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Healthy Japan 21

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Key words: National health promotion; Life-long health project; Investment in health

Background of New Concepts

The Ministry of Health and Welfare (currently the Ministry of Health, Labor and Welfare) has been working to prepare infrastructure that will enhance the health of the Japanese people by establishing a system of medical check-ups for the elderly, creating local health centers and other facilities, and training fitness instructors, as a part of the "First-phase Measures for National Health Promotion" begun in 1978 and the "Second-phase Measures for National Health Promotion" begun in 1988.

Based on the results of these efforts to promote health and on public health activities taking place both inside and outside Japan, a task force to plan Healthy Japan 21 and a task force to set up the Healthy Japan 21 Project were organized in November 1999, drawing together a number of experts sanctioned by the Public Health Council. Issues were discussed by the task forces for about one and a half years, and the results of their activities were compiled in the Report of the Task Forces for Planning Healthy Japan 21 and Framing the Healthy Japan 21 Project.

On the basis of these reports, the Ministry of Health and Welfare issued a communication from the permanent vice-minister for health and welfare entitled "National Health Promotion Movement in the 21st Century (Healthy Japan 21)" on March 31, 2001. The Ministry selected as targets of the Tertiary National Health Promotion Movement issues relevant to improving cancer, heart disease, stroke, lifestyle-related diseases such as diabetes mellitus, and underlying lifestyle factors, and provided goals for these targets, aiming at implementation by 2010. These actions facilitated and extended the health promotion movement, in which self-motivated individuals are involved in their own health and quality of life, and solicited widespread cooperation and support from private associations and various administrative bodies.

This large-scale project to promote national health is what is known by the term "Healthy Japan 21."

Basic Policies and Goals

The four basic policies of "Healthy Japan 21" are as follows: (1) the importance of primary prevention; (2) creation of a supportive environment for the enhancement of health; (3) goal setting and assessment; and (4) the promotion

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of effective, well-coordinated activities by the various implementing bodies.

These activities are intended to cover nine specific areas: (1) diet and nutrition; (2) physical activity and exercise; (3) leisure and mental health; (4) smoking; (5) alcohol; (6) dental health; (7) diabetes; (8) cardiovascular disease; and (9) cancer.

Because these activities are slated to be implemented nationwide, the organizations responsible for their implementation, including local public organizations, are expected to formulate goals that are held in common among the participating organizations and are relevant to their actual situations, while keeping in mind the overall goals of Healthy Japan 21. The goals for promoting the health of participants should be individual and specific, based on the participant's health status and view of good health, also with reference to the overall goals of the project. The proposed goals are expected to be expanded or reviewed as occasion demands.

In addition, under the heading "Promotion of health in communities" Healthy Japan 21 has directed that specific plans for the promotion of health be formulated in the manner best suited to the actual situation of that particular area (local plans) by enlisting the cooperation of residents and various community health organizations, in order to effectively promote the plan.

Problems

The author participated as a member of all the task forces and committees responsible for development of the "Healthy Japan 21" project (Task Force for Planning Healthy Japan 21, Task Force for Framing the Healthy Japan 21 Project, Expert Committee for Framing the Healthy Japan 21 Project, and Public Health Council).

While fully appreciating the importance of the Healthy Japan 21 project, the author also would like to point out certain issues raised by the project.

(1) The project places too much emphasis on measures against lifestyle-related diseases (formerly called adult diseases), focusing its attention on a healthy adult life while disregarding measures for maternal and child health, infant health, and the health of schoolchildren. In response to such criticism, the "Healthy Parent and Child 21" project was hastily formulated, but it is mainly a supplementary, patchwork plan.
(2) The importance of primary prevention received too much emphasis. In particular, Task Force for Planning presented certain negative opinions as to the contributions made by the medical community in prolonging the life span of Japanese people and questioned some of the benefits of secondary prevention. Eventually, however, these views were altered to a great extent, reflecting the opinions of the Japan Medical Association and other critics.
(3) Another criticism was that the project imitated similar projects in other countries, as represented by "Healthy People 2000" in the U.S., and was not an original Japanese health plan designed specifically for the Japanese people.
(4) Although this project is one that aims at promoting health and fostering independent, individual participation, there is a great deal of national and local government involvement. It is also problematic that the national government set forth basic principles for the formulation of local plans that were intended to be specific to the realities of the particular region.

Policies of the Japan Medical Association

On the other hand, the Japan Medical Association (JMA) is proposing a life-long health project as one of its five specific plans for medical structural reform. The plan is grounded in a report issued in March 1998 by the Health Investment Project Committee (formed in 1997

by JMA), "Systematization of activities of maintaining and promoting life-long health."

The life-long health projects proposed by JMA are based on the idea that health is a form of capital, and the promotion of health projects throughout the life span is actually an investment in health. JMA has offered the following two suggestions based on the idea of investment in health: (1) enactment of the Basic Health Law and (2) the value of daily clinical practice.

In addition, the specific themes of life-long health projects cited by JMA include (1) measures against lifestyle-related diseases as primary prevention, (2) improvement of health examinations as secondary prevention, (3) guidance based on the results of health examinations as secondary prevention, and (4) prevention of the development or aggravation of illness and recovery of impaired function.

In addition, it was decided that health projects should cover the entire life span and involve all periods of life, from the fetal stage (including the health of the expectant mother) to infancy, childhood, puberty, and adolescence, young adulthood, middle and late middle age, and advanced and late advanced age.

Based on the above concerns, JMA considers Healthy Japan 21 to lack the concept of health as an investment, as proposed in JMA's life-long health projects.

Unlike previous projects on maternal and child health, school health, industrial health, and elder health, Healthy Japan 21 has not been implemented to conform to laws that have already been enacted; rather, it is being promoted through the spontaneous participation of individuals, communities, and groups, who then set and accomplish goals. In this regard, the project should expand its horizons in order to fulfill its mission, namely, promotion of people's health in the 21st century.

Therefore, for Healthy Japan 21 to succeed, it is vitally important that family physicians, who are familiar with community health needs, and JMA, which has as its mission the support of family physicians, take part and cooperate in the project.

It is desirable that Healthy Japan 21 be promoted through strategies that are aligned with the purpose of the life-long health projects proposed by JMA.

Stress and Immune Function

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Abstract: In the presence of internal and external stress, homeostasis of the internal environment of the body is maintained through the regulatory functions of the nervous, endocrine and immune systems. These three systems, sharing an information transmitting mechanism, function as an integrated regulatory system of the body. The information-transmitting factors include hormones, cytokines, and neurotransmitters. Stress influences the immune system through two routes, the hypothalamus-pituitary-adrenal axis and the autonomic nervous system. The response to the immune system through these pathways differs according to stress type, amount, and duration, and the condition of the body receiving the stress. Clinical and basic research will be reviewed to show the influences of stress on the immune system.

Key words: Stress; Immune function; Hormone; Neurotransmitter; Homeostasis

Introduction

In the presence of internal and external stress, homeostasis of the body's internal environment is maintained through the regulatory functions of the nervous, endocrine and immune systems. These three systems, sharing an information-transmitting mechanism, function as an integrated regulatory system of the body. The information-transmitting factors include hormones, cytokines, and neurotransmitters.

Stress affects the immune system through two pathways, the hypothalamus-pituitary-adrenal axis and the autonomic nervous system. The response of the immune system through these pathways differs according to the type, amount, and duration of stress and the condition of the organism subjected to stress. Also, the extent to which the endocrine and nervous systems modulate the response of the immune system to stress differs according to the type of target immune system.

Clinical Studies

In various circumstances where individuals experience worry, grief or depression, the rate of infectious diseases, allergic diseases, autoimmune diseases, and cancer has been reported to increase.

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Table 1 Suppression of Immune Function by Stress

Types of stressors	Immune function	Published
Mental and social stress	Increased morbidity rate by upper bronchial infection	1962, Jacob
Chronic daily stress	Reduced resistance to streptococcal infection	1962, Meyer
Sleep disorder	Reduced phagocytic capacity against streptococcus, reduced production of interferon	1976, Palmbland
Death of a spouse	Reduced T cell function	1977, Bartrop
Effect of stress due to changes in life	Reduced cytotoxic function	1978, Green
Certification examination	Reduced lymphocyte PHA response	1982, Dorlan
Worry or depression with changes in life	Reduced NK cell activity	1983, Gottschalk
Depression	Reduced lymphocyte response	1986, Kronfol
Death of a spouse	Reduced lymphocyte PHA and PWM response	1983, Schleifer
The elderly without social support	Reduced lymphocyte PHA response	1985, Thomas
Mental stress	Increased morbidity rate from common colds	1991, Cohen
Loss experience, interpersonal stress	Increased herpes labialis recurrence	1991, Schmidt
Natural disaster (hurricane)	Reduced NK cell activity	1997, Ironson

PHA: phytohemagglutinin PWM: pokeweed mitogen

Bartrop *et al.* reported that the immune response of bereaved spouses decreased within 2–8 weeks after the death of their mates.[1)]

Schleifer *et al.* reported a significant reduction of lymphocyte blastogenesis capability in men after the death of their wives from breast cancer.[2)]

In addition, the suppression of PHA response (proliferation of phytohemagglutinin) of lymphocytes in peripheral blood, reduced production of interferon, and reduced activity of NK cells[3,4)] during stress tests have been reported.

An epidemiological study by Cohen *et al.* reported the occurrence of respiratory infections, viral isolation, and increased antibody levels when rhinovirus, a causal virus of the common cold, was dropped into the noses of healthy subjects.[5)] They found that the susceptibility to viral infection differs according to the subjective intensity of stress.

It has recently been reported that depression is partly responsible for cancer because of reduced immune function.[6)] In patients with depression, a reduction in lymphocyte blastogenesis capability in peripheral blood in response to mitogen (activity promoting mitoses of lymphocyte) was observed, and it was found that the more severe the depression, the lower the blastogenesis response.

Additionally, a reduction in the number and activity of NK cells was reported in depression. This finding can be attributed to the acceleration of the hypothalamus-pituitary-adrenal axis.

Thus, it has been shown that mental condition significantly influences the immune function. In humans, the response differs according to the personality and physical factors of the person under stress. Table 1 summarizes the major reports on stress and suppressed immune function.

Basic Studies

Many basic studies have been conducted using animal models. Reduction in the activity of NK cells in response to low- or high-temperature stress has been reported in rats. It has also been reported that lymphocyte blastogenesis in response to mitogen is suppressed in mice in response to short-term exposure to noise. However, it was also reported that immune function is sometimes enhanced by short-term fasting or pain stimulation.[7)]

The effect on immune response depends on

individual ability to control stress.[8] When rats or mice were given uncontrollable electroshocks, blastogenesis PHA and Con A lymphocyte response and NK cell activity were reduced. In contrast, when electroshock was self-controllable, the immune responses were not suppressed even when the same voltage was administered.

