to the fact that differences in living environment and differences in living habits between towns & cities and farming villages & mountain villages have an effect, but also to the fact that people cannot use primary health care facilities because they are inaccessible.

As shown in Fig. 3, the onset of illness is determined through an interaction of genetic factors and environmental factors, and among environmental factors, for children, the maternal environment at the fetal stage, food & nutrition nota-



(WHO, 1997)

Fig. 4 Causes of infant deaths



(UNICEF/WHO, 2005)

Fig. 5 Cause-specific proportional mortality —WPR high mortality countries (2000–2003)—

bly breast milk at the infant stage and a sanitary living environment are particularly decisive factors. Everything to do with the mother, including the mother's state of nutrition, perinatal infections, her lifestyle and her work affect the growth & development of the fetus via the placenta, umbilical cord and amniotic fluid. In other words, the prevention of illness and promotion of health in children will not be resolved simply by biomedical prevention or the improvement of medical technology, and it is clearly important to improve the living environment and improve the primary health care environment.

Causes of Infant Deaths (See Figs. 4 and 5)

The causes of deaths in children worldwide have begun to change in recent years. Figure 4 shows data released by WHO in 1997. Diarrhea, acute respiratory infection (ARI), measles and malaria account for 50%. In other words, half of infant deaths were caused by infectious diseases. On the other hand, perinatal disorders accounted for only 18% of the causes of infant deaths, but, according to 2003 statistics, this has risen to 33%. One factor behind this rise is an increase in records due to the fact that, led by UNICEF and WHO, safe motherhood programs and child survival programs in cooperation with the ODA and NGOs have increased and as a result institutional deliveries as opposed to home deliveries have increased. However, another factor is a reduction in the number of deaths resulting from vaccine preventable infectious diseases like measles, whooping cough and tetanus owing to the effectiveness of the expanded program for immu-

nization (EPI). There is also a tendency for an increase in deaths caused by HIV/AIDS and accidental death.

Global Strategy for Infant Health

(1) Control strategies by illness

WHO and UNICEF have long since established preventative measures against single illnesses, developed and trained experts in such illnesses, and produced results. Smallpox, polio, TB and the expanded program for immunization are good examples of this. Smallpox has been successfully eradicated worldwide, and polio has been declared eradicated in North & South America and the Western Pacific Region. However, TB, Malaria and in recent years HIV/AIDS are still far from being under control let alone eradicated, and every country is struggling with their prevention. Particularly in relation to illnesses where there is an established method of control by vaccination, thorough going implementation of vaccination holds the key. However, in developing countries there are many problems such as the storage and quality control of vaccines, the transportation of vaccines to regional public health centers, the training of vaccinators and the enhancement of people's awareness about sanitation, and it is no easy task.

(2) Primary Health Care (PHC)

It is a long time since the Alma-Ata declaration on primary health care was proclaimed in 1978. This clearly stated that it is difficult to solve health problems simply through improvement of medical care and public health, and comprehen-

Table 1 Country groups for implementing child survival actions (EAPRO/UNICEF, WPRO/WHO, 2005)

Group	Countries	Interventions (interventions in bold indicate strategic priorities)
1	Cambodia, Kiribati, Marshall Islands, Lao PDR, Papua New Guinea, Solomon Islands, Vanuatu	<ul style="list-style-type: none"> • Essential package for child survival • Deworming of children 6–59 months and pregnant women
2	China, Fiji, Micronesia, Mongolia, Nauru, Philippines, Samoa, Tonga, Tuvalu, Viet Nam	<ul style="list-style-type: none"> • Essential package for child survival with geographic targeting in underserved areas • Improvement in comprehensive perinatal and neonatal care • Promotion of childhood safety • Introduction of new or underused vaccines: rotavirus, conjugate pneumococcal vaccine, haemophilus influenzae type B, hepatitis B
3	American Samoa, Australia, Brunei Darussalam, Cook Islands, French Polynesia, Guam, Japan, Korea, Republic of Malaysia, New Caledonia, New Zealand, Niue, Northern Mariana Is., Palau, Republic of Singapore, Tokelau, Wallis and Futuna	<ul style="list-style-type: none"> • Essential package for child survival with targeting of the socio-economically under-privileged and marginalised • Emphasis on institutional deliveries with comprehensive newborn care • Promotion of childhood safety • Introduction of new or underused vaccines: rotavirus, conjugate pneumococcal vaccine, haemophilus influenzae type B, hepatitis B

sive measures including political, economic and social measures are necessary. The declaration was triggered by the fact that particularly in developing countries health problems had not been resolved simply through the introduction of modern medicine, while in industrially advanced nations sophisticated state-of-the-art medical technologies and industrial technologies had not only promoted people's physical and mental health, but, conversely, had also brought about an increasing deterioration in the living environment and increasing health threats. In this context, with the global common goal of "Health for All by the Year 2000", the declaration is a theory to promote health incorporating components such as appropriate technologies & methods that are not only medically justified but also socially valid, the development & utilization of regional human resources and resources, resident's needs & equity, and cooperation with other fields. Therefore, there have been diverse programs for the practice of PHC covering education about public health and sanitation, safe drinking water supply and improvement of basic sanitation, improvement of food and nutrition, maternal and child health, family planning, vaccination and prevention of infectious diseases, and essential drugs, and each program has produced its own results.

(3) Integrated Management of Childhood Illness (IMCI)

In view of MDG4 (reduction of the 1990 infant mortality rate by at least two thirds by 2015), which came after the Year 2000 goal, when establishing the next strategy for PHC, WHO and UNICEF reevaluated the public health care indicator data to date and investigated the illnesses and health problems of children worldwide. Based on their findings, for example, that food & nutrition problems, living habits and living environments are related not only to the development of children but also to the onset and exacerbation of virtually all illnesses, and that quality control, storage and distribution systems of essential drugs, access to public health facilities, national/regional priority issues and budget allocation require close cooperation to implement, integrated management (IMCI) with effective utilization of limited human resources and resources for diagnosis, treatment and prevention to secure children's health was proposed and deployed worldwide. This comprises clinical IMCI, which consists of checklists and flow charts that allow diagnosis and treatment guidelines to be put together easily on a first line level as well as the appropriate distribution of essential drugs, and community IMCI, which includes the creation of a referral system for transferring serious cases

Table 2 Essential package for child survival (EAPRO/UNICEF, WPRO/WHO, 2005)

1. Skilled attendance during pregnancy, childbirth and the immediate postpartum period with essential newborn care and care of the sick newborn
2. Exclusive breastfeeding for six months, and adequate and safe complementary feeding from six months onwards with continued breastfeeding and micronutrient supplementation
3. Vaccination against vaccine preventable diseases
4. Case management of pneumonia
5. Case management of diarrhea
6. Use of insecticide treated bed nets and prompt treatment of malaria where indicated
7. Prevention of mother-to-child transmission of HIV

to secondary facilities, a patient follow-up and advisory system in the community, food & nutrition guidance, health promotion, expansion of vaccinations and sanitation education programs.

However, since IMCI itself is a strategy and not a specific program, some countries and regions where guidance was not specific enough lagged behind. Also some countries that are not economically wealthy were unable to develop effective programs due to budget restrictions. As a result, many countries have emerged that have no prospect of attaining MDG4 by 2015. These are disparities in U5MRs resulting from the regional differences and income gap described earlier, and revision of the IMCI strategy itself from the perspective of equity is now necessary.

In May 2005 UNICEF and WHO divided countries and regions into three groups based on factors such as U5MR, infant mortality rate, maternal mortality rate, causes of infant deaths and GNP (See Table 1) and discussed the strategy of incorporating into the primary health care interventions program a means of selecting the essential package plus an optional program according to the situation. As shown in Table 2, the essential package consists of the importance of perinatal particularly neonatal care, complementary feeding and micronutrient supplementation following exclusive breastfeeding, expansion of the six basic vaccinations, case management including follow-up guidance for ARI and diarrhea, malaria prevention and prevention of mother-to-child transmission of HIV. Options include deworming as an intervention from the perspective of nutrition, promotion of childhood safety, vaccinations for illnesses such as rotavirus, conjugate pneumococcal vaccine, haemophilus influenzae type 1b and hepatitis B, and the improvement of neonatal care facilities. These

IMCI revisions have recently been announced and will be put into practice.

To produce results, it is important to properly understand the strategy and to put together specific programs. Cost effectiveness is also important, and IMCI requires not only cooperation between departments within health ministries such as the Child Health Division, Nutrition Division and Drug Delivery Division, but also cooperation with other fields like education, agriculture and fisheries and industrial distribution is also necessary. Monitoring and follow-up as part of case management also requires cooperation with NGOs. Nepal's TB and Lung Health Project applied the DOTS strategy for TB and, to prevent children's ARI on a local level, third-day follow-up by female community health volunteers and on-the-spot advice and guidance using check lists and flow charts were provided. The outcome was a treatment rate for influenza of 87.3%. Integrated programs in collaboration with other fields in each region are what IMCI needs.

Conclusion

Children are a country's riches. However, it is important that an environment allowing children to access and choose health care equally be created by countries and regions not from the perspective of protecting children and safeguarding their health, but as their basic right. The governing power of a particular country, the prioritization of medical policies, budget allocation and the leadership of health ministries are key factors, but it is necessary for international organizations and each country to effectively bring out their respective strengths and cooperate in promoting the health of children.

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The Life-Threat of Everyday Disasters to Children in Japan and the Need for Safety Promotion as a Public Health Policy

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Abstract

According to comparative research on the injury to children in 26 OECD countries conducted by the UNICEF Innocenti Research Centre, Japan is ranked 12th among the 26 countries in the lowness of child-injury mortality rate (ages from 1 to 14), and Japan is ranked 18th when only ages 1 to 4 years are considered. This is a serious situation for Japan.

Although we tend to focus on major disasters in discussing disasters, the lives of children in Japan are threatened by injury from everyday disasters such as traffic accidents. This article compares the situation of child-injury death in Japan with that in Sweden, where the child-injury death rate is the lowest in the world. By reviewing the death rates associated with various causes of injury, we show that childhood mortality rates due to pedestrian injury, pedal cyclist injury, falling, choking on food or nonfood materials, accidental drowning, and interpersonal violence are higher in Japan than in Sweden, and clarify how the lives of children in Japan are threatened by everyday disasters.

Next, we explain how the low child-injury mortality rate in Sweden is supported by implementing safety promotion as a public health policy, and emphasize the need to introduce safety promotion and a national program to protect Japanese children from everyday disasters.