In addition, the authors investigated the relationship between restraint stress and immune function in mice.[9]

A study of the number and subsets of cells in the organs of mice under restraint stress reported that the ratio of CD4, CD8, and B cells in the spleen and mesenteric lymph nodes remained the same, but that the number of cells was significantly decreased at 12-hours and recovered to the original level within 24 hours. Under the restraint stress, a decrease of lymphocytes was observed in organs such as the thymus and liver, while the ratio of lymphocyte subsets and the number of cells such as CD4, CD8, and B cells was increased in bone marrow.

The effect of 12-hour restraint stress on antibody production was found a reduction of IgE, IgG 1, and IgG 2a antibodies in blood collected over time from mice immunized with OVA.

The effect of stress on the immune system differs depending on the type, amount, duration of the stress, and the condition of the individual subjected to stress.

Correlation between Stress and the Nervous, Endocrine and Immune Systems

Stress affects the central nerve system through sensory systems, such as auditory and visual, and then it affects the immune system through the hypothalamus-pituitary-adrenal axis or the autonomic nervous system.

1. Stress and the endocrine and immune systems

Emotional stress activates CRH (corticotropin-releasing hormone) neurons in the nucleus paraventricularis of the hypothalamus by stimulating the limbic system, especially the amygdaloid nucleus, causing the hypothalamus to secrete ACTH (adrenocorticotropic hormone), after which the adrenals are stimulated to secrete glucocorticoids.

On the other hand, the hippocampus exerts a suppressive action on the CRH neurons. The CRH neurons send fibers to POMC (proopiomelanocortin) neurons of the arcuate nuclei, which allows stimulation and secretion of β-endorphins, α-MSH (α-melanocyte-stimulating hormone), and ACTH, leading to the modulation of various immune functions. β-endorphin and ACTH are antagonists to the secretion of CRH from the paraventricularis.

Generally speaking, increased glucocorticoid binding to the receptors of the hippocampus antagonizes the secretion of CRH through the paraventricularis under acute stress. In contrast, glucocorticoidemia downregulates the receptors of the hippocampus, attenuating the antagonistic response, and glucocorticoidemia persists under chronic stress. Decreased lymphocytes and eosinophils in blood and increased excretion of 17KS (an intermediate sex steroid) and 17OHCS (a glucocorticoid indicators) in urine are observed under stress.

Adrenocortical hormones such as glucocorticoids have anti-inflammatory, immunosuppressive, and anti-tumor actions. Glucocorticoid receptors are found in almost all cells except for erythrocytes. The antagonist action of glucocorticoids on the immune system is expressed directly or indirectly by suppressing mediators.

Moreover, growth hormones, gonadotropin, and prolactin are susceptible to stress. Those hormones are known to affect the immune system.

2. Stress and the nervous and immune systems

The nervous system transmits external stimulation received by receptors through the neu-

rons, and responds to external changes through effectors. Additionally, a part of the nervous system, the autonomic nervous system, maintains homeostasis of the internal environment.

Organs are regulated by the functions of the sympathetic and parasympathetic nerves. The immune tissue also has many autonomic nerves. The core of the autonomic nervous system is found in the hypothalamus, and it has been shown that the core of emotion is also in the hypothalamus and the limbic system. Emotion also influences immune function through autonomic nerves. Immune tissues such as the thymus, bone marrow, spleen, and lymph nodes are controlled by both sympathetic and parasympathetic nerves.

The autonomic nervous system regulates not only microcirculation of lymphatic tissue through vessels, but also controls lymphocytes directly, through the action of nerve fibers extending to the parenchyma which is full of lymphocytes. T and B lymphocytes have α- and β-adrenoceptors through which immune response is modulated by the autonomic nervous system. Stimulated α-receptors promote immune responses by reducing intracellular cAMP, while stimulated β-receptors suppress lymphocyte function by increasing intracellular cAMP.

Under stress, β-endorphin is excreted from the anterior hypothalamus and enkephalins from the adrenal medulla. Weigent *et al.* reported that receptors specific to nerve peptides were found on immunocytes.[10] They include VIP (vasoactive intestinal polypeptides), substance P, catecholamines, and acetylcholine.

Those neurotransmitters modulate cell function by activating secondary messengers such as cAMP and cGMP through specific receptors. In addition, the neurotransmitters affecting the production of cytokines and physiological activity modulate indirectly immune responses.

The nucleus of the solitary tract, the core of the sympathetic nerves in the brainstem, sends noradrenergic fibers to sites full of CRH cells in the internal nucleus paraventricularis. The ceruleus nucleus has similar fibers connected to the nucleus periventricularis and the cerebral cortex which have thyrotropin-releasing hormone, somatostatin, and dopamine-containing cells.

Both nervous nuclei stimulate CRH secretion from the nucleus paraventricularis in parallel, forming a network with splanchnic nerve stimulation such as bleeding, and somatosensory stimulation such as pain. Thus, there is an interaction between the CRH secreted in the hypothalamus and in the sympathetic nerves.

Conclusion

Stress affects mental condition through the sensory system (nervous system) and the nonsensory system (immune system). Mental condition stimulates a homeostasis triangle: the nervous, endocrine, and immune systems.

In brief, emotions such as worry, depression, anger, grief, and pleasure induced by stress affect the immune system through nerves and endocrine system. Further investigation of the relationships between emotions and immune function from molecular-biological standpoint is essential.

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Mental Health and Stress

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Abstract: Within the field of mental health care, family, school, and work are the three areas of importance. In this paper we mainly focus on one area, that of the workplace where 65 million workers are engaged in Japan. The increased demand for economic efficiency, technical innovation, and structural changes that has been induced by the globalization of the economy and the economic recession in recent years has resulted in many workers having to work under stressful condition in Japan. In the national survey of mental and physical conditions of 16,000 workers conducted in 1997 by the Ministry of Labor, 62.8% of workers responded by stating that they felt anxiety, worry and stress in their working life. In addition to this, the number of suicides due to economic problems has increased markedly from 3,600 in 1997, to more than 6,000 in the years 1998, 1999, and 2000. This paper discusses job stress models regarding the relationship between job stressors, health outcome and modulating factors in relation to field studies. The paper also reviews the onset mechanism and contents of job stressors observed among workers with occupational maladjustment syndrome, the current situation of and issues in stress management at work, and policies being implemented by the Ministry of Health, Labor and Welfare concerning occupational mental health.

Key words: Mental health; Job stress;
Occupational maladjustment syndrome;
Occupational mental health promotion

Introduction

The contemporary period is positioned as an age of great innovation in modern history and changes are on going in various fields. Mental health at the levels of home, schools, and work, and that in the younger and aged generation have become important issues. The present study

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mainly discusses mental health in the workplace which is attracting particular interest among clinicians and occupational physicians.

Currently Japan has a workforce of approximately 65 million. They work in a rapidly changing environment which has been profoundly affected by economic depression. In industry, restructuring, and organizational reforms are rapidly occurring in order to enhance economic efficiency by promoting information technology, computerization, technical innovation, achievement-based wage system (annual salary system), discretionary work, management by objectives and self-responsibility. Many workers are suffering from various types of stress as a result of these changes. Some of them lapse into occupational maladjustment syndrome leading to mental and physical disorder.

This paper discusses the background of increasing job stress, the present conditions of mental health, job stress models, occupational maladjustment syndrome, and measures to promote occupational mental health.

Increases in Job Stress and Present Conditions of Mental Health

Currently Japan is experiencing ongoing changes that are having significant effects on society, industry, the economy, medical care, and education. The factors which are accelerating these changes are the promotion of information technology, the pursuit of economic efficiency via technological innovation and economic globalization, the introduction of the theory of competition into various fields, individualism, and diversification of sense of value.

These changes inevitably have significant effects on the working environment. Typical Japanese systems of employment and management are losing their original forms, and increases in the numbers of contracted and temporary employees indicate the demise of the life-time employment system. The seniority wage system and periodic employment system are being replaced by new systems such as performance-based wage rating (annual salary system), results-based service rating, and discretionary labor. More companies are adopting the theory of competition and self-responsibility in the management of their employees.[1)]

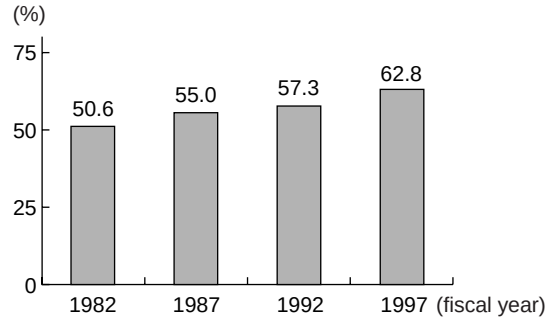

Fig. 1 Changes in the percentages of workers with anxiety, worry, and stress in their working life (A survey conducted by the former Ministry of Labor) [Prepared using reference 2)]

These rapid changes are imposing an increasing amount of stress on workers who are forced to adapt to the changing environment. The Ministry of Labor (the current Ministry of Health, Labor and Welfare) conducts a questionnaire on workers' mental and physical conditions every five years. According to the results obtained in the survey (on 16,000 workers), the percentage of workers who complained of serious anxiety, anguish, and stress showed a constant increase from 50.6% in fiscal 1982 to 62.8% in fiscal 1997 (Fig. 1).

Their anxieties included problems with interpersonal conflict in the workplace (46.2%), qualitative work load (33.5%), quantitative work load (33.3%), vocational aptitude (22.8%), promotion and rise in rank (19.8%), and job insecurity (13.1%).[2)]

In this situation, an increasing number of workers are failing to adjust to the changing work environment and are suffering from impaired health and psychosomatic symptoms. Many researchers point out increased anxiety due to job insecurity and maladjustment relating to restructuring, increases in depressive workers, increases among those who have diffi-

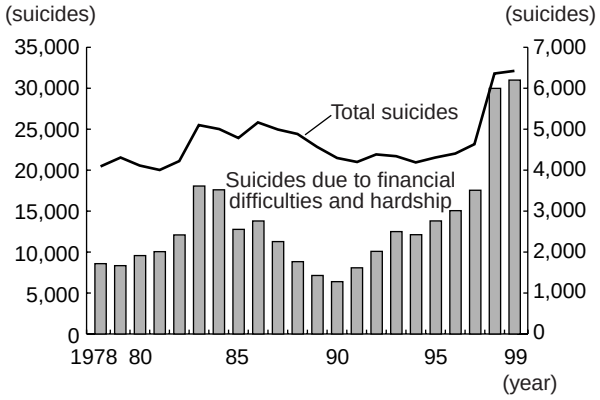

Fig. 2 Changes in the number of suicide (Statistic data issued by the National Police Agency)
[Prepared using reference 3)]
(Note: The left scale indicates the total number of suicides and the right scale indicates the number of suicides due to financial difficulties and hardship.)

culty in returning to their former positions, and worsening of the atmosphere in the workplace.[1)]

Overwork not only causes death from heart diseases and cerebrovascular diseases (death from overwork, so-called "karoshi") but also suicides from work-related depression (so-called "karojisatsu"). The number of these deaths was at the 24,000 level in 1997, while it has exceeded 32,000 since 1998. This increase indicates that more people are committing suicide because of hardships and financial difficulties[3)] (Fig. 2). In view of the current situation, the Ministry of Labor (the current Ministry of Health, Labor and Welfare) prepared a draft of guidelines for the approval of overwork-related mental disorder as an occupational injury in 1999, and established the Guidelines for the Promotion of Mental Health in the Workplace in 2000.[4)]

Impairment of health due to job stress occurs in various forms ranging from psychiatric symptoms to physical disorders such as diabetes mellitus, hypertension, and ischemic heart diseases, indicating that occupational diseases are being replaced by work-related diseases induced by job stress. There are many reports on the higher incidence of work-related disease.[5)]

Stress Models

Regarding the impairment of health resulting from job stress, several job stress models have been proposed.[6–8)] The generic model of job stress proposed by the National Institute for Occupational Safety and Health (NIOSH)[6)] is more comprehensive than other models.