Key words Child-injury, Disaster, Safety promotion, WHO, Japan, Sweden

Introduction

Recently in Japan, a significant number of individuals and organizations are concerned about developments threatening the safety of children, such as child abuse by parents, abduction of children by strangers, and assault in schools, and proactive measures are being taken to correct this situation. Measures against earthquakes and other natural disasters are also implemented in an organized manner, covering children as well as other members of society. However, it should be emphasized that the lives of children are threatened not only by crime, major disasters,

and diseases, but also by injury from everyday disasters such as traffic accidents. Injury from everyday disasters, except those resulting from domestic accidents, has not been regarded as a health care problem, and such injury has not been addressed with sufficient prevention efforts in Japan.¹

According to comparative research on the injury of children in 26 OECD countries conducted by the UNICEF Innocenti Research Centre,² Japan is ranked 12th among the 26 countries in the lowness of child-injury mortality rate (ages 1 to 14), and Japan is ranked 18th when only ages 1 to 4 years are considered. This is a serious situation for Japan. On the other hand,

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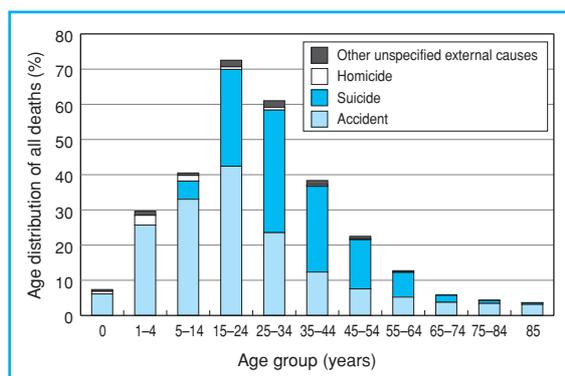


Fig. 1-M Percentage of injury deaths to all deaths in age groups, Males (1999–2001)

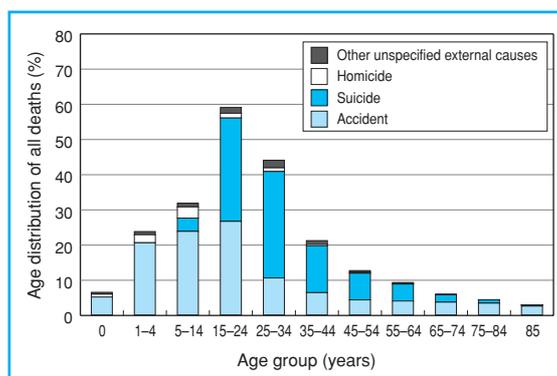


Fig. 1-F Percentage of injury deaths to all deaths in age groups, Females (1999–2001)

Sweden records the lowest child-injury mortality rate among the 26 countries.²

This article examines the situation of child-injury death in Japan compared with that in Sweden, where the child-injury death rate is the lowest in the world. By reviewing the death rates associated with various causes of injury, we clarify how the lives of children in Japan are threatened by everyday disasters. Next, we explain the safety promotion program^{3,4} that is implemented in Sweden as a public health approach to prevent accidents, interpersonal violence, and self-inflicted violence, which supports the low child-injury death rate in the country. Finally, we emphasize the need to introduce safety promotion and a national program to protect Japanese children from everyday disasters.

Japanese-Swedish Comparison of Child-Injury Mortality from Various Causes

Before making a Japanese-Swedish comparison, we look into the ratio of death from injury to death from all causes in Japan by sex and age. Figures 1-M and 1-F show the data from vital statistics (1999–2001) compiled according to major categories in the “manner of death,” such as accident, suicide, homicide, other and undetermined external causes, etc. For either sex, death from all injury and death from accidents present high peaks in the 15–24 age bracket, and decrease with age thereafter. Death from suicide shows a peak in the 15–34 age bracket both for males and for females. While homicide (interpersonal violence) represents only a small percentage of all

deaths, it tends to be higher in children aged from 1 to 14 than in other age groups. While males tend to show a higher rate of death from injury than females, no notable sex-related difference is seen in terms of injury type and peak pattern.

Next, we compared the mortality rates from various injuries among children in Japan and Sweden, using vital statistics (1999–2001) in these countries. Considering the relatively small population of Sweden (approx. 9 million), we pooled the data for population and mortality by sex and age over the period from 1999 to 2001 to avoid the effect of random variation on the numerical stability of analysis, and then calculated the mortality rate by sex and age for all types of injury. Only the injury types showing remarkable international differences among children (ages 0 to 14 throughout this study) are reported here (Figs. 2 through 7). The classification of injury was made according to the International Classification of Diseases 10th Revision (ICD-10) Chapter XX, “External Causes of Morbidity and Mortality” (Table 1).

The mortality rate from pedestrian injury in the 0–9 age bracket is remarkably higher in Japan than in Sweden both for males and for females. In the 10–14 age bracket, it shows little international difference for males and an excess in Sweden for females (Figs. 2-M and 2-F). Pedal cyclist injury shows higher rates in Japan than in Sweden in the 0–14 age bracket for males and in the 5–14 age bracket for females (Figs. 3-M and 3-F). The remarkable excess of death from pedestrian injury and pedal cyclist injury among children in Japan compared with Sweden may reflect the difference in measures for traffic accident

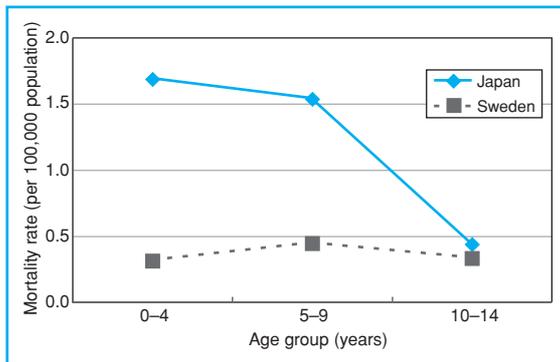


Fig. 2-M Japanese-Swedish comparison of pedestrian injury in children, Males

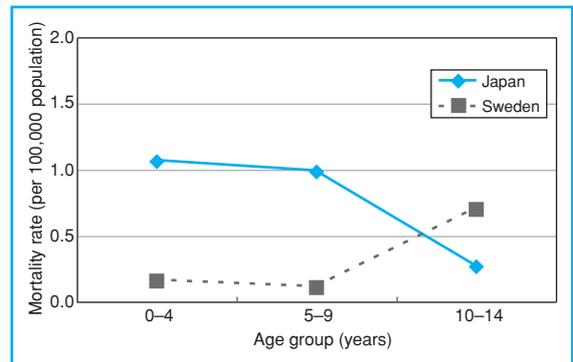


Fig. 2-F Japanese-Swedish comparison of pedestrian injury in children, Females

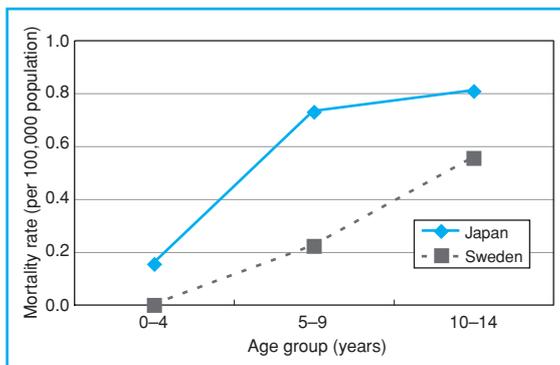


Fig. 3-M Japanese-Swedish comparison of pedal cyclist injury in children, Males

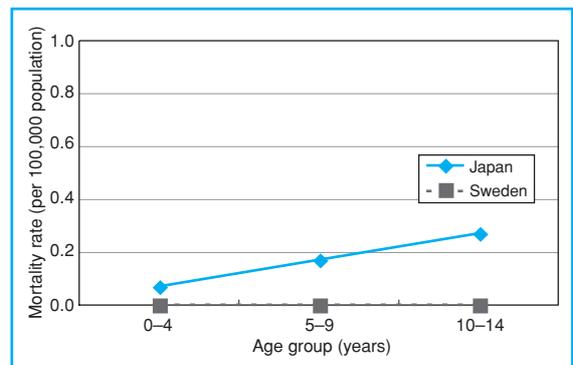


Fig. 3-F Japanese-Swedish comparison of pedal cyclist injury in children, Females

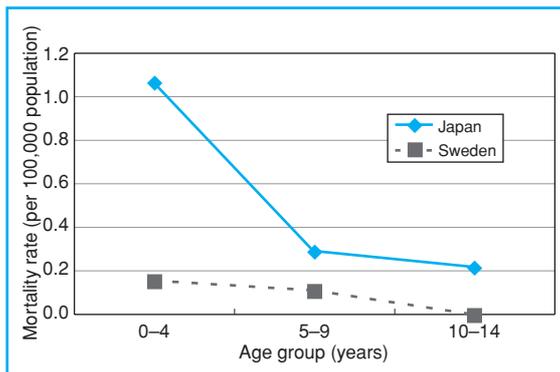


Fig. 4-M Japanese-Swedish comparison of fall injury in children, Males

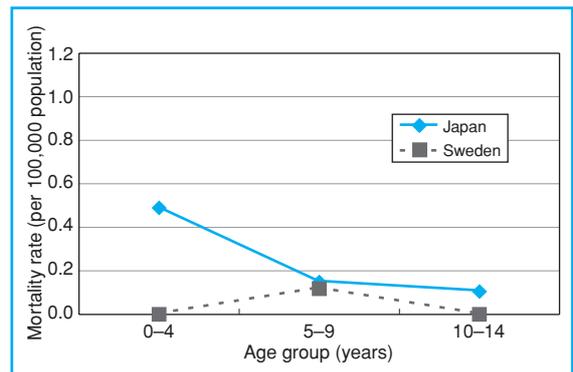


Fig. 4-F Japanese-Swedish comparison of fall injury in children, Females

prevention in these countries.⁵

The mortality rate from injury due to falling is higher in Japan than in Sweden in all groups except for females aged 5–9 years (Figs. 4-M and

4-F). Although the reason for this difference is not clear, a factor may be the widespread use of safety devices to prevent falling down stairs and other hazards in Swedish households.