The NIOSH model of job stress describes the relationship between a job stressor, the resulting stress reaction and health impairment, the factors which modify the intensity of stress reaction such as personal factors and factors not related to the job, and the factors which reduce stress reactions such as social support from superiors, colleagues, family members, and friends. Hurrel *et al.*[6)] in NIOSH established this model by analyzing a large volumes of currently available data and have prepared a questionnaire to obtain data corresponding to the categories of the model.

This questionnaire was used to conduct a large-scale survey in Japan. It has been reported that overwork, anxiety about future employment, and lack of sufficient support from superiors contribute to the creation of depressive mood.[9)] The authors also used this questionnaire to investigate the health of local government employees and evaluated the results by multiple regression analysis. This investigation demonstrated a clear correlation between the degree of impairment of mental health and the following items: variance in work load, interpersonal conflicts among groups, lower self-esteem, lower job satisfaction, and insufficient social support.[10)] Recently, Japanese researchers have simplified this questionnaire and developed a brief occupational stress questionnaire for practical purposes.[4)]

Karasek and Johnson *et al.*[9)] conducted surveys using the questionnaire corresponding to the demand-control-support-model and reported a higher incidence of depression and ischemic heart diseases among workers with high job strain and insufficient social support and a lower incidence among workers with suf-

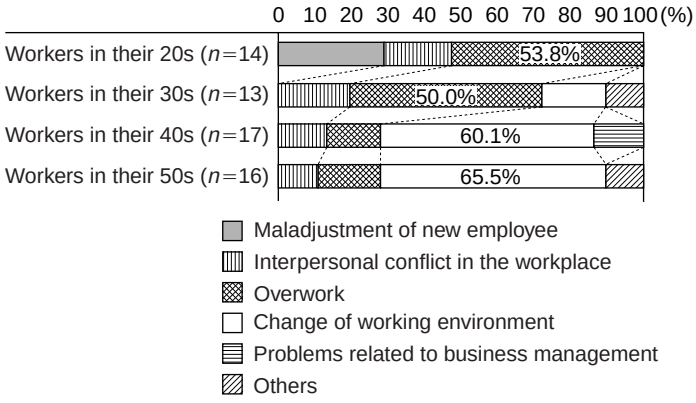

Fig. 3 Occupational maladjustment syndrome stressors by age groups [Cited from the reference 11)]

ficient social support.

There are many reports suggesting that job stress may accelerate the development of depression, neurosis, and psychosomatic disorders.

Occupational Maladjustment Syndrome

Some workers are unable to adjust to job stress and show various symptoms and require medical treatment. These workers are recognized that they have occupational maladjustment syndrome. This symptom is produced by a mismatch between individual factors including work ability, personality and behavioral patterns, and occupational factors including work-related problems and interpersonal relations.[11] Generally, many of these workers are clinically diagnosed with depression although some patients suffer from psychosomatic disorders, characterized by the aggravation of symptoms by stress, alone or in combination, with an underlying disease.

Sixty cases with occupational maladjustment syndrome were studied in order to clarify the causative factors. The results obtained demonstrated several characteristic tendencies in each age group[11] (Fig. 3). Some of the workers in their 20s who have just started to work recognize a gap between their expectations and reality and a difficulty in participating in group work, and find themselves unable to adjust to the new jobs and working environment. Many workers in their 20s and 30s suffer from burnout syndrome due to overwork. Intermediate managers in their 40s recognize their responsibility in the workplace but face conflicts in interpersonal relations, conflicts with their superiors, and conflicts with their subordinates. Furthermore, the introduction of new personnel rating systems and unexpected changes in roles and the working environment following temporary transfer and personnel changes frequently cause depressive state or depression accompanying "maladjustment between individual and workplace".

The next section on occupational mental health promotion explains the prevention and treatment of these cases. Special attention should be directed to the fact that approximately 80% of these patients recovered and have succeeded in returning to their former positions.

Occupational Mental Health Promotion

There are two major pillars in the promotion

Table 1 Guidelines for Promoting Mental Health in the Workplace
[Cited from reference 4)]

1) Employers are to draw up "plans to promote mental health" consisting of practical countermeasures.
2) In accordance with the plan, they are to promote the following four types of care:
   - "Self-care" by workers themselves
   - "Care by a line of managerial persons" to be extended to subordinates by superiors
   - "Care by occupational health care staff members" to be extended by persons in charge of in-house health management
   - "Care by external resources" to be provided by external specialists
3) Employers are to adopt the following approaches to smoothly provide these types of care for their employees:
   - Hold educational seminars for workers in various positions including managers
   - Improve the working environment
   - Establish a counseling system to encourage workers to receive mental health care voluntarily

(Issued by the former Ministry of Labor, August 9, 2000)

of occupational mental health.[1] One is how to manage workers who suffer an impairment to their health. It is necessary to identify such workers, provide appropriate medical care, and support their rehabilitation. Medical care, which is usually provided in facilities other than workplaces, consists of pharmacotherapy using hypnotics, anxiolytic agents and antidepressants, and counseling. Clinicians need to listen sympathetically to these workers and clarify the problems being faced by such individuals in the workplace and at home. They then need to provide appropriate mental care and support so that they can cope with and resolve their problems. In some cases, clinicians may need to consult with the worker's superior in order to improve their working environment by transferring them to a different position or department.

The other pillar is the establishment of effective preventive measures consisting of a reduction of stressors in the workplace and the enhancement of individual tolerance to stress. It is necessary to provide employees with a comfortable working environment, optimize the quality and quantity of work, improve communication in the workplace, provide superiors with educational programs so that they can provide appropriate support to their subordinates, provide mental health seminars, ameliorate job stress, and implement necessary promotional measures.

These promotional measures function appropriately when the employers understand job stress and collaboration between employers, the director of the personnel department, managers, and occupational health care staff members.[1]

In August 2000, the Ministry of Labor (the current Ministry of Health, Labor and Welfare) established the Guidelines for the Promotion of Mental Health in the Workplace[4] (Table 1) and recommended employers to draw up plans to promote mental health in the workplace. Such plans are to include the following four types of care: self-care by workers themselves, care to be extended to subordinates by superiors, care to be extended by persons in charge of occupational health care and care to be provided by external resources such as medical care facilities, local occupational health centers, and occupational health promotion centers. The practical activities are shown in the reference material.[4]

Conclusion

The authors discussed mental health in the workplace focusing on the following three points.

1) Recent rapid changes in social and economic systems resulting in an increase in job stress leading to an increase in the incidence of mental and physical health impairment and suicide among Japanese workers.

2) A job stress model was used to conduct a survey of job stress in the workplace and the results obtained were reported.
3) Measures to promote occupational mental health were suggested to cope with various work-related problems including occupational maladjustment syndrome.

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Peptic Ulcer

JMAJ 46(2): 61–65, 2003

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Abstract: The conventional biomedical model used for medical research and disease management is a linear model in which the cause-effect relationship is important. In contrast, the model used in psychosomatic medicine is a bio-psycho-social model in which much importance is attached to interactions and relationships among various factors, as well as to the individuality of the patients. When peptic ulcer is studied or treated, it is meaningless to argue about whether this is an infectious or a stress-related disease. Although there is a lot of evidence that the eradication of *Helicobacter pylori* (*H. pylori*) prevents ulcer recurrence, the development of ulcers only occurs in several percent of persons infected with *H. pylori*. It has been estimated that 70–80% of the population aged 40 years or older are infected with *H. pylori*. Although stress is associated with ulcer development in 30–40% of all patients with peptic ulcer, many persons who are under stress do not suffer from this disease. The organ affected by stress varies depending on many factors, including individual predisposition (vulnerable organ), smoking, drinking, and dietary habits. Because peptic ulcer is a multifactorial disease, a bio-psycho-social approach adjusted for the individual patient should be applied to its diagnosis and management, with careful consideration of the association of this disease with many factors including *H. pylori* and stress.

Key words: Peptic ulcer; Stress; Psychosomatic disorder; Lifestyle; *Helicobacter pylori*

Introduction

Alexis Carrel (who died in 1944) developed the technique of arterial anastomosis and won the Nobel Prize. In his book entitled "Man the Unknown," he wrote: Despite the remarkable progress in science, little is known about human beings because the mentality of man is not designed to know himself, because his ancestors were too busy, and because he is too complicated. This discrepancy is fundamental. We must clearly recognize the fact that "human science" is the most difficult among all sciences. (The Japanese version of this book was translated by Shoichi Watanabe and published by Mikasa Shobo.)

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He was warning that the mankind stood on the brink of ruin because Europeans were not adequately aware of human nature despite their enormous power attained as a consequence of scientific progress. Whenever I think about peptic ulcer, this warning by Carrel, who was also a critic of civilization, is full of meaning.

Is Ulcer an Infectious or a Stress-Related Disease?

I would like to state my conclusion first: this question is irrelevant. In the biomedical model, a linear model in which clarification of the cause-effect sequence is important, ulcer would be an infectious disease rather than a stress-related disease. There is a lot of evidence that eradication of *H. pylori* prevents the recurrence of peptic ulcer, particularly duodenal ulcer. It is believed that 70–80% of individuals aged 40 years or older are infected with *H. pylori*. Among them, however, only a few percent develop ulcers.

With respect to the association between peptic ulcer and stress (a psychosocial factor), numerous animal experiments performed to date have demonstrated a strong association of stress with the development and recurrence of ulcer disease.[1)] However, ulcers are related to stress in only 30–65% of the patients.[2)] Do all individuals who are under stress suffer from peptic ulcer? The answer to this question is also obviously negative. In the biomedical model, the cause-effect relationship is important. However, in persons exposed to stress, the organs that are affected tend to vary depending on the interaction of stress with individual predisposition (the vulnerable organ concept) and many other risk factors. Consequently, peptic ulcer is a multifactorial disease.[2)]

According to a recent report, whether bacterial infections become manifest or not depends on the presence or absence of stress and on the state of immunity.[3)]

The Bio-Psycho-Social Viewpoint

Engle advocated use of the bio-psycho-social model for psychosomatic medicine.[4)] He stated, "In diseases for which the pathogenesis involves multiple factors, it is impossible and meaningless to identify individual etiologic factors. The system as a whole, as well as interactions and relationships among individual risk factors, is important."