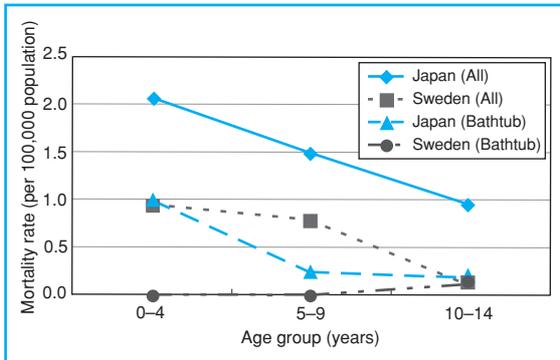


Fig. 5-M Japanese-Swedish comparison of all drowning and drowning in bathtub in children, Males

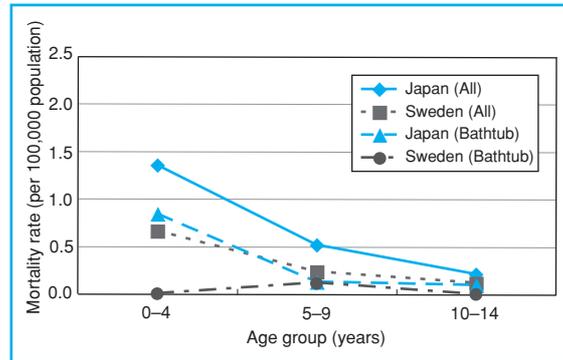


Fig. 5-F Japanese-Swedish comparison of all drowning and drowning in bathtub in children, Females

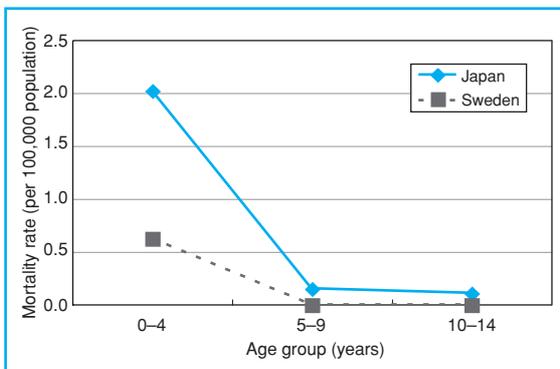


Fig. 6-M Japanese-Swedish comparison of choking in children, Males

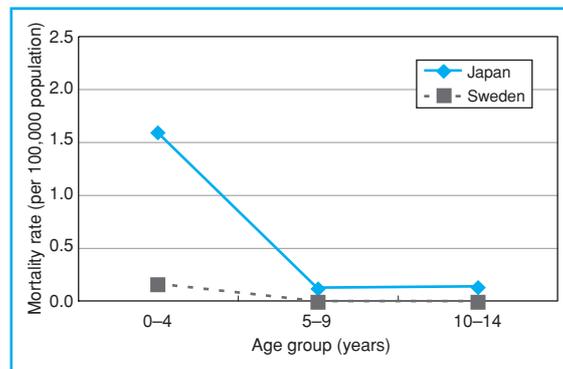


Fig. 6-F Japanese-Swedish comparison of choking in children, Females

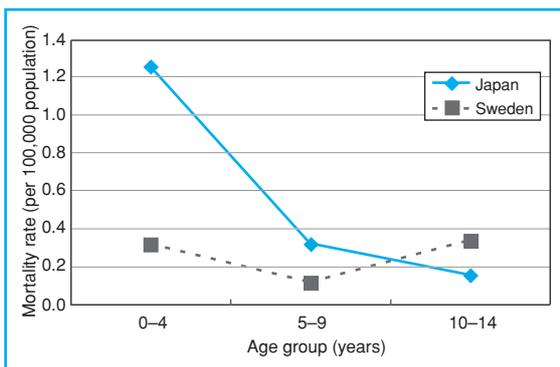


Fig. 7-M Japanese-Swedish comparison of homicide (interpersonal violence) in children, Males

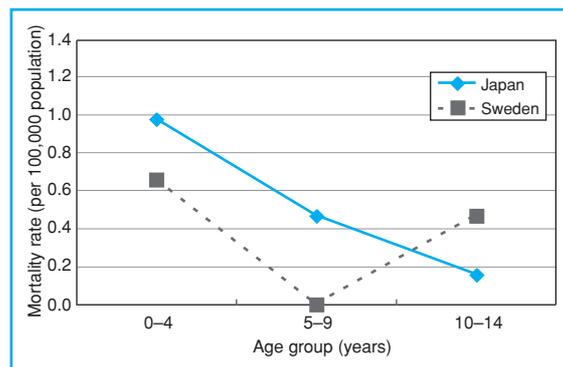


Fig. 7-F Japanese-Swedish comparison of homicide (interpersonal violence) in children, Females

Accidental drowning shows higher rates in Japan than in Sweden for males and females of all ages. Among the causes of accidental drowning, drowning in the bathtub is very rare in Swe-

den, while it is considerably common in Japan. For both males and females, most of the difference in the incidence of accidental drowning in the 0-4 age bracket is explained by the difference

Table 1 External causes of injury and corresponding ICD-10 (International Classification of Diseases 10th revision) codes

External causes of injury	ICD-10 codes
All injury	V01–Y98
Unintentional injury = All accidents	V01–X59, Y40–Y86, Y88, Y89
Land traffic accident	V01–V89, Y85.0
Pedestrian	V01–V09
Pedal cyclist	V10–V19
Motorcycle rider	V20–V29
Car occupant	V40–V49
Accidental poisoning	X40–X49
Fall	W00–W19
Exposure to fire	X00–X09
Accidental drowning	W65–W74
Drowning in bathtub	W65–W66
Other accidental suffocation	W75–W84
Choking on food or nonfood	W78–W80
Intentional injury	X60–Y09, Y35–Y36
Self harm	X60–X84
Interpersonal violence	X85–Y09
Other and undetermined injury	Y10–Y36, Y87

in the incidence of drowning in the bathtub (Figs. 5-M and 5-F). The excess of drowning in the bathtub among Japanese children may reflect the difference in the frequency of bathing, the difference between the deep Japanese and the shallow Swedish bathtub designs, and the practice of keeping water in the bathtub for later use for washing clothes.¹

The mortality rate from choking on food or nonfood materials at ages from 0 to 4 is higher in Japan than in Sweden both for males and for females (Figs. 6-M and 6-F). It has been pointed out that the high rate of choking in children may be attributable partly to the Japanese custom of living on *tatami* mats involving the presence of items that may cause choking within the reach of infants. The difference between Japan and Sweden confirmed in this study supports this remark.⁶

The mortality rate from interpersonal violence (homicide) is higher in Japan than in Sweden for males aged 0–4 and for females aged 0–9 (Figs. 7-M and 7-F). The high childhood mortality rate from interpersonal violence in Japan may be a result of the lack of systematic efforts to prevent child abuse until recent years in Japan,

in contrast to the proactive measures taken in Sweden, including the enactment of a law prohibiting corporal punishment by guardians (1979).⁷ Another factor that may be reflected in the difference is the occurrence of homicide in the form of so-called murder-suicide, which is very low in Sweden and considerably high in Japan.

The large Japanese-Swedish differences in pedestrian injury, pedal cyclist injury, car occupant injury, choking, and interpersonal violence in the 0–4 age bracket seems to correspond to the fact that Japan was ranked 18th among 26 countries in the international comparison of child-injury mortality rate conducted by the UNICEF Innocenti Research Centre in 26 industrialized OECD countries.

From an epidemiological point of view, death as the result of injury may not be evaluated sufficiently based on per-population mortality rates alone, and consideration of the exposure to injury risks is required. Although it is difficult to calculate exposure to risks regarding all types of injury, indices associated with exposure to risks are available in the case of traffic injuries, such as the number of registered automobiles, the total elongation of roads, and the number of persons

with a driving license. We should perform analysis using such indices in the future. However, the data discussed above clearly show the fact that the lives of children in Japan are threatened by everyday disasters more seriously than those in Sweden, and there is an urgent need for measures to protect children from these threats.

Why Does Sweden Record the World's Lowest Child-Injury Mortality Rate? —Safety Promotion as a Public Health Policy Supporting This Situation

It is not by good luck that Sweden maintains the world's lowest child-injury mortality rate. In the background, there are not only the renowned social security system and programs supporting child rearing, but also a public health policy called safety promotion.³⁻⁵

Here, we briefly describe safety promotion, which emerged in Sweden about 30 years ago and spread all over the world to become a part of the policies of the WHO headquarters.^{3,4} Safety promotion is a public health policy intended to prevent injury from accidents, self-inflicted violence, interpersonal violence, etc. and the associated threat to security and safety from a public health approach.^{3,4}

The core element of this approach is community safety promotion (CSP) based on regional communities. CSP was first developed in Falköping, a local city in Sweden, in the latter half of the 1970s. It was implemented following the steps of (1) forming networks transcending the boundaries of departments and professions under the lead of the health care sector, (2) constructing an injury surveillance system using patient information from medical institutions, (3) preparing a sketch map of injuries in the community, (4) developing a comprehensive preventive intervention program addressing various injuries in each age group, (5) implementing this program, (6) conducting scientific evaluation of the results using surveillance, and (7) providing feedback to improve the program. This program achieved such a remarkable outcome that traffic injury, injury from industrial accidents, and injury from domestic accidents decreased by 28%, 28%, and 27%, respectively, over a period of 2 and a half years.⁸

The principles of the Ottawa Charter for Health Promotion in 1986 served as the spring-

board for safety promotion to spread to the world. The First World Conference on Accident and Injury Prevention held in Stockholm in 1989 adopted the Manifesto for Safe Communities, stating, "All human beings have an equal right to health and safety." To this end, the Manifesto called for measures to reduce accidents and injuries without social discrimination and emphasized that a safe community program is the key to this goal.⁹ Put briefly, the safe community mentioned here refers to the development of a community ensuring safe and carefree living across the area using CSP in the same manner as the aforementioned efforts in Falköping City. In the same year, 1989, the WHO Collaboration Centre on Community Safety Promotion (abbreviated to the WHO Collaboration Centre in this paper) was established in the Karolinska Institute, Sweden. Under the lead of this Centre, a movement to develop safe communities based on CSP was promoted all over the world.⁹

In the meantime, the WHO headquarters has highlighted the prevention of injuries, including traffic injuries, as one of the most important public health problems in the 21st century.¹⁰ It established an independent department called the Department of Injuries and Violence Prevention, which has been operating incorporating safety promotion in its policies.¹¹ Publishing the World Report on Road Traffic Injury Prevention, the WHO headquarters has been promoting a worldwide campaign for traffic injury prevention and selected "road safety" as the theme of World Health Day 2004.¹²

The effectiveness of WHO safe community in injury prevention was evaluated by the Cochrane Collaboration. This organization systematically reviewed programs implemented in areas designated as safe communities by the WHO Collaboration Centre. Although they remarked that the accumulation of data was not sufficient for meta-analysis and the effectiveness in developing countries was unknown, they concluded that the effectiveness was supported by evidence in 2004.¹³ This fact is considered to demonstrate the scientific effectiveness of the CSP model as a means of preventing injury. Safety promotion has gained not only practical but also scientific evaluation.