From this viewpoint, both *H. pylori* infection and stress are important for, but are only two of many factors pertaining to, the development and recurrence of peptic ulcer. Thus, it is better to consider that the addition of *H. pylori* as an important factor in the pathogenesis has expanded the bio-psycho-social scope of peptic ulcer disease, allowing us to expect further elucidation of the pathophysiology and more progress in diagnosis and management.

Multivariate Analysis of Factors Related to Peptic Ulcer

The author and his colleagues performed a multivariate analysis to identify the factors that were most important in relation to the development and recurrence of peptic ulcer.[5)] As shown in Fig. 1, 1) smoking, 2) the method of coping with stress, 3) anti-*H. pylori* antibodies, 4) the speed of eating, 5) an ulcerogenic personality, 6) a regular diet, and 7) daily stress were closely associated with the presence or absence of ulcer in this order. The presence or absence of ulcer could be accurately predicted using these factors in 38 (79.2%) out of 48 patients.

A graphical assessment showed that 1) an irregular diet and 2) smoking were most closely associated with recurrence in this order. In the case of association with recurrence, positivity for anti-*H. pylori* antibodies and compliance with therapy were comparable in importance.

From the results described above, in addition to *H. pylori* infection, several risk factors are important as etiologic factors, including life-

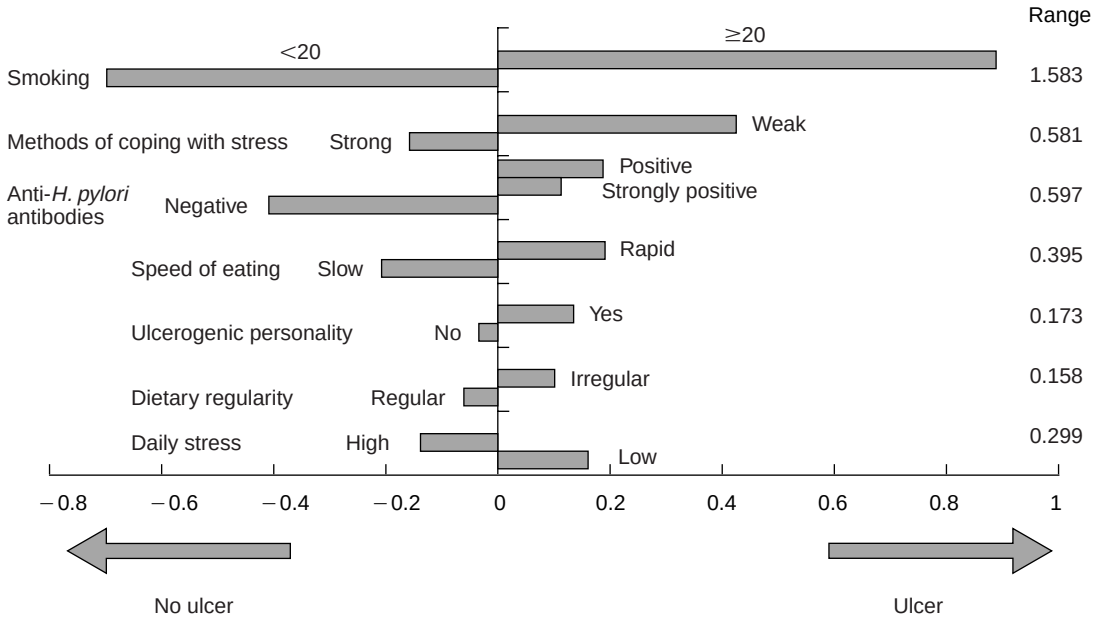

Fig. 1 Comparison between patients with and without peptic ulcer[5]

style, smoking, and behavioral factors such as the mode of coping with stress. The extent of the involvement of these individual factors in the pathogenesis of ulcer cannot be assessed without a new method such as one based on non-elementalism.

Diagnosis of Peptic Ulcer as a Psychosomatic Disease

A set of diagnostic criteria for peptic ulcer was drafted depending on the results of the above-mentioned multivariate analysis.[6] According to these criteria, peptic ulcer could be considered a psychosomatic disease in 39 (76.5%) out of 51 patients; a diagnosis of psychosomatic ulcer was established in 13 patients (25.5%) and was suspected in 26 patients (51.0%). Most of the diagnoses agreed with those made by psychosomatic physicians.

Ishikawa *et al.*[7] previously reported another set of diagnostic criteria. They assessed the value of their criteria by dividing patients into two categories, i.e., those with psychosomatic ulcer and those with suspected psychosomatic ulcer. Their criteria and ours share many features. According to their criteria, peptic ulcer was psychosomatic in more than 66% of patients, which was a similar rate to that estimated according to our criteria.

There is a problem in relation to the "Human Science" advocated by Carrel that was mentioned at the beginning of this article. The prevalence of psychosomatic ulcer will vary depending on the ability of the physician to understand human nature and the ability of patients to notice their own internal stress. In traditional medicine, peptic ulcer is regarded as a disease caused by infection, stress, or non-steroidal anti-inflammatory drugs. In conventional medical methodology, even lifestyle factors, psychological factors, social factors, and behavioral patterns, all of which vary between individual patients, are separately quantified and expressed numerically to reach a statistical conclusion. This is the present status of the medical approach to peptic ulcer.

Unexpectedly, the patients are often aware of the association of their peptic ulcer with stress.[8] A questionnaire study was performed

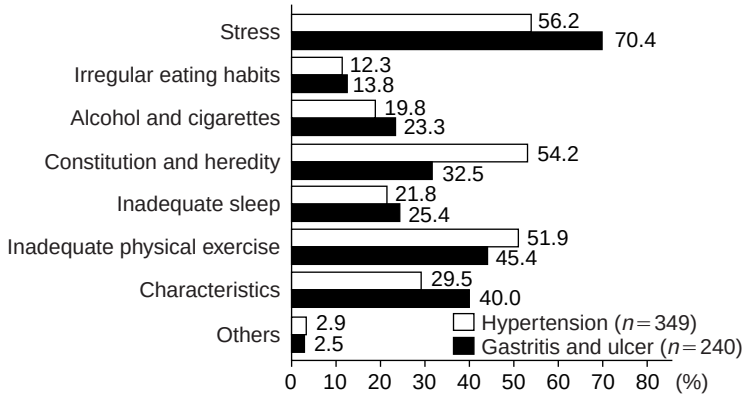

Fig. 2 Factors that you think are associated with your disease (more than one factor can be chosen)[8]

in patients with gastritis, peptic ulcer, and hypertension, who were asked to describe one or more risk factors that were considered to be involved in their disease. The factors that they chose are listed in Fig. 2. Among the patients with gastritis or peptic ulcer, 70.4% considered that their disease was associated with stress. Other factors chosen were those related to lifestyle, which is an item included among the diagnostic criteria described above. Lifestyle is deeply associated with human nature, society, behavior, economic status, and education. In other words, it should be understood that behavior and lifestyle reflect the individual personality and social milieu.[9]

Conclusion

If the natural banks of a river are broken, the breach may be filled with concrete along with reinforcement of the riverbed using concrete and construction of a dam upstream to control the flow of water. Bacterial eradication and the administration of proton pump inhibitors and other drugs in the treatment of ulcer are analagous to civil engineering for river management.

In conventional medical treatment for ulcer, unhealthy lifestyle factors (including smoking, drinking, and stress) are left unchanged. If disease is a signal from the body and mind, even if the signal is removed, the underlying health problems have a high potential to give rise to diabetes, cancer, and other diseases instead of peptic ulcer. A construction project designed to prevent a river from breaking its banks makes the river unable to function as part of the ecosystem, and makes it hard for living things grow and survive in it. In addition, it causes pollution of the sea, and makes the land less fertile, while damaging the fields, forests, and mountains.

Like civil engineering for rivers, the medical management of ulcer should not be based on a simple cause-effect relationship. Treatment should be adjusted to individual patients and should be designed by taking the involvement of many causative factors (including *H. pylori* and stress) into consideration. In other words, the bio-psycho-social approach is essential for the treatment of peptic ulcer.

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Irritable Bowel Syndrome and Stress

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Abstract: The aim of this review is to make clear the relationship between irritable bowel syndrome (IBS) and stress. From a pathophysiological viewpoint, IBS is an abnormality in brain-gut interaction, motility of the digestive tract and visceral perception. Confirmation of the stress itself is not necessary to make the diagnosis but it relates to the onset, severity, or course of the disease. Cognitive behavior therapy may reduce the symptoms and stress. Even if the patients succeed in coping with their stress, some of their symptoms may last for a long time. The therapeutic goal is not a symptom free state but self-control of symptoms. These therapies rely on the relationship between the patient and the therapist.

Key words: Irritable bowel syndrome; Stress; Brain-gut interaction; Cognitive behavior therapy

Introduction

The enteric nervous system (ENS) contains almost as many neurotransmitters as the brain itself. This fact suggests that the brain-gut axis may play an important role in the pathogenesis of stress-related diseases. It is well known that stress affects gut motility and perception. The most popular conceptualization of irritable bowel syndrome (IBS) is as one of the stress-related disorders, and that its symptoms are generally manifest in the presence of intense emotional or psychological stimuli. The aim of this review is to present the diagnosis, pathophysiology, therapies, and stress coping methods of IBS.

Definition of IBS

IBS is a functional gastrointestinal disorder, a term which covers a range of symptom complexes affecting the gastrointestinal tract. There has been a Rome working team report on diagnostic criteria for IBS. The Rome II working team developed new criteria (Table 1).[1)]

The Rome II criteria is simple, the diagnosis of IBS being based on the presence of two out of three main diagnostic criteria alone. In recognizing IBS, careful interpretation of the abdominal pain and stool form is needed. Abdominal pain related to defecation is likely to be a bowel pain, while that associated with exercise, movement, urination, or menstruation may have a different cause. Postprandial

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Table 1 Diagnostic Criteria* for IBS

At least 12 weeks or more, which need not be consecutive, in the preceding 12 months of abdominal discomfort or pain that has two out of three features:

(1) Relieved with defecation; and/or

(2) Onset associated with a change in frequency of stool; and/or

(3) Onset associated with a change in form (appearance) of stool

* In the absence of structural or metabolic abnormalities to explain the symptoms. (From Thompson, W.G. *et al.*: *Gut* 1999; 45(Supple 2): II43–II47)

Table 2 Investigation of IBS, Alarm Symptoms and Signs

1. Test	1) Full blood count (WBC, RBC, Hb), C-reactive protein, Urinary analysis, Blood biochemistry (total protein, GOT, GPT, γ-GTP) 2) Fecal occult blood (immunochemical method)
2. Alarm symptoms or signs	1) Abnormal physical examination 2) Loss of body weight within 6 months (over 3kg) 3) History of organic colon diseases/family history 4) Age over 50 years 5) Nocturnal abdominal pain 6) Fever, joint pain 7) Bloody mucus in stools

symptoms have little value in discriminating IBS from other diseases. Many women with IBS consult a gynecologist for lower abdominal pain (pelvic pain). There are other gastrointestinal, somatic, and psychological symptoms, so-called non-colonic symptoms, in patients with IBS. These may include globus, headache, backache, urinary symptoms, and psychogenic symptoms. But, non-colonic symptoms are not essential for the diagnosis. Among patients with IBS, stress produced changes in bowel function, but no particular stress events or bowel responses were found to be characteristic of IBS. The alarm symptoms or signs that are not explained by functional disturbance of the digestive tract should be determined (Table 2).[2] A physical examination is important to exclude other diseases and, to provide the reassurance for the patient by the physician. Unnecessary investigations should be avoided.

Brain-Gut Interaction

It has been a popular notion that the manifestations of IBS include emotional and perceptual components, which are suggestive of the brain-gut interaction. Several studies have shown an alteration in bowel function during sleep and specific sleep disturbances in patients with IBS, suggesting that altered CNS function may be playing an important role in the pathogenesis of IBS. Using PET (positron-emission tomography) scanning, it appears that the activated portions of the brain cortex by the stimulation of sigmoid distention in patients with IBS are different from control subjects.[3] The enteric nervous system contains almost as many neurotransmitters as the brain itself. These transmitters form important relationships between gut function and stress.

Motility, Perception, and Stress

Acute stress and emotional arousal may induce the change of the colonic motilities. Colonic motilities show exaggerated patterns when IBS patients are under the stress. There are no specific findings of the colonic motility pattern seen in IBS, but several principal motility abnormalities are seen in it. IBS patients report pains to be less intense when a balloon is inflated in the colonic lumen. It is assumed that visceral hyperalgesia is seen in IBS patients due to the decrease of the perceptual sensitivity threshold induced by intraluminal balloon distention. Whitehead *et al.*[4] examined by meta-analysis whether visceral heperalgesia is a diagnostic biological marker of IBS, and psychological factors have an influence on perceptual sensitivity in IBS patients or not. Many of these findings cannot be explained on the basis of biological differences between patients with IBS and controls. It may be confirmed that psychosocial stressors have an influence on the pain threshold in patients with IBS.

Therapies in Primary Care

There are no convincingly effective therapies for IBS. In IBS patients, there is much heterogeneity in disease severity, nature of symptoms, pathophysiologies, and psychosocial factors. The ideal therapy for IBS may be individual treatment planned out for each condition, but it may be difficult to make treatment strategies due to the great number of profiles of IBS patients. The clinical trial evidence for the efficacy of drugs is relatively thin. Physicians can only use several psychotherapies skillfully.

1. Explanation and therapeutic relationship

The important therapeutic tools for the physician are listening to the patients' worries with a sympathetic attitude, and careful explanation of the examined data and pathophysiologies of the IBS. These must be done based on effective patient-doctor relationship.

2. Life style modification

Some IBS patients may have an impaired life style. Habitual bad conditioning may produce abnormal bowel movement or abdominal pain. Physicians must point out these factors and environmental stress surrounding the patient, and give advice about life style modification and environmental adjustment. Cognitive behavior therapy may be helpful for reduction of patient's symptoms and to change their way of thinking about their symptoms. Self-monitoring by the patients is usually very beneficial and an important method in cognitive behavior therapy. Homework diaries on diet, bowel movement, sleep quality, and stress are useful as they enable the patient to understand the relation between their symptoms and stress.

3. Dietary modification

Consumption of adequate amount of soluble fiber may alleviate symptoms of the patients with IBS. Insoluble fiber also improves bowel movement, but it often increases gas production in the intestine, and causes abdominal fullness.

4. Drug treatment

(1) **Pharmacological therapy targeted at somatic symptoms**

The drugs for treatment of IBS should be chosen for target symptoms of the patients. Symptoms are likely to include bowel symptoms and extra-colonic symptoms. For abdominal pain, tricyclic antidepressants are used in lower doses than are needed for depression because of analgesic effects on visceral sensation. In patients with diarrhea-predominant IBS, antidiarrhoeal agents, such as loperamide are useful, and when constipation is predominant, stool softeners such as low doses of magnesium oxide are useful. But, these drugs are limited to only symptomatic treatment. Calcium polycarbophil is a synthetic soluble fiber, and effective for both diarrhea and constipation.

(2) **Psychopharmacologic drugs**

Anxiolytics are occasionally used to help ameliorate stress-induced anxiety and nervous tension, or fear caused by physical symptoms.

Tricyclic antidepressants should be given in full doses when depression can be identified. A poor clinical response may be due to insufficient doses.

5. Stress management

Once the patients have recognized that stress triggered disease onset, or affected their symptoms and course of disease, they should identify the following facts by self-monitoring, and listing.

(1) their signs of stress
(2) the probable cause of their stress
(3) the changes in the nature, severity, and duration of their stress

There are two strategies to defend against stress. One is mental fitness and the other is physical fitness.

1) Mental fitness includes self-control of symptoms such as looking out for unhelpful thoughts that do not have factual basis, and thinking of new solutions or trying to reduce stress by having interests. Relaxation techniques are useful. Autogenic training or progressive relaxation may be helpful for self-control of symptoms.
2) Physical fitness means regular exercise, aerobic dance, sports, and so on, enjoying oneself within the limits of physical abilities and interest.

Social support from the patient's friends, neighbors, colleagues, or pets may help for reducing stress.

Therapy by Specialist

There are a few IBS patients who resist to standard therapies, so are called super-patients. Primary care physicians do not treat these patients for a long time, and it is better to send them to specialists.

Conclusion

IBS is a disease suffered by both the brain and the gut. Stress itself is not necessary to make the diagnosis but it is related to disease onset, severity, or course of the disease. One good way to cope with stress is cognitive behavior therapy. Even if the patients succeed in reducing their stress, some of their symptoms may last for a long time. The therapeutic goal is not a symptom free state but self-control of symptoms.

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Changes in the Child-Rearing Environment and Their Effect on Child-Rearing Anxiety

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Abstract: The child-rearing environment has drastically changed over the past fifty years. Many factors associated with the changes in the environment have resulted in heightened child-rearing anxiety among mothers. For example, advancement of industries, urbanization, and expansion of the information society have led to a change in family structure. Nuclear families that consist of only a few members have been replacing traditional extended families. In addition, close ties to neighbors in the community are extremely decreasing. Under such conditions, many women have no experience of playing with small children until they become mothers. Feeling a great deal of perplexity and anxiety in child rearing, many mothers cannot find anyone they can consult with nearby and they have a sense of isolation. It is an important goal to foster a support system for child rearing in which mothers can enjoy taking care of their children without isolating from a society. For this purpose, it is necessary to construct a community-based system according to the current social conditions, and child-rearing environment to support mothers in their fight against child-rearing anxiety.

Key words: Child-rearing environment; Child-rearing anxiety; Child abuse; Support for child rearing; Fathers' participation in child rearing

Introduction

Child-rearing anxiety is a major concern among childcare experts today. Various analyses and studies have been done regarding its causal factors. Among them, a change in the child-rearing environment surrounding children has had a great influence on the way children are taken care of. Therefore, it is important to study how this factor is related to child-rearing anxiety.

Changes in the Child-Rearing Environment

How the environment surrounding children has changed during the past half century will be illustrated in this section.

It is certain that the social structure has drastically changed, which has also resulted in a

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profound change in the family structure.

With high economic growth, industries have advanced and the information society has prevailed in this half century. Urbanization has also advanced and new cities with many high-rise buildings have been born one after another. On the other hand, open areas and green spaces where children can play have rapidly shrunk.

The status of women has also changed: The level of women's academic achievement has become higher and many women have entered the workforce seeking self-realization.

Naturally, these social changes have affected the conditions of the family.

In the past, a family was large, consisting of three generations including children, their parents, and grandparents. Families with more than ten members were common in those days. On the other hand, nuclear families consisting of three to five members are prevalent today. In addition, many different forms of families have emerged, reflecting today's social conditions. For example, the number of new family types, such as households consisting of singles, single parent families and households without a father due to his transfer to a remote workplace, has been increasing.

The role of the community regarding child rearing has also changed. Communication among neighbors used to be frequent and people living in the same town used to know each other's family members and circumstances very well. Nowadays, urbanization has advanced and many people live in condominiums or apartments rather than in single family homes. Consequently, it has become typical for people to want to avoid seeming to invade others' privacy, and as a result they do not know their neighbors' family structures or occupations.

A good example of this is the following: A three year-old child was temporary placed under the protection of the Children's Welfare Agency because child abuse was suspected. When the investigation was carried out, it turned out that the neighbors did not know much about the child's family, although the family had lived in the same apartment for more than half a year. Moreover, although the neighbors were aware of the child's frequent cries day and night, they did not pay any particular attention to them.

How Changes in the Child-Rearing Environment Affect Childcare

Considering the description of changes in the child-rearing environment as described above, let us now examine how these changes have affected the way children are taken care of.

In the past, children grew up surrounded not only by their parents but also by many other adults and children, including other family members, relatives, and neighbors. Various people around a child played different roles in childcare depending on their relationship to the child.

Compared to today's one-to-one basis childcare, the way a group of adults would care for a group of children better enabled caregivers to openly share their experiences, although an individual's privacy was likely to be ignored. In my childhood, for example, my family consisted of six children including myself, my parents, my grandparents, and two relatives who were helping my family with housework and childcare.

In those days, this was not a mere case. A friend of mine was one of five brothers and sisters, and many people were always around his family because his parents ran a small business. Adults who were not even relatives cared for the five children during the daytime. Also, older brothers and sisters took care of the younger ones and they all played together. Their way of living left a good impression on me because the brothers and sisters seemed to enjoy it, experiencing many different phases of each other's everyday lives.

Many young women of the present generation have been brought up in nuclear families. They have grown up with little experience of holding a baby in their arms, trying to make a baby happy, or playing with children, reflecting

the decreasing number of children in the society. Then, they get married and give birth to their own child. Therefore, in many cases, the first baby a woman hugs is her own — when she must begin caring for a child for the first time in her life.

A decade ago, I was surprised at a question asked by a mother who had to take her one month-old baby for a medical checkup. She asked me how she should touch and hold her baby. I thought she was joking, but she continued seriously, "My baby does not stop crying when I hold her in my arms. I could not find any direction for holding a baby in my arms in my childcare book, and there is no manual for mothers. Please tell me a good way to hold a baby in my arms."