In the background of the world's lowest child-injury mortality rate in Sweden, there are national programs employing safety promotion as a public health policy.¹⁴

Situation of Japan Concerning the Prevention of Childhood Injury from Everyday Disasters and the Need for Safety Promotion

Let us look back to the situation of Japan. Because Japan is a country with many natural disasters, including earthquakes, typhoons, and other storm and flood disasters, there are disaster control programs against natural disasters established at national and local level, and we can expect systematic responses of the relevant organizations to be ensured to a reasonable extent. (However, the aspect of natural disasters as a public health problem is not always recognized, and the systematic involvement of the health care sector in disaster response is not sufficient.) Japan also has an internationally recognized high level of engineering and technological approaches to safety in preventing damage from natural disasters. (For example, Japan is at the leading edge of the world's research on the alarm system against *tsunami*.)

On the other hand, how are traffic accidents and other everyday disasters addressed in Japan? As mentioned above, the WHO headquarters has positioned the prevention of injuries from everyday disasters including traffic injuries as one of the most important public health problems in the 21st century. However, the recognition of traffic injury as a public health problem is not sufficient in Japan. The national movement toward better

public health in the 21st century, entitled "Kenkou Nippon 21" and formulated in 2000, does not include prevention of injury from accidents as a main theme, in contrast to the Healthy People 2010 in the U.S. incorporating injury and violence as major themes.¹⁵ In another program called "Sukoyaka Oyako 21," sort of a child version of Kenkou Nippon 21, a goal has been set to reduce the childhood death rate from accidents by half,¹⁶ but this program does not specify concrete target figures that can be used in prefectural and municipal efforts, and "Sukoyaka Oyako 21" has not been fully utilized for community-level prevention of accidents and injury. In addition, there are no national-level policies or programs based on necessary interagency cooperation (including not only the Ministry of Health, Labour and Welfare and the Ministry of Education, Culture, Sports, Science and Technology, but also the National Police Agency and the Ministry of Land Infrastructure and Transport) for promoting comprehensive measures to prevent childhood injuries from everyday accidents.

The authors propose that the public health policies of Japan should promptly incorporate safety promotion, which originated in Sweden, has later developed all over the world, has been incorporated in the public health policies of the WHO headquarters, and has been demonstrated as effective by the Cochrane Collaboration. On this basis, a national program to prevent the death of children from everyday disasters should be formulated.

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Menstruation-related Syndrome: Clinical relations and treatment

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Abstract

Mental and physical conditions associated with the menstrual cycle are often left untreated unless they become severe or are accompanied by psychiatric concomitants, by which time treatment may be ineffective. This paper introduces the pathophysiology and treatment of premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) and offers comments and conclusions based on a discussion of their relation to atypical psychosis. Menstruation-related syndrome (MRS) is a group of diseases in which the menstrual cycle is related to various mental and physical symptoms and influences the clinical course. Although specific abnormalities of gonadal hormones are not apparent, serotonin dysfunction is thought to be present because selective serotonin reuptake inhibitors are effective for premenstrual dysphoric disorder. MRS and atypical psychosis have many similar pathophysiologic and clinical features. I propose a new clinical classification of all menstruation-related conditions which provides a contrast between MRS and atypical psychosis.

Key words Menstruation-related syndrome, Premenstrual syndrome, Premenstrual dysphoric disorder, Atypical psychosis

Introduction

A variety of conditions associated with the menstrual cycle produce mental changes or physical changes or both. Although biological and sociopsychological factors are clearly involved in the pathogenesis of these conditions is unclear, these factors are often discussed separately because of the obscure definitions and concepts associated with them. The concept of menstrual psychosis (also known as cyclic psychosis and considered a type of atypical psychosis) has been used in the field of psychiatry, but different diagnoses have been given to cases with the same pathologic features.

To eliminate confusion, operational diagnoses based on the International Classification of Diseases, 10th revision (ICD-10) or the Diagnostic and Statistical Manual of Mental Disorders,

fourth edition (DSM-IV)¹ have been introduced, but a group of diseases with short, cyclic, morbid phases were eventually excluded because of the difficulties of diagnosis. This exclusion has led to further confusion.

Premenstrual syndrome (PMS), ovulatory disorders, and climacteric syndrome have been investigated on the basis of endocrine function (hypothalamic-pituitary system), age, parity, level of activity, and nutritional status. However, mental or physical symptoms are experienced by many women during the menstrual cycle, they tend to be regarded as common or trivial problems not requiring medical attention and are therefore left untreated.

In contrast, because premenstrual dysphoric disorder (PMDD) is considered a severe condition, diagnostic criteria are provided in DSM-IV and have gradually attracted attention. In addition to PMS/PMDD and menstrual psychosis, a

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Table 1 Diseases in the broad-based category of MRS

1. Perimenarche syndrome
2. Pubertal periodic psychosis
3. Premenstrual tension syndrome (PMS)
4. Premenstrual dysphoric disorder (PMDD)
5. Periodic psychosis (synchronous to menstrual cycles)
6. Puerperal mental disorders
7. Climacteric disorder
8. Ovulation disorders (e.g., those related to the hypothalamus-pituitary system and PCOS)
9. Atypical psychosis (including periodic psychosis)
10. Eating disorder
11. Seasonal affective disorder
12. Others

Table 2 Menstruation-related syndrome from the aspect of based on classification of the atypical psychosis-like disease group

1. Menstruation-related syndrome (MRS) (narrow sense)
1) PMS, PMDD
2) Periodic psychosis (synchronous to menstrual cycles)
3) Puerperal mental disorders
4) Climacteric disorder
5) Others (e.g., PCOS)
2. Atypical psychosis
1) Periodic psychosis
2) Acute transient psychotic disorder
3) Schizoaffective disorder
4) Catchall category
3. Organic mental disorders

variety of psychosomatic medical conditions are associated with menstrual disorders.² Because I do not consider these menstruation-related conditions to be independent clinical entities, I have suggested establishing a separate field of medicine to address menstruation-related conditions by defining, classifying, and specifying the subjects of research.³ For this reason, I have defined menstruation-related syndrome (MRS) as a condition in which menstruation is closely involved in the pathophysiology and symptom formation of these disease entities and results in both mental and physical symptoms. With this definition, I have attempted to clarify the pathology of the various conditions that are related to menstruation and have not yet been fully clarified and to develop treatments for them.

This paper outlines the clinical position and treatment of MRS and compares it with so-called atypical psychosis, which is thought to have similar pathophysiological features.

Clinical Position of MRS

The conditions I have included in MRS are listed in Table 1. Although conditions 9 through 11 are also found in male patients, they are included in this table as reflecting the broad sense of MRS because most patients are women and these symptoms are closely related to menstruation.

If attention is focused on the mental symptoms of these conditions, a clinical picture of atypical psychosis-like disease usually, but not always, emerges. An atypical psychosis-like condition

is characterized by abrupt onset; a complex of disturbances of consciousness and affective and psychomotor disorders; and a periodic, transient course. Clinical symptoms vary widely from reduced alertness and bradykinesia to an abnormal sleep-wakefulness cycle, abnormal eating patterns, depression, impatience, irritability, impulsivity, excitation, hyperkinesia, mania, and hallucination, and paranoia.

Table 2 shows the proposed reclassification of MRS, with attention focused on the mental symptoms and the menstrual cycle. Initially, the overall clinical picture was regarded as fitting the atypical psychosis-like disease group. This classification may require some explanation.

1. MRS in the narrow sense

- 1) PMS and PMDD are the main axes of this syndrome and represent the main topics of this paper. Their symptoms and treatments will be described later.
- 2) Periodic psychosis (synchronous with the menstrual cycle) is characterized by the common features of atypical psychosis-like disease. Periodic psychosis is classified both under MRS in the narrow sense and as a type of atypical psychosis, as described later (section 2). Periodic psychosis is included in both categories because not all cases show synchronicity with the menstrual cycle.
- 3) Mental symptoms in patients with puerperal mental disorders have been cited as typical features of atypical psychosis-like disease.
- 4) Some patients with climacteric disorder exhibit

a clinical picture of atypical psychosis-like disease. This type of disorder may develop after bilateral ovariectomy.

- 5) Other disorders of MRS in the narrow sense include polycystic ovary syndrome (PCOS). Although no symptoms are diagnostic for this PCOS, the clinical picture is occasionally that of an atypical psychosis-like disease. Attention should also be paid to eating disorders and seasonal affective disorders.⁹

2. Atypical psychosis

The concept of atypical psychosis was developed in Japan. Although this condition is not limited to women, female patients outnumber male patients by 7 or 8 to 1, and attention has focused on the co-existence of PMS or endocrine disease. Because of this focus, several neuroendocrinologic studies have been performed and have found vulnerability in the diencephalic-hypothalamic system. This finding explains why atypical psychosis is included MRS when broadly defined (Table 1). However, the symptoms of atypical psychosis-like disease suggest that this condition also occurs in men. Therefore, the diagnosis of atypical psychosis has come to be applied to a wide spectrum of cases. Because atypical psychosis also occurs in men, it cannot be classified solely under the category of MRS. Thus, a separate category that represents the conventional diagnosis of atypical psychosis has been differentiated from narrowly defined MRS.

Atypical psychosis can be subclassified as 1) periodic psychosis (a subgroup closer to MRS); 2) acute transient psychotic disorder, a diagnosis described in DSM-IV and ICD-10, corresponding to atypical psychosis; 3) schizoaffective disorder; and 4) a catchall category (unspecified atypical clinical picture). In fact, the techniques of operational diagnosis are not appropriate for diagnosing a disease group with this clinical picture. For this reason, the conventional diagnosis of atypical psychosis seems to be more suitable and more useful because it is based on symptoms and disease stage.

3. Organic mental disorder

Mental symptoms in patients with symptomatic mental disorders and organic brain damage form the clinical picture of an atypical psychosis-like disease.