She told me that she had never held a baby in her arms before. Because it was the first time that I had met a mother in such circumstances, I concluded that the generation affected by the decreasing rate of childbirth had finally arrived. Above all, I was amazed that there was no one for her to ask such a simple question until she came to me.

It was in fact true that she was holding her baby very tightly so that she would not drop her. Her baby seemed unable to move and looked uncomfortable because her mother held her so tightly.

I explained to her that there was no correct way to hold a baby, and that the mother and baby come to know how to hold and be held respectively after the mother tries holding her baby many times. I also told her that the time would come when she would know the most comfortable way for herself and her baby to hold her baby in her arms, and at that point the baby would not accept the way others would hold her and she would cry until her mother held her. Then, I had the mother try holding her baby many times until she got accustomed to doing it and felt relieved.

Since her case, I have been asked the same question from time to time. Therefore, I have come to think that the isolation of mothers has to be taken into serious consideration, rather than merely looked at in surprise.

She was an ordinary, rather intellectual woman who lived with her husband and baby in a block of high-rise apartments. Her husband was busy with work and both pairs of their parents lived far from them. She did not have friends nearby either. Accordingly, no one could come to help her in caring for her child or in solving her problems.

We have to recognize that there are many mothers like her and that it is natural for them to feel a great deal of perplexity and anxiety because they do not have experience in caring for children. Furthermore, their perplexity and anxiety will be even greater when they believe they cannot make any mistake on child rearing because they should not acquire the skill of childcare by repeating mistakes.

In the past, there were many people around young mothers who helped them or gave them advice. Not only relatives, but also neighbors gave advice when they knew that an inexperienced mother was having problems in the care of her children.

Today, people are reluctant to seem to be invading an individual mother's privacy and childcare is carried out behind the closed door of an apartment. Inexperienced mothers are at a disadvantage when facing childcare, and something has to be done right away to help them.

Although a great deal of information is available in the present information age, mothers do not necessarily know which information to rely on. It is probable for example that they cannot find any information that fits their specific problems, which would heighten their anxiety even more.

Improvement in the Child-Rearing Environment and Alleviation of Child-Rearing Anxiety

Measures against child-rearing anxiety among isolated mothers under today's child-rearing

environment are discussed in this section.

From the standpoint of improving the childcare environment, it is most important to prevent mothers from becoming isolated. In short, mothers need someone to support them so that they will avoid the sense of isolation.

The following is an example of an isolated mother who successfully alleviated her child-rearing anxiety.

A competent woman working for a publisher quit the workforce when she had a baby. She wanted to take care of her baby by herself as a mother, rather than asking someone else to do it. Her life with a baby was stimulating and satisfying in the beginning. Soon her baby began what was called, "evening colic," which lasted for several hours in the evening. She had to spend two hours struggling with the housework and her baby's crying every evening.

She began to wonder why she had to be with her crying baby, and remembered the days when she was at work actively editing magazines. Once when her baby would not stop crying, despite hugging or rocking the infant, her frustration reached a point where she covered the baby's nose and mouth with her hand. The baby stopped crying for a moment and stared at her with a reproachful look. The expression on the infant's face made the mother realize the seriousness of her actions and this is when she thought of seeking the advice of a third party for the first time.

The mother then remembered a notice of a child-rearing group posted on the wall of the entrance to the apartment building. Although she did not expect much, she joined the group and told of her experience honestly to the group members. She received positive comments from many of the members and was encouraged by them. They told her that it was not worthwhile to worry excessively about such a single problem and that her experience was very common. She was relieved to know that it was not herself alone who had worries about child rearing. What was particularly interesting was that her baby did not cry that evening. Subsequently, she became the leader of the child-rearing group.

Someone close to the situation needs to support a mother with child-rearing anxiety by listening to her, encouraging her, and thinking about the most constructive way to help her remove her child-rearing anxiety, and which is the most quick and sure method.

Fathers are the most appropriate supporters for mothers who have child-rearing anxiety. It is natural that fathers should share the burden of childcare because they are one of the parents and close to the mothers and their children. Without fail, fathers can alleviate child-rearing anxiety among mothers who tend to have a sense of isolation.

In the past, housework and childcare were regarded as women's duties — not men's. However, in the year before last the Ministry of Health and Welfare (restructured into the Ministry of Health, Labour, and Welfare) produced a poster that said, "A man who does not look after his child is not qualified as a father." The Ministry seemed to be encouraging fathers to participate in caring for their children in order to promote childcare that is free from anxiety in a natural way. Actually, today's fathers often actively participate in caring for their children, and not because they are forced to do so. Many fathers can be seen enjoying child rearing in a positive manner.

It is not only fathers though who can help mothers — friends, parents, brothers, and sisters, or relatives can help them. In the medical field, doctors, nurses, public health organization representatives, clinical psychologists, and caseworkers can provide them with assistance. In the community, public health organization nurses, nursery school teachers, and volunteers at public health centers, nursery schools and children's halls can cooperate with mothers to solve their childcare problems.

The most important thing in alleviating child-rearing anxiety is to recognize that such anxiety is very common among mothers and a mother is not alone.

There is a great difference between childcare conditions fifty years ago and those today; however, it is not a question of which is right or wrong, or that is, it is not possible or necessary to rebuild the child-rearing environment of fifty years ago.

From the standpoint of public health, today's childcare conditions are excellent: As knowledge of hygiene has been disseminated among the public and cities have acquired advanced sanitation facilities, infectious diseases have drastically decreased. The fatality rates among babies and perinatal mortality rates, which are barometers for the maternal and child health standards, are among the lowest in the world. Commodities are abundant and convenience in everyday life has increased. Accordingly, it has become easier, in a way, to raise children.

Despite all the advantages described above, many mothers have child-rearing anxiety. Therefore, it is important to analyze the cause of such anxiety and to construct a system to support them in order that they can enjoy caring for their children under the current social conditions. This is the most efficient way to alleviate mothers' child-rearing anxiety and to promote the sound growth of children.

Measures to Support Child Rearing

The widely adopted measures to support childcare consist of various forms of child-rearing groups. The scale of such groups varies depending on the community. In most cases, a new group leader replaces the existing one when the latter finishes raising her own children. Despite occasional changes and diversity in the forms of child-rearing groups, they continue to exist because group members are aware of the necessity of such groups and they cooperate with each other in continuing the groups' activities.

Some child-rearing groups originate when four or five mothers who have children in the same age group gather over tea and sweets in the home of one of the mothers. The members of such groups gradually increase and they come to use the meeting room of one's apartment building. Some groups are organized by the local nursery center as a childcare support center for mothers in the community. Others are organized by children's halls for the young mothers of the residents, so that they are provided with various events, study sessions, and opportunities to talk to other mothers.

Recently, various types of information on child rearing as well as support for group activities have been provided through the Internet. A list of childcare support groups is available through Internet web sites. Details of childcare support activities by medical organizations and community health centers are also available through Internet web sites.

While, childcare support staff work in a wide range of fields. In order to develop human resources associated with childcare support, deliberate consideration should be given to the content of staff training and basic instruction to be given. Close communication among workers in these areas is also necessary.

Conclusion

The child-rearing environment has drastically changed during the last fifty years, producing many causal factors for child-rearing anxiety. In order to alleviate anxiety among mothers under current social and childcare conditions, it is not sufficient to support only those who are involved in maternal and child health. It is vital to construct a community-wide system to support childcare, which will lead to building the community of the twenty-first century in which everyone believes in child rearing that is anxiety-free and meaningful.

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Psychology of Parent-Child Relationship

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Abstract: Findings that have been gained from psychological studies on parent-child relationship desired for the healthy development of the mind in infants, with particular emphasis on how to raise infants are discussed herein. First, a conceptual scheme to examine mother-infant relationship, the most important aspect of early parent-child relationship, is presented. For instance, structural components of mother-infant interactions are shown diagrammatically. Based on the figures, development of infants during the first two years since birth is discussed in relation to the mother-infant interactions by dividing it into three phases. Specifically, primary characteristics of developmental changes in the ability of infants to communicate during the first two months of life, two to six months, and six to 18 months are exemplified, and the characteristics of the mother-infant interactions strongly related to such changes are organized. Subsequently, how the behavioral changes in parent-child relationship might be related to the tasks concerning mind development in infants is clarified. Finally, the current situation of the parenting environment in Japan, including the issue of participation by fathers, and clinical tasks are presented.

Key words: Early mother-infant interaction; Developmental task; Parent-child relationship; Parenting environment in Japan; Affect attunement

Introduction

For this article, I have been asked to discuss the parent-child relationship recommended for healthy development of the mind in infants, with particular emphasis on how to raise infants, based on findings that have been gleaned from psychological studies. First, the basic components of parent-child relationship are summarized. Subsequently, the relationship between tasks concerning psychological development of infants and parenting environment is discussed. Finally, the future parenting environment, including the issue of participation by fathers, is mentioned.

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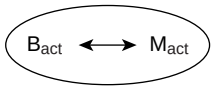
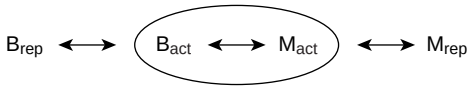


Note) B_{act}: Infant's actions
M_{act}: Mother's actions

Fig. 1 Interactions between an infant and a mother[7)]



Note) B_{rep}: Infant's representations
M_{rep}: Mother's representations

Fig. 2 Experience of the interactions between an infant and a mother[7)]

Behavioral Exchanges and Exchange of Minds

"Relationships" are "exchanges" that exist among people. Early parent-child relationships are often discussed in terms of the importance of the mother-infant relationship. In psychology, exchanges between a mother and an infant is called "mother-infant interaction" and studied commonly. Mother-infant interaction is developed not only one-sidedly, but as a mother and an infant affect each other, each changing their own behavior to match the other's, and vise versa. From birth, a child takes the initiative to actively exercise his or her abilities to communicate depending on the development stage (Fig. 1).

Characteristics of the interactions up to two years are summarized by each primary developmental transition. The subjective experience of a child in the mother-infant interaction during these two years is qualitatively different from how things are experienced thereafter, due to how infants develop during this phase, which is very important to know if one is to offer advice on how to take care of and raise infants.

1. Up to two months of age

What is required during the initial stage of early mother-infant relationship is for both to share the moment they interact with each other.[1)] For example, newborns have characteristic behaviors and affective expression patterns at different conditions of alertness that overall "appeal" to mothers for something. Namely, interactive experiences start irrespective of the intent of the newborn when the mother seeks out meaning in the behavior of the newborn.

Although infants cannot subjectively experience these interactions as adults do, there is at least a "world of meanings" from the perspective of the mother that supports visual behavioral exchanges. In other words, this is a qualitative aspect of the interaction that concerns how a mother is experiencing what the child is experiencing. Expanding the basic components of mother-infant interaction in Fig. 1 to Fig. 2 may be of clinical help in understanding parent-child relationships.