The above explanation presents the clinical

picture of MRS from the viewpoint of the clinical picture of atypical psychosis-like disease. Although this classification may be flawed and controversial, a more clinically realistic tool was the goal of this classification, which is based on conventional and operational diagnostic techniques. I intend to review and improve this classification from the perspective of evidence-based medicine.

PMS/PMDD

1. History of the diagnosis of PMS/PMDD

After Frank proposed the concept of PMS in 1931,⁴ the diagnostic criteria for this condition were first presented in the DSM-III-R in 1987 as late luteal phase dysphoric disorder (LLPDD), a mental disorder not otherwise specified. This condition was classified as premenstrual dysphoric disorder (PMDD) in DSM-IV and as PMS in ICD-10 in 1994.

2. Differences between PMS and PMDD

The major symptoms of PMS, which are seen in 50% to 70% of menstruating women, include various types of pain, such as breast pain and lower back pain, and other physical symptoms, such as swelling and weight gain. Mild depression, irritability, and sleep disorder may also occur. PMDD is considered to be a severe type of PMS, present in 2% to 8% of patients with PMS. The symptoms of PMDD include physical symptoms and mood disorders. Characteristic symptoms are marked depression, anxiety, emotional lability, difficulty concentrating, altered eating behavior, sleep disorders (hypersomnia or insomnia), and various types of pain. The most important symptom is tendency for uncontrollable anger (a feeling of being out of control). Like patients with depression, patients with PMDD have behavioral difficulties, both social (including work) and interpersonal.

3. Pathophysiology of PMDD

Despite years of endocrinologic research on PMDD, there is no clear evidence that abnormal hormone regulation plays a role. Schmidt et al. have reported that an abnormal reaction to the normal secretion of gonadal steroid hormones, e.g., hyperreactivity of receptors and neurotransmitters, is responsible for PMDD.⁵ Among the possible mechanisms, abnormality in the

serotonergic nervous system has long been the most likely theory, for the following reasons.

- 1) Serotonin suppresses the major symptoms of PMDD, i.e., irritability, tendency for uncontrollable anger, depression, abnormal appetite (hyperphagia), and sleep disorders (hypersomnia or insomnia).
- 2) Studies of serotonin dysfunction in PMDD have shown decreases in serotonin reuptake by and content of platelets.
- 3) Serotonergic agents are clinically effective. As documented in several case reports and clinical trials, both selective serotonin reuptake inhibitors (SSRIs) and serotonin agonists produce improvements in symptoms which could be blocked by serotonin antagonists.^{6,7}

Thus, serotonin dysfunction triggered by gonadal steroid hormones has been suggested to result in psychological, physical, and behavioral disorders.

4. Treatment of PMDD

The main methods of treatment for PMDD are the inhibition of ovulation and the use of antidepressants (e.g., SSRIs).

(1) Psychotropic drugs

i) Efficacy of antidepressants

Clinical studies have shown that SSRIs (e.g., citalopram, fluoxetine, paroxetine, sertraline, and fluvoxamine) and the tricyclic serotonergic agent clomipramine are significantly more effective than placebo in patients with PMDD. These agents are also more effective than nonserotonergic drugs. These drugs usually act quickly on the predicted disease phase. These agents are effective at low doses for both mental and physical symptoms. Discontinuation of SSRI therapy allows symptoms to return. However, intermittent administration is also effective.

ii) Anxiolytic drugs

Alprazolam and buspirone (5HT_{1A} agonist) are particularly effective for treating irritability.

(2) Ovulation inhibition

Ovulation inhibition, considered the definitive treatment, eliminates an important trigger of PMDD. Various types of ovulation-inhibitors are available: gonadotropin-releasing hormone agonists, such as leuprolide, goserelin, and nafarelin; danazol, a gonadotropin antagonist; and estrogen/progesterone oral contraceptives. However, ovulation-inhibitors can induce climacteric symptoms. Therefore, ovulation inhibition

is indicated only for patients who have severe symptoms that justify this risk. Thus far, however, the results of ovulation inhibition therapy have been mixed, with inconsistent or disappointing outcomes and even the worsening of symptoms.

(3) Other agents

Although the efficacy of SSRIs suggests that the serotonergic agent fenfluramine will also be useful, another effective drug, the dopaminergic agent bromocriptine, promotes, rather than inhibits, ovulation.⁸ Although opposing methods may be effective in regulating ovulation, ovulation inhibition seems to be effective in patients with periodic psychosis and psychopathic symptoms. The fact that fenfluramine and bromocriptine are effective despite opposing actions (ovulation inhibition and promotion, respectively) implies that this group of analogous diseases has a complicated pathophysiology.⁹⁻¹¹ Other agents recently reported to be useful include calcium, vitamin B₆, and Chinese herbal remedies, such as kamishoyosan, tokishakuyakusan, and keishibukuryogan.

(4) Treatments other than drug therapy

Sociopsychological support includes such therapies as cognitive behavioral therapy, group therapy, aerobic exercise, and dietary therapy with a carbohydrate-rich diet. In addition, I have previously reported the efficacy of phototherapy, in which the patient is exposed to bright lights during the luteal phase. If the treatment is done in the follicular phase, ovulation is inhibited.

Conclusion

Conditions with both mental and physical components which occur in association with the menstrual cycle often remain untreated if they are mild. Even if these conditions are severe, treatment may be withheld because they are regarded as a normal part of menstruation. If psychotic features are present, treatment will be started. However, the condition may be resistant to conventional chemotherapy or to ovulation inhibition, which is generally considered a definitive treatment. Unexpectedly, no specific abnormality in gonadal hormones is present.

Atypical psychosis, a concept that grew out of periodic psychosis, came to include cases in men after initial studies of cases in women progressed to include peripheral complaints. As a result, the concept and definition of atypical psychosis

has become increasingly unclear. No specific endocrine abnormalities are apparent in these conditions. However, after the vulnerability of the hypothalamic-pituitary system was discovered,

research on these conditions has decreased. I intend to focus on core cases and study the pathophysiology and treatment of MRS.

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Bile Peritonitis due to Spontaneous Perforation of the Left Hepatic Duct: A case report

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Abstract

This case report concerns a patient with bile peritonitis due to spontaneous perforation of the intrahepatic bile duct. A 67-year-old woman underwent an emergency laparotomy for acute abdomen with a tentative diagnosis of acute cholangitis with a calculus in the common bile duct. Intraoperatively, however, bile peritonitis due to perforation of the peripheral left hepatic duct was found. After cholecystectomy and common bile duct exploration, intraoperative cholangiography was performed, and the perforation site was suture ligated. She was discharged from the surgical service 31 days after surgery with complete recovery.

Key words Bile peritonitis, Spontaneous perforation, Intrahepatic bile duct

Introduction

Spontaneous perforation of the intrahepatic bile duct is an extremely rare event in adults. This rare form of bile peritonitis results in a 30 to 50% mortality in spite of adequate surgical therapy and postoperative intensive care.¹ We report on a patient with bile peritonitis due to spontaneous perforation of the left hepatic duct and review the literature.

Case Report

A 67-year-old female, who had undergone ventriculo-peritoneal shunt operation 3 years previously, complained of abdominal discomfort with nausea and two episodes of nonbilious vomiting. She had neither prior episodes of abdominal pain nor history of trauma. She was initially admitted to the department of internal medicine in our hospital with a clinical diagnosis of entero-

colitis and was given intravenous antibiotics. On the third day of admission, she started to complain of diffuse abdominal pain. She underwent computed tomography (CT) and ultrasonography (US), which was compatible with cholecystitis and choledocholithiasis.

On referral to our surgical service, her vital signs were as follows: body temperature 36.9°C, blood pressure 147/90 mmHg, heart rate 76/min. Physical examination revealed a thin female in severe distress due to abdominal pain. Her bowel sounds were diminished, and diffuse abdominal tenderness was noted with maximum rebound tenderness in the upper abdomen. A knock pain in the right upper quadrant of the abdomen was significant and Murphy's sign was positive. Significant laboratory data were as follows: white blood cell count 15,200/ μ L, hemoglobin 12.9 g/dL, platelets 199,000/ μ L, total bilirubin 2.0 mg/dL, direct bilirubin 1.5 mg/dL, alkaline phosphatase 1,105 units/L, serum amylase 37 units/L. Chest radiograph revealed no free intraperitoneal air

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and no acute pulmonary process. No dilated bowel loops were seen in a flat abdominal film. An upright abdominal film demonstrated a non-specific bowel gas pattern without air-fluid levels in the intestines. The abdominal US showed cholecystitis with a small gallstone and sludge associated with wall thickening of the gallbladder (Fig. 1a). The US also identified the dilated intrahepatic bile duct (Fig. 1b). The CT of the abdomen and pelvis confirmed the gallbladder wall thickening (Fig. 2a). A calculus in the common bile duct and moderate ascites were also noted (Fig. 2b). No free air was identified in accordance with the chest radiograph. The preoperative diag-

nosis was acute abdomen possibly due to gangrenous cholecystitis with a concomitant choledocholithiasis.

At operation, the gallbladder was edematous and severely inflamed, and bilious peritoneal fluid and diffuse fibro-purulent exudates covered the visceral peritoneum. In addition, dark-colored ascites was found in the left subhepatic area and the left subphrenic fossa. We therefore performed full abdominal exploration (Fig. 3a). The left lobe of the liver revealed a minor bile leak emanating from the peripheral biliary tree (Fig. 3b). Cholecystectomy was performed, and an intraoperative cholangiogram through the cystic

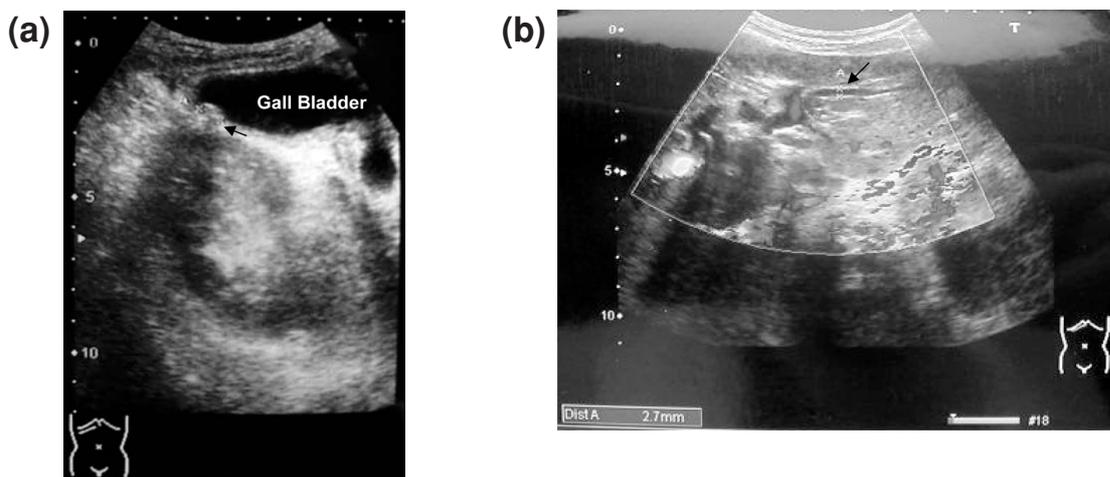


Fig. 1 (a) Ultrasonography showing a small gall stone with an acoustic shadow. The wall thickening of the gall bladder is also observed.
(b) The black arrow indicates a dilated intrahepatic bile duct.

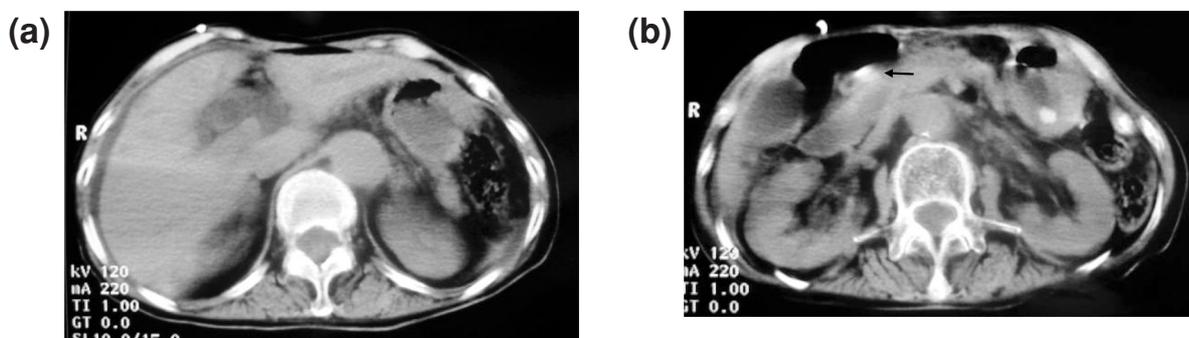


Fig. 2 (a) Computed tomography revealing fluid collection in the right subphrenic fossa.
(b) A stone in the common bile duct (arrow).

duct stump showed the presence of a perforation in the anterior aspect of the lateral segment of the liver indicated by the leakage of the contrast material from the perforation site. The cholangiogram also identified a stone incarcerated in the common bile duct. A 3 mm plastic tube was successfully inserted through the perforated hole, and we confirmed that a perforation occurred at a terminal branch of the left hepatic duct by the tube cholangiography (Fig. 4). The perforation site was suture-obligated with interrupted 4-0 Vicryl, which was followed by choledocholithotomy and T-tube drainage.

The postoperative course was uneventful. No retained stone was found on a T-tube cholangiogram at 3 weeks after surgery, when T-tube was removed. The patient was discharged 31 days after surgery. She was well with regard to the

hepatobiliary system at 6 months postoperatively, and she remains well except for a fracture of the left hip by trauma.

Discussion

Rupture of the hepatic duct in the absence of operative injury or severe trauma is an extremely rare cause of bile peritonitis in adults.^{2,3} Since the first description by Freeland in 1882, 22 cases of spontaneous perforation of the intrahepatic bile duct have been reported in the English literatures.^{2,4-16} McWilliams, in 1912, reviewed 108 cases of bile peritonitis in which hepatic duct perforation accounted for only one case.⁵ Perforation in the hepatic duct was also the rarest cause of bile peritonitis in a review by Nomura et al.¹⁷

Several possible mechanisms have been advocated for spontaneous perforation of the biliary system,³ which include: (a) increased intraductal pressure due to either mechanical blockade by stones or reflex spasm of the sphincter of Oddi, or both; (b) intramural infection which weakens the duct wall and lowers its resistance to intraductal pressure increase; (c) thrombosis of a mural ves-

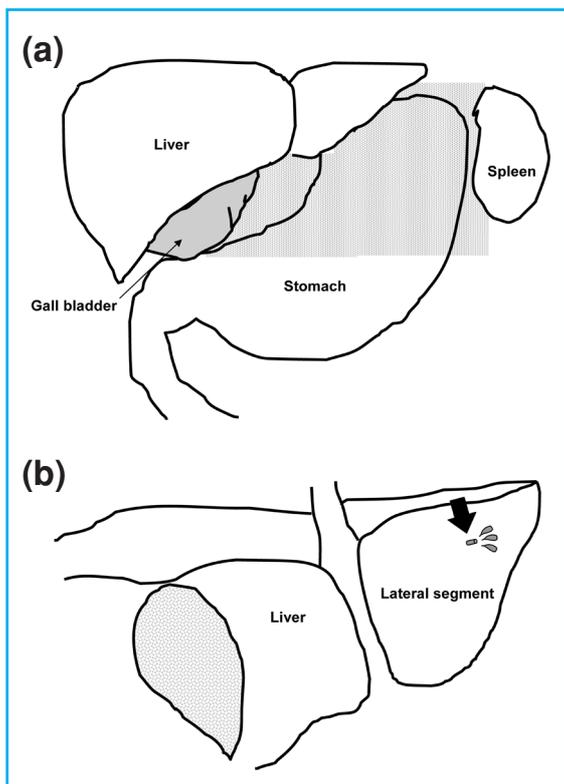


Fig. 3 Schematic representation of intraoperative findings is shown.

- (a) Dark colored bilious peritoneal fluid was observed at shadowed area.
- (b) Bile leak was observed from a perforation site in the anterior aspect of the lateral segment of the liver (arrow).

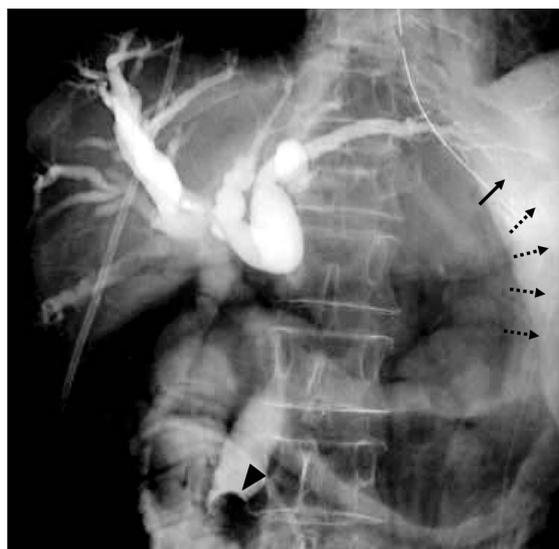


Fig. 4 An intraoperative cholangiography demonstrated a stone in the dilated common bile duct.

Contrast material was infused through a small caliber tube inserted into the bile leakage point (arrow). The dotted arrow indicated the inserted catheter, and the calculus incarcerated in the distal common bile duct is identified (arrow head).

sel leading to necrosis of the affected part of the bile duct wall; (d) reflux pancreatic secretions resulting in autodigestion; (e) diverticulum. In the present case, the putative cause seems to be incarceration of a calculus in the distal common bile duct which increased intraductal pressure and resulted in the perforation of the periphery of the intrahepatic bile duct. Other reasons, such as acute infection, might have contributed to the development of the perforation.

US is a noninvasive and rapid examination which is recommended as a first choice to evaluate abnormalities in the biliary system. CT should also be performed to detect calculi in the common bile duct or abnormal fluid collection. In our case, US showed severe cholecystitis and a mildly dilated intrahepatic bile duct, and CT

revealed cholecystitis and ascites also, which led us to a diagnosis of peritonitis due to severe acute cholangitis and cholecystitis. Retrospectively, we might have been able to suspect bile peritonitis due to perforation in the biliary system based on the findings of dilated intrahepatic bile duct and fluid collection in the abdominal cavity.

In the present case, intraoperative cholangiography was a very useful diagnostic technique to identify the site of perforation. Nobusawa et al. reported the usefulness of intraoperative cholangiography using indigo carmine.⁹ Fortunately, the perforation site in our case could be detected easily by retrograde cholangiography through the perforated hole in an aberrant hepatic duct which is located at the end of the left hepatic triangular ligament.¹⁸

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Medical Disputes and Countermeasures in Japan

JMAJ 48(8): 426–428, 2005

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Key words Medical dispute, Medical malpractice, Professional Medical Liability Insurance Program, Patient safety, Medical liability review board, Medical association

Introduction

The annual number of lawsuit cases related to medical malpractice filed with district courts has been increasing and doubled during the past decade in Japan. The duration of court deliberations for medical malpractice is much longer than general civil lawsuits.

The Japan Medical Association (JMA) created its Professional Medical Liability Insurance Program in 1973 to reduce the economical damages from which the members suffered and stimulate faster resolution of the disputes. Its foremost characteristic or the most fundamental basis is the fact that the program is working under the neutral review board. The JMA also provides the optional Special Clause Insurance that is supplementary and covers the amount in excess of the maximum coverage of the basic scheme.

It is crucial to take immediate action to prevent medical malpractice to avoid facing malpractice crises. The JMA has been also promoting CME activities for its members to support patient safety measures. The JMA has also been analyzing the past cases as part of its efforts to prevent the recurrence of medical malpractice.

The following is the outline of the JMA Professional Medical Liability Insurance Program.

1. Current Medical Lawsuits

Medical errors result in tragic consequences for

both the patient and physician, and the utmost effort should be made to prevent them from occurring. A study by the supreme court on medical malpractice lawsuits in Japan showed that the number of cases has been increasing and doubled in the past decade (Fig. 1).

Considering this growing trend of pending litigations at district courts nationwide, if the number of out-of-court settlements and arbitrations is included, it is thought that malpractice related disputes are becoming frequent and common.

The average duration of court deliberations for medical litigation cases is very long in comparison to deliberations made for ordinary cases (Fig. 2). Thus, the number of pending first malpractice trial cases that remained unresolved in 2002 was 2,063. In reviewing the results of past decisions, although less than half of the decisions were against the physician, there are much more cases that have been decided against the physician if amicable settlements are included.