The most important point in clinical psychology during the parenting phase is to listen to how a mother feels regarding her involvement with a child. Stern[2)] calls what parties involved in an interaction subjectively experience "representation." The world of infant's representation remains in a speculative territory since we cannot ask an infant, "What is your experience?"

2. Two to six months of age

Qualitative changes occur in the ability a newborn is either born with or rapidly develops each day. Transition from spontaneous smiles to social smiles occurs, and infants begin to smile at their mothers as though they are full of affection. They also become able to look into another person's eyes, which increases the moments when mothers feel that they have built a mutual relationship. Although it has not been thoroughly determined why this sort of dramatic developmental changes occur at two months of age, it can be said that infants are

further involved in human interactions during this stage of mother-infant interaction.

Mothers continually but finely adjust how they communicate with the infant and adjust the alertness of the infant in order to draw the infant's attention and to keep the infant happy. It is important to maintain the best possible condition of alertness in an infant to make communication with others possible under favorable conditions. This is not a matter dependent only on the mother.

For example, due to individual differences among infants, some infants may be temperamentally irritable and not very good at calming down. In such cases, they would get easily excited, but start crying or break down with little stimulation, making it difficult to carry on long interactions with other people.

However, during this phase, many healthy mothers are deeply involved with their relationship to their children that such objective individual differences in how infants react does not seem to affect the subjective experiences of mother-infant interaction from the perspective of mothers. Namely, all mothers tend to overlook the difficulty in dealing with infants, viewing it rather as individuality, which is preferable. Resultantly, this likely protects mothers from the hurt that comes from failed interactions.

On the other hand, infants also adjust their own alertness in their own way by interrupting and resuming interactions. For example, infants are known to commonly look away as though to reject any involvement when a mother's response is too strong and stimulating. By this behavior, the flow of interaction becomes temporarily uncomfortable, causing the mother to immediately correct the intensity of her response, which in turn resumes the interaction.

3. Six to 18 months of age

During this phase, qualitatively great changes occur in the mother-infant interactions as it becomes possible for an infant to have intersubjective involvement[3] with others. Specifically, infants begin to understand not only their own intentions and feelings, but also that others have them also.

For example, we begin to observe social referencing when the infant determines the next action based on the mother's affective expression when faced with uncertainty of her own judgement.

There is also a concept called affect attunement[2] in relation to sharing intersubjective affects between a mother and an infant. This is a series of interactions that occurs when a mother senses the affective condition within the infant from the infant's behaviors, and responds to the infant in a way that reflects how the infant is feeling, thereby enabling the infant to feel that the same affective condition that is shared by the mother.

For example, let us say that an infant raised a toy and vocalized to the mother with a happy look. The mother will likely respond, "Oh, wow!" subconsciously nodding her head to a degree that would match the intensity of the infant's hand motion or voice. When the infant then goes back to playing by taking toys up and down with great satisfaction, we would say that affect attunement has occurred. The internal understanding that the mother shares the amusement of playing with toys enables the infant to store this experience of interaction as an experience of even greater joy. The presence of these interactions teaches us that an exchange of "mind" between a mother and an infant has been established.

In clinical situations, I occasionally see parent-child relationships that do not seem to be right even though there may be no specific behaviors out of the ordinary. At times like this, observation of the parent-child interactions from the perspective of the infant has sometimes revealed that there is a slight repetition of mismatched response on the parent's part to the affective expression of the infant. This is called mis-attunement, and it is one of the characteristics of parents and children who have relational problems.

Psychological Development of Infants and Parent-Child Relationship

Early mother-infant interactions begin by the mother adding meaning to the child's behaviors, which move on to mutual adjustment of emotions as exchanges increase, and then the interactions begin to be experienced intersubjectively as the infant begins to understand the presence of intentions and minds in other people. Mother-infant interaction begins to have significance called "shared experience of emotions (mind)" that is essential for affective development of infants or the personality formation.

The important qualitative aspect of mother-infant interaction will have already been established by the time the infant begins to interact with others using words during the second half of the two years since birth.

Let us think about this in relation to the tasks of psychological development during this phase, based on Erikson's theory.[4] It is well known that he stated that the task of psychological development for the fist year of life is to gain basic trust, and the task around the age of two is to gain autonomy.

Erikson says that these tasks for development are achieved through an appropriate parenting environment for the infant, namely, a qualitatively favorable maternal relationship. What is a "favorable maternal relationship"? Actually, this does not imply a one-sided relationship offered by the mother. Rather, as Emde *et al.*[5] put it, it signifies the reciprocating relationship that psychologically rewards the parent as well when the infant expresses emotions in response to the mother's response. This is no different from the development of healthy mother-infant interactions mentioned earlier.

Therefore, maternal relationships required for the infant to develop basic trust and to perform tasks of psychological development imply repeatedly shared experiences of the infant asking for something, the parent fulfilling this need, and the parent being fulfilled by seeing the infant fulfilled. Because there is such a reciprocal aspect to the mother-infant relationship, an intimate relationship where the mother and child are a pair, such as one described by Winnicott[6] in his statement "there is no baby who is alone," can be maintained.

Various System that Surrounds the Parent-Child Relationship

Anyone would admit that a good parenting environment is essential for the healthy development of a child's body and mind. However, in our society today, people have started to recognize the wrongfulness of burdening the mother with the entire responsibility to create a good parenting environment.[7] The most significant problem ought to be the fact that realistic measures in response to the rapidly declining parenting function in local areas due to reduced birthrates are overdue, while delusions that women can naturally carry out parenting when they give birth to a child remain unexamined.

The heavier burden of parenting a mother carries, amidst the trend toward the nuclear family, may reflect the reality that the father cannot take on the role expected of him in accordance with the changes in family structures. The Ministry of Health and Welfare (currently, the Ministry of Health, Labour, and Welfare) created a catch phrase in 1999 as one of their measures to support reduced birthrates and parenting which goes, "Men not involved in parenting will not be called fathers." I recall there were various discussions surrounding the issue of whether or not this was appropriate at the time. It is clear fathers are not commonly involved with parenting in Japan from surveys that have been conducted in Japan and overseas.

For example, a basic survey on social life conducted by the Census Bureau of the Management and Coordination Agency (currently, the Ministry of Public Management, Home Affairs, Posts and Telecommunications) in 1996

showed that even the generation of fathers that is most involved with parenting (25–29 years of age) spend only 12 minutes on an average each day "parenting" (2 hrs 02 min. for mothers). A survey conducted to determine the reasons for such little involvement in parenting on the part of men disclosed three primary reasons: "business with work," "views of gender roles" (men are to work and women are to take care of the home), and "fathers' views of children" (for example, people who think "children will grow without parents" are less involved with parenting).[8)]

All three reasons are greatly affected by our social model. What jumps into a clinician's eyes first in clinical psychology is the presence of a mother heavily involved with her children's problems. However, in my clinical experience, such cases are most often not free of the problem of poor parenting function on the father's part.

Family is the strongest cooperator of cares surrounding children. Even family members who do not directly affect the act of raising children have important roles of supporting the family member with the heaviest parenting burden.

In addition, there is a multifarious system that supports the relationship between a parent-child pair. It may also be important to look around the surrounding environment of the parent-child relationship that needs to change and consider supportive resources that could be used.

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Prevention of Child Abuse

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Abstract: Child abuse has recently become the focus of attention as a significant social problem with the number of related consultations drastically increasing 15-fold in the past 10 years. The "Law Concerning Prevention of Child Abuse" also came into force in 2000. The law stipulates the obligation of physicians to take appropriate measures to detect any abuse in its early stages and to report any such abuse once detected based on Article 25 of the Child Welfare Law. The major objective in preventing abuse is to protect children from physical and psychological risks. To achieve this objective, medical personnel are requested to take measures to protect children in conjunction with other organizations. Their protective role is a broad one that includes not only the detection of abuse but also the medical evaluation of such abuse, treatment, legal measures, in-home care, and prevention itself. This paper explains the definitions of abuse, its classification (physical abuse, neglect, sexual abuse, psychological abuse, and special forms noted clinically) and the role of medical care.

Key words: Child abuse; Role of medical treatment; Child abuse prevention law; Children's rights

Introduction

Recently, child abuse has been capturing the attention of this society. The number of consultations brought to children's counseling centers throughout the country has rapidly risen by approximately 15 times in 10 years, from 1,171 cases in 1991 to 18,804 cases in 2000 (Fig. 1). This increase, however, could be representing an increase in the discovery of abuse due to enhanced social awareness rather than an increase in the rate of abuse itself. However, it is true that some individuals directly involved with the issue claim that the actual number of abuse is also increasing. The number only represents the number of incidents of consultations at children's counseling centers, which is only the tip of the iceberg of large scale abuse. In reality, it is thought that many more children suffer abuse.

The role of physicians is significant in protecting such children. The duty of early discovery

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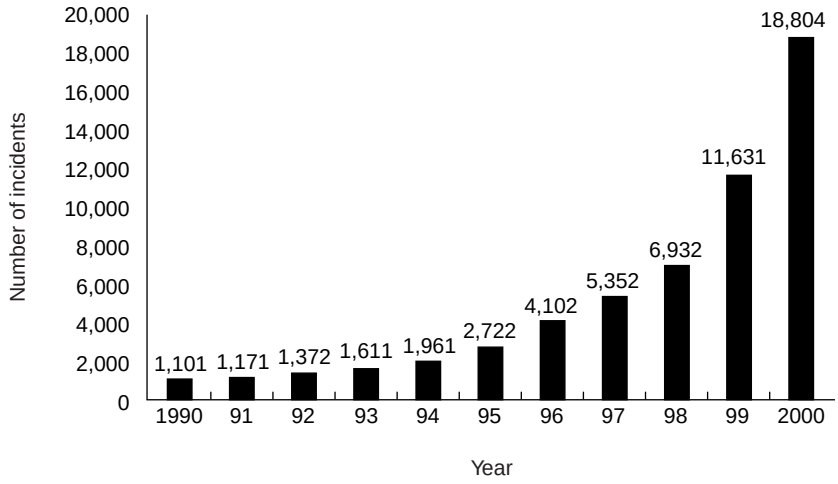

Fig. 1 Incidents of consultation concerning abuse

on the part of a physician is explicitly stated in Article 5 of "the Law Concerning Prevention of Child Abuse (henceforth, Child Abuse Prevention Law)" that was put into effect in 2002. It has also been reemphasized that those who discover signs of abuse must report to a children's counseling center or a welfare office in accordance with Article 25 of the Child Welfare Law. However, the role of healthcare professionals is not limited to discovery and prevention. Protection of children, medical evaluation of the abuse, physical and mental treatment of children and their family, and prevention of abuse are also important roles of healthcare professionals.

What is Child Abuse?

Child abuse is a serious violation for the rights of children, as the minority status in our society. Specifically, it includes physical abuse, neglect, sexual abuse, and psychological abuse.