2. Professional Medical Liability Insurance Program

There are two types of medical liability insurances in Japan—one is the JMA Professional Medical Liability Insurance Program that is managed by the JMA for its members and the other is the general medical liability insurance program that is provided by non-life insurance companies. The liability insurance for individual employed physicians is available through medical specialty

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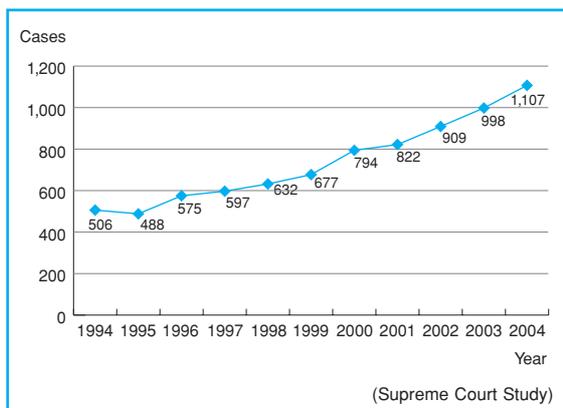


Fig. 1 Transitions in medical malpractice lawsuits, the leading number of new cases nationwide

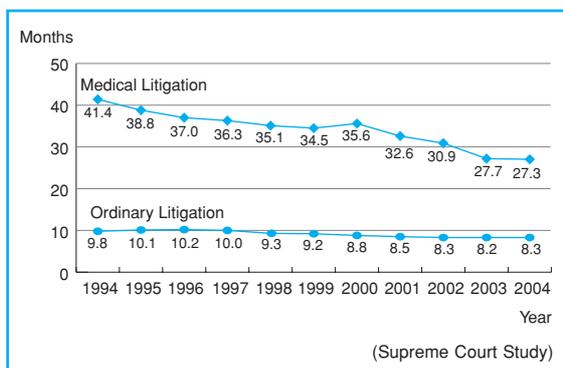


Fig. 2 Average deliberation period for pending first trial ordinary and medical malpractice litigation cases

societies.

The JMA created its Professional Medical Liability Insurance Program in 1973 to cover the economical damages from which the members suffered and make faster resolution of the disputes. It is provided for all JMA Category A Members.* The members are automatically insured by paying the membership fee.

The liability limit guaranteed by this Program per year per insured party is 100 million yen (about US\$950,000) with 1 million yen (about US\$9,500) deductible per medical act. The annual premium for JMA Category A₁ Member who is founder or administrator of medical facility is 70,000 yen (about US\$670) and Category A₂

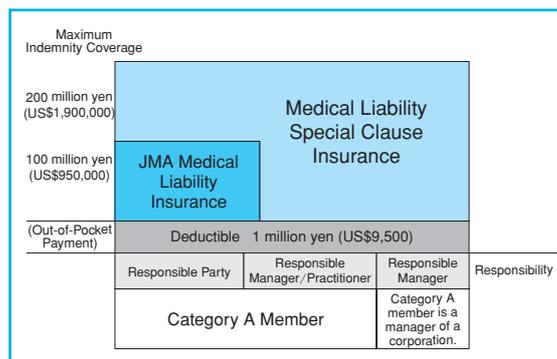


Fig. 3 Relationship between JMA Medical Liability Insurance and the Special Clause Medical Liability Insurance

Member who is employed physician is 55,000 yen (about US\$520).

The JMA also provides the optional Special Clause Insurance. It is supplementary and covers the amount in excess of the maximum coverage of the basic scheme. A special feature of the Special Clause Insurance is that the maximum limit of liability has been increased to 200 million yen (US\$1,900,000) per case. And for the members of Category A₁ as founders and administrators of medical facilities, it will include coverage per facility. If another physician who is not a Category A member is the cause of medical malpractice at that facility, the founder or administrator is covered with this Special Clause (Fig. 3).

3. Medical Liability Review Board

The foremost characteristic or the most fundamental basis of this program is the fact that it is working under the Medical Liability Review Board which is an impartial and neutral third-party institution. The JMA, the prefectural medical associations, and insurance companies coordinate together in dealing with examinations by the Review Board to settle medical malpractice disputes. Medical dispute cases that are covered by the JMA Program support the decisions of the Review Board, which decides the existence of liability, the amount of liability to be paid, and other details.

The JMA, the prefectural medical associa-

* The JMA Category A₁ is a group of its membership who are a founder or administrator of medical facility. The JMA Membership of Category A₂ is a group of employed physicians enrolled in the JMA insurance.

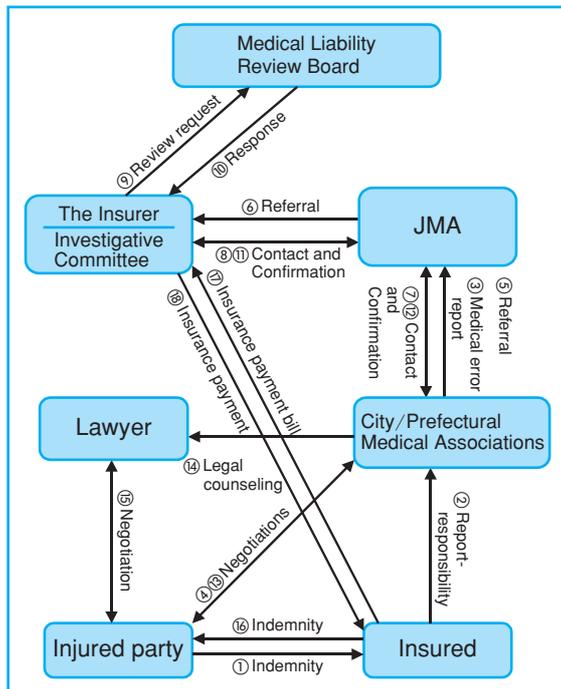


Fig. 4 Flow chart of dispute settlement

tions, and insurance company have cooperated to create a system that allows the JMA Insurance Program to efficiently resolve the medical disputes for its members (Fig. 4).

For example, based on deliberations by all three parties, legal counsel will be sought at the expense of the insurance company or academic review will be made to corroborate the medical position as needed.

The number of malpractice cases referred to the JMA has been increasing. The number of cases examined by the Review Board grew from 1 in 1993 to 1.5 in 2003. Even in the cumulative total of payments alone that was made in the past is in excess. If pending cases where payments will be made in future are projected, the balance in revenue and expenditure is in a severe condition.

The specialty with highest ratio for the total

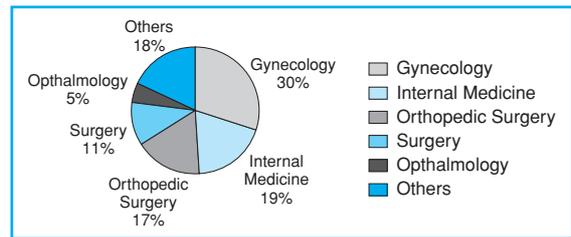


Fig. 5 Ratio of cases according to medical field (cumulative total for the past decade)

number of cases handled by the Review Board over the past decade according to medical specialty is gynecology at 30 percents, followed by internal medicine, orthopedics, and surgery (Fig. 5).

4. Patient Safety

In Japan it is crucial to take immediate action to prevent medical malpractice to avoid facing similar malpractice crises. The JMA set up the Medical Safety Policy Committee in 1997. Through this committee, the JMA has supported its members in the patient safety activities and has been engaged in further CME activities together with continuous efforts to enhance member awareness of medical ethics. It will be starting the reeducation program in 2005 for JMA members who repeat medical malpractices.

To prevent medical malpractice from occurring, past cases will be analyzed and the findings will be used in recurrence prevention measures. In addition to analyzing data from JMA Professional Medical Liability Insurance, other data will be collected from the local medical associations and a nationwide survey will also be in the future plan.

The JMA has also set up a project committee which is responsible to study the compensation system for the disabilities stemming from medical care including non-fault compensation.

Guidelines on Genetic Testing

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Yoshimitsu Fukushima*^{1,2}

Key words Genetic test, Genetic counseling, Medical genetics, Clinical geneticist, Certified genetic counselor

Introduction

Because human genetic data is so markedly different from any other kind of human data, guidelines have to be established and observed. The International Declaration on Human Genetic Data¹ adopted by UNESCO (United Nations Educational, Scientific and Cultural Organization) in 2003 states that human genetic data should be given a special status because:

- 1) they can be predictive of genetic predispositions concerning individuals;
- 2) they may have a significant impact on the family, including offspring, extending over generations, and in some instances on the whole group to which the person concerned belongs;
- 3) they may contain information the significance of which is not necessarily known at the time of collection of biological samples; and
- 4) they may have cultural significance for persons or groups.

The declaration states, therefore, that human genetic data should be used only for purposes such as 1) health care, 2) medical and scientific research and 3) legal proceedings, and that genetic counseling should be made available in an appropriate manner to persons involved in genetic testing that may have significant implications for their health.

In Japan, as a result of the complete enforcement of the Personal Data Protection Law in April 2005, as shown in Table 1, policies and guidelines

have been drawn up in the respective areas of 1. research, 2. clinical practice and 3. industry, incorporating the aims of the UNESCO International Declaration on Human Genetic Data. This paper introduces guidelines directly relating to genetic testing drawn up by the Ministry of Health, Labor and Welfare (MHLW) [Table 1, 2.1)] and ten genetic-medicine-related societies [Table 1, 2.2)].

MHLW Guidelines for the Appropriate Handling of Personal Information by Health Care Providers

Because genetic data is a special type of personal data, MHLW established as the tenth item of these Guidelines “Handling of Genetic Data Used for Clinical Practice”, stating that “Any medical institution, etc. engaged in genetic testing must provide genetic counseling by persons who have specialist knowledge of clinical genetics and can provide psychosocial support to the individuals concerned and their families, etc.” (See Table 2).

In Japan, the Guidelines for Research on the Human Genome and Genes at 1 in Table 1 state that facilities engaged in genetic analysis and research should endeavour to establish systems enabling them to provide genetic counseling, and, prompted by this, a clinical section for medical genetics was set up in most university hospitals. (Since 2003 a National Liaison Meeting for Clinical Sections of Medical Genetics has been held, where representatives of these clinical sections

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Table 1 Policies and guidelines for genetic analysis

<p>1. Guidelines for research</p> <p>Ethics Guidelines for Human Genome/Gene Analysis Research (Ministry of Education, Culture, Sports, Science and Technology, Ministry of Health, Labor and Welfare, Ministry of Economy, Trade and Industry) (Notified 28/12/2004)</p> <p><http://www.mext.go.jp/a_menu/shinkou/seimei/main.htm></p> <p>2. Guidelines for clinical practice</p> <p>1) Guidelines for the Appropriate Handling of Personal Information by Health Care Providers (MHLW) (Notified 24/12/2004)</p> <p><http://www.mhlw.go.jp/shingi/2004/12/s1224-11.html></p> <p>2) Guidelines for Genetic Testing by ten genetic-medicine-related societies [Japan Society of Human Genetics, Japan Society of Obstetrics and Gynecology, Japan Society for Pediatric Genetics, Japanese Society for Family Tumor, Japanese Society for Gene Diagnosis and Therapy, Japanese Society for Genetic Counseling, Japanese Society for Inherited Metabolic Diseases, Japanese Society of Laboratory Medicine, Japanese Society for Mass-screening, and Japanese Teratology Society (alphabetically)] (August 2001)</p> <p><http://jshg.jp></p> <p>3) Ethical Guideline for Contractual Human Genetic Testing (Japan Registered Clinical Laboratories Association (March 31, 2001)</p> <p><http://www.jrcla.or.jp/news.html></p> <p>3. Guidelines in the industrial field</p> <p>Guidelines on Personal Data Protection in Fields of Economic and Industrial Enterprise Using Personal Genetic Data (METI)</p> <p><http://www.meti.go.jp/press/20041217010/041217iden.pdf></p>

Table 2 Handling of genetic data used for diagnosis and therapy described in Guidelines for the Appropriate Handling of Personal Information by Health Care Providers (MHLW notified December 24, 2004)

Since genetic data obtained from genetic tests, etc. not only includes data concerning the disposition of the individuals concerned or the development of a disease, etc. based on genetic or karyotypic changes, but is also data that does not change in the lifetime of the individuals concerned and is data relating to their blood relatives, if such data were leaked, the damage or pain suffered by the individuals concerned and their blood relatives could be huge. It is, therefore, necessary to pay particular attention when handling test results or biological samples of blood, etc., with reference to the UNESCO International Declaration and relevant guidelines in the area of medical research and guidelines prescribed by relevant groups, etc.

The individuals concerned and their families, etc. are often very anxious when consenting to testing, for example, they find it difficult to accurately understand the significance of the test results or do not know who to deal with the predictability of disease. Therefore, medical institutions, etc. engaged in genetic testing must provide genetic counseling by persons who have specialist knowledge of clinical genetics and can provide psychosocial support to the individuals concerned and their families.

for medical genetics gather to exchange information. Details of the first and second liaison meetings (2003 and 2004 respectively) are shown on the Home Page of the Division of Clinical and Molecular Genetics, Shinshu University Hospital.²

As a result of the establishment of these Guidelines by MHLW, medical organizations besides university hospitals will now also be required to establish systems enabling them to practice in appropriate medical genetics includ-

ing genetic counseling in the future.

Guidelines for Genetic Testing by Ten Genetic-Medicine-Related Societies [Table 1, 2.2]

The MHLW Guidelines [Table 2] show only principles for handling genetic data used for actual clinical practice, but these Guidelines, which are also formally quoted in the MHLW guidelines,

serve as a more detailed reference.

If we look at the overall structure, the Introduction section explains how these Guidelines came to be drawn up and their main aims, and then I. Testing to be Directed by the Guidelines, II. Practice of Genetic Testing, III. Disclosure of Genetic Test Results and IV. Genetic Testing and Genetic Counseling give a general description of important points when conducting genetic tests. There is then the section V. Important Points Concerning Genetic Testing for Specific Subjects, which gives a detailed description of points to remember in six scenarios in which genetic testing is considered (1. genetic tests for persons who have developed a disease, 2. genetic testing for carrier detection, 3. genetic testing to predict disorders “pre-symptomatic testing and disease susceptibility testing”, 4. genetic testing for individual, differential drug response, 5. prenatal testing and diagnosis and 6. mass screening for newborn infants). Initially, these Guidelines were drawn up for members of genetic-medicine-related societies, but because they were formally quoted in the MHLW guidelines, in the future medical research bodies, medical institutions, clinical testing companies, genetic analysis centers, genetic analysis agencies, health-related companies, mass media and other parties concerned that are not members of genetic-medicine-related societies will be required to understand the significance of genetic testing via these Guidelines and observe these Guidelines, and it is hoped that genetic testing will come to contribute to the health and welfare of humankind.

Conclusion

This paper introduced policies and guidelines for genetic analysis in Japan. We can easily recognize that a keyword common to them all is “genetic counseling”. Genetic counseling is the medical activity of performing clinical genetic diagnosis on patients with genetic diseases, their families and people who may have genetic diseases and providing them with appropriate information and support based on medical judgment so that they can make life choices and take action of their own free will.³ Currently most medical initiatives are being taken for different internal organs, but there are genetic diseases that are present in each organ. To know how to make appropriate use of hereditary and genetic data in clinical practice, people need special education, training and experience covering the skills and methods of genetic counseling. Initiatives by internal organ alone are not enough. Initiatives to train human resources to provide genetic counseling include the “Clinical Geneticists Program”⁴ for medical doctors and “the Certified Genetic Counselors Program”⁵ for non-medical doctors. All medical doctors living in the genome era of the twenty-first century must understand the various ethical aspects of genetic data revealed by genetic testing, and must have a good understanding of the kinds of situations in which they must work in cooperation with a clinical geneticist or a certified genetic counselor.

Acknowledgements

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4. <http://jshg.jp/> For details contact the Secretariat (Secretariat of the Committee of the Japanese Board of Medical Genetics, Clinical Geneticist: Division of Genetic Diseases, Department of Pediatric Medicine, Tohoku University Graduate School of Medicine, 1-1 Seiryomachi, Aoba-ku, Sendai, Miyagi 980-8574. Tel: 81-22-717-8141, Fax: 81-22-717-8141, Fax: 81-22-717-8142, E-mail: idensenmoni@ped.med.tohoku.ac.jp)
5. Certified Genetic Counselors Program <<http://plaza.umin.ac.jp/~GC/>>

Using Clinical Indicators to Improve the Quality of Medical Care

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Yoshio Yazaki*¹

Key words Clinical indicator, Quality of medical care, Patient-oriented medicine, Medical safety management

Introduction

Clinical indicators are indicators for objectively evaluating medical care, especially its outcomes, and recently they have begun to be used widely at medical facilities to improve the quality of medical care.

Basic Requirements of Clinical Indicators

The requirements of clinical indicators used in the evaluation of medical care are measurability, comparability and improvability.

Measurability means that physicians can collect the data necessary for evaluation using the existing infrastructure of the medical institution. Another key point is that the medical institution will not have to start introducing electronic medical records or creating networks, etc., in order to create such clinical indicators.

Moving onto comparability, the use of the words of common diseases, common concepts of pathological states and common terms to enable as much information sharing as possible and some degree of standardized management are preconditions of comparability. Of course, comparison is only possible if there is no excessive bias in the amount of data, for example, the number of patients. However, a lack of progress with standardization in concepts of diseases, pathological states, etc. would not preclude the

introduction of clinical indicators.

Improvability means using clinical indicators to review operational procedures and, thereby, being able to establish specific plans for improvement. Improvement measures must use the existing infrastructure, and evaluation criteria for which there is no obvious means of improvement are unsuitable because they can be difficult to use.

Subjective Points on Creating Clinical Indicators

The diversification of medical care makes evaluation and the creation of medical indicators extremely difficult. And so, one approach to proceeding with evaluation is to lay down indicators by proceeding with an examination based on a framework that divides medical activities into three stages. The first stage is to create indicators to evaluate the basic functions and capacity of the medical institution, as these are the easiest aspects to express numerically. To be more specific, indicators would include structure and equipment in relation to the facilities of the medical institution and staffing i.e. doctors and nurses. However, depending on the scale of the medical institution and the medical care it provides, indexing based on numerical values alone is not always possible. For example, if we compare a facility that deals with acute illness and a hospital that treats chronic illness, nursing standards are different, and this point also needs

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to be adequately considered. The number of doctors is also not just a question of actual numbers, information like the system in each therapeutic department and whether or not the number of doctors includes specialists in that particular area is also important.

The second stage is to evaluate the medical activities performed in terms of their respective processes. To be more precise, it is a fundamental part of an evaluation to show that doctors are implementing initiatives as a medical institution towards evidence based medicine (EBM). For example, criteria would include therapeutic guidelines for each patient, protocol conformity and the number of critical paths implemented.

The final stage is evaluation of the outcome of therapy, which is the most difficult to express numerically. Evaluation criteria consist of criteria shared throughout the whole medical institution on the one hand and criteria for each therapeutic area on the other.

Criteria from a shared standpoint can be broadly subdivided into criteria such as whether the medical institution practices safe medical care, whether it provides efficient, high quality medical care, whether it provides medical care to patients referred from regional medical institutions and whether it provides patient-oriented medical care. Specific criteria include the establishment of a medical safety management system, for example, the activities of risk managers and the rate of prevention of medical accidents, while other indispensable evaluation criteria include the state of implementation of measures to prevent in-hospital infections and the number of adverse drug reaction reports, etc. Criteria evaluated for the provision of patient-oriented medicine are the results of satisfaction surveys for in-patients and outpatients, the number of inquiries from patients and families dealt with and also whether there is a section for a second opinion.

Turning to indicators for individual therapeutic areas, in the cancer field these would cover aspects such as the number of patients, number

of surgical operations and the post-operative survival rate for different degrees of progression. In the cardiovascular field indicators would include the number of patients suffering acute myocardial infarction or apoplexy and death rate according to severity.

Utilization and Effects of Clinical Indicators

To begin with, the act of making a decision as a hospital organization to evaluate medical care based on clinical indicators will on its own increase awareness among all members of staff, because objective identification of the actual medical care provided by the hospital itself will give all members of staff a concrete understanding of this. The results of the evaluation will not just be used to rate the hospital, because a comparison of the results with those of other medical institutions or a comparison with general standards will not only reveal the strengths and weaknesses of the medical care provided at one's own hospital and instill confidence and awareness, but will also make it possible to focus on improvements in the quality of the medical care and take efficient action. Other expected benefits are that the level of awareness of each individual will be raised, and also that a systematic response as a hospital will be made, therapeutic departments and nursing departments will cooperate with each other in practicing medical care as a team and the quality of medical care will be raised further still.

The use of clinical indicators makes it possible to set the objectives and required levels of one's own hospital more clearly and promises more reliable results.

Conclusion

This article has shown that the evaluation of the medical care provided by a hospital based on objectively indexed criteria and utilization of the results serve as powerful tools for improving the content and quality of medical care.