Physical abuse is physical violence such as hitting, kicking, and burning. Fracture, intracranial hemorrhage, and internal hemorrhage are also common besides skin injuries that can be seen. This is a type of abuse that must not be missed by physicians. Early protection is particularly important for infants who tend to be under greater danger.

Subdural hemorrhage and retinal hemorrhage by the rapture of bridging vein caused by being shaken is not uncommon among infants, whose heads are relatively heavy, making it difficult to keep their necks steady. This is called "shaken baby syndrome."[1] This may also accompany fracture of ribs or limbs where the infant was grabbed for shaking, although such findings are not required for the diagnosis of this syndrome. There is also a special form of abuse called "Munchausen by proxy."[2] This diagnosis is used for parents who create diseases for their children so that they can be admitted to hospitals repeatedly. For example, some parents may give large doses of purgatives for another hospital admission, endangering the child's life. Those parents seem to desire medical attention.

Neglect refers to not providing care necessary for children. This includes not only failure to care for children physically, such as not giving nutrition, not keeping them clean, and not maintaining livable temperatures, but also not giving their emotional need or endangering children by neglecting to keep an eye on them. For example, leaving a child alone in the parking lot while playing *pachinko* for a long time also falls under the category of neglect. Neglect

also includes healthcare neglect, which refers to neglecting to have children receive healthcare such as vaccinations, and medical neglect, which refers to not providing the child necessary medical attention. In any of these cases, early intervention is important as life can be endangered.

Sexual abuse is referred to exposing a child to sexual stimulation inappropriate to their developmental age. Even when there is no sexual contact, taking pornographic pictures of children or showing pornography to children also falls under the category of sexual abuse. Victims are not necessarily girls, and also include boys; the age ranges from infancy through adolescence. While the "Child Abuse Prevention Law" limits the term for cases when the offender is the guardian of the child, all adults including grandparents, relatives, and acquaintances are also considered potential offenders of sexual abuse in most developed countries. While sexual abuse may also entail medical harm to the body, such as laceration of genitals and sexually transmitted diseases, it also puts children at a high risk for mental damage such as dissociative disorders and sexual acting out.[3] Early separation from the abuser and mental care are absolute requirements.

Due to a high risk for mental damage, psychological abuse is the most difficult abuse to handle. Much attention has been paid by those living in countries well advanced in dealing with abuse, such as in North American countries. This includes verbal abuse, such as repeatedly telling a child, "You should not have been born" or "You are a demon," speaking words that are degrading to a child, putting a child through a frightening experience, showing favoritism among siblings, forcing a child to commit crimes such as theft, and continually putting excessive expectations on a child to achieve what the child cannot do.[4]

Discovery of Abuse

Parents or children involved in the abuse will hardly ever report it themselves. Discovery of abuse, therefore, always begins with suspicions. Since healthcare providers are not used to doubting people, they may even feel a sense of guilt associated with such suspicion. Nonetheless, the goal is not to punish the parents but to support parents and children so that children are protected, which can not be happened without suspicion. Suspicion is important.

We suspect abuse when we notice anything "unnatural." For example, we need to notice the unnatural nature of things such as frequent accidents that would not occur under normal conditions, an injury that one would not get simply by falling, an unnaturally long period before seeing a doctor, an explanation that does not make sense in light of the injury or disease or one which changes with time, and medically unexplainable malnutrition or short height. Even in relation to a child's behavior, it is important to suspect abuse when there is lack of expression, overly affectionate behavior towards anyone, fear or tension in the presence of parents, or sexual behaviors and comments unbefitting of age.

Initial Intervention

Initial intervention is needed when abuse is suspected. The most important objective of intervening to abuse is to protect children from physical and mental risk. There are four dangers children are exposed to in abuse: danger to life or danger that leaves permanent bodily injury, danger that leads to mental disorders, danger that certain behaviors might cause abuse to recur, and danger that a person might turn into an offender who physically abuses the weak or abuses one's own child. The objective is to protect children from such dangers.

If abuse is actually suspected, it is important to listen to children and parents separately, if the child is old enough to talk. Physicians can be creative in doing this, such as by asking the child questions during examination in a separate room or by having a nurse to ask the child

questions as the nurse plays with the child while the physician is talking to the parent. Abusive parents do not always appear to be violent people. Appearance should not be the basis of judgement, and attention should be paid to the content of the story and how it may change. Content of what parents and children tell should be recorded as precisely as possible. Other thing should be recorded is how the child or parent acts or interacts.

Then, before physical examination children must be given an adequate age-dependent explanation so that they do not feel anxious. After having them take their clothes off, condition of skin, presence of any scars, body proportion, and symmetry should be examined. Physical examination of the entire body should then begin, and conducted thoroughly. If violence to the face is suspected, it may be necessary to have the child examined at an ophthalmology or ENT clinic.

However, since children who have undergone sexual abuse may experience further psychological damage by being seen without clothes, there may be situations when physical examination should not be performed or performed only by an experienced physician or a female doctor. When physical examination needs to be conducted immediately, the child must be fully convinced of the purpose and methods of the examination, and examined slowly so as to alleviate any anxiety. It may be a good idea to have a nurse continually speak to the child so that the child will feel safe. Visual inspection is generally considered sufficient when examining the genitals in the case of sexual abuse.[5)] One must be careful not to unnecessarily cause further psychological invasion. It is also important to record findings that have been obtained through the examination.

When neglect is suspected, it is important to take a look at the "maternal and child health handbook." This may be helpful in verifying whether there has been failure to keep records and whether the infant has been receiving routine check-ups and vaccinations, as well as in determining when the child might have been most neglected by drawing a growth curve based on the information on height and body weight. Also, systemic bone imaging may be required when physical abuse is suspected, and blood tests may be helpful when malnutrition is suspected.

It is also meaningful to ask nurses and receptionists about their impression of the parent and child, since parents who may show commendable behavior before physicians may act more aggressively in front of nurses or hit the child in front of receptionists. Children should be actively admitted not only when their physical condition medically requires admission, but also when treatment could be given at home under normal circumstance, so that the child can be protected.

When it seems that there is abuse, it should be reported to the child guidance center. There is no need to prove abuse. A report must be filed if there is any reason for suspicion. However, notifying parents about the report is a very sensitive matter. It seems that it is commonly more effective to notify parents upon consulting the child guidance center. When notifying parents, it is important not to accuse them, but to explain that it is necessary to ensure a good parent-child relationship. Parents who abuse their children are not necessarily evil people. It is not uncommon that they are troubled by or that they are anxious about the vicious cycle of their relationship with their children. Physicians can explain to the parent the fact that physicians have the duty to report to the child guidance center when abuse is suspected, and let the guidance center handle the subsequent notification.

Medical Evaluation of Abuse

Medical institutions may be asked to perform medical evaluations of a child suspected of having been abused. When physical abuse is suspected, detailed systemic examination and systemic bone imaging are required, and when

head injury is suspected, facial bone CT, head CT, ophthalmologic examinations, ENT examinations, and EEG will be required.[6] However, since x-ray findings can be very difficult to interpret in the case of abuse, it would be desirable to consult a pediatric radiologist. Additional examination may also be required; for example, dermatological findings will be required for burns, and echography will be needed to verify the presence of any internal hemorrhage when there is abdominal pain.

When there are growth problems or slow development possibly caused by neglect, nutritional conditions and the state of development should be examined in order to differentiate them from metabolic diseases or endocrine diseases. When sexual abuse is suspected, the presence of sexually transmitted diseases should also be verified in addition to examination of genitalia.[7]

While mental evaluations of children should be made in all abuse cases including psychological abuse, this may not necessarily be possible due to limited number of specialists. Nevertheless, any notable behaviors should at least be recorded.

Abuse is made through holistic judgement. Although one finding renders the possibility of abuse low, multiple findings may reveal a very high possibility of abuse. It is, therefore, important to always keep in mind the importance of seeing the big picture rather than only one finding. Request for such systemic assessment will likely increase in the future. While the topic of abuse is given a chapter in pediatric textbooks overseas, it is not yet mentioned in most Japanese textbooks. Physicians who see children will need more knowledge on medical findings of abuse.

Treatment

Some children may require treatment of physical injuries and medical rehabilitation for sequelae as a result of abuse. It is not uncommon for parents not to follow instructions in the case of abuse. Therefore, it is important that we make sure they are being compliant with drug treatment and other necessary care for their children. Mental care is also commonly required for children and parents. Besides post-traumatic problem of an abused child, mental problems in a child that have been caused by abusive or neglectful parent-child relationships are also said to commonly lead to a high risk such as personality disorders in the future.[8] The need for mental care may increase in the future also from a social standpoint.

Legal Response

Chances of physicians encountering legal situations other than situations of abuse may be increasing. Physicians should not feel uncomfortable dealing with law, and thereby avoid any involvement, but rather, they should respond in a proper manner so that many children can be helped. Even when it is difficult to verify that a child has been abused, physicians should be able to at least prove their own findings. Further development of forensic medicine may be needed.

Home Support

There may be times when providing home support becomes necessary, rather than separating parent and child, even when abuse exists. In such cases, healthcare professionals may need to function as members of a supportive network for the parent and child, cooperating with the team so that the parent-child relationship will improve, while monitoring them from a medical standpoint. Many parents wish to correct their children's behaviors by scolding them very harshly or by giving them physical punishment. This, however, frequently causes the children's behaviors to worsen in the long run. Parents would then continue to try to correct the worsening behaviors by hitting and scolding them very strongly. A lot of parents will continue using the same methods even

when they seem futile because they do not know any other methods. Sometimes it is helpful to teach parents alternate methods of handling their children, such as the "time out" method rather than those that aggravate their children.

Also, it is not uncommon for parents themselves to have been abused as children or to have grown up feeling unloved. There is a growing number of places that support parents such as through counseling and support groups. There are times when we need to refer parents to such supportive places. Phone counseling conducted by civilian networks is also often helpful for parents. This requires us to be resourceful in information on our local society and to deepen our connections.

Abuse may worsen even when many organizations are cooperatively supporting families at home. When heightened danger is sensed, intervention is necessary in cooperation with the child guidance center. It is a tragedy not only for children themselves but also for parents when a child dies or develops sequelae. Protecting both parents and children from such danger is the least that is required of us.

Prevention

It would be ideal if we can prevent abuse from happening to children. In particular, studies have shown that premature babies who were immediately separated from parents upon birth, and children who are difficult to raise, such as those with disabilities, are more prone to abuse. Since healthcare professionals are more likely to encounter such parents and children, it is important that they offer appropriate support and prevent abuse.

Conclusion

Although healthcare professionals have only just started to get involved with child abuse, the expectations of people in other fields have for them are surging. It is, therefore, with great urgency that healthcare professionals need to prepare themselves to deal with such situations.

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Post-Transfusion GVHD

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Abstract: The Japanese Red Cross Society has appointed representatives to Blood Centers nationwide to collect information on blood transfusion-associated adverse reactions, and data on 310 suspected cases of post-transfusion GVHD were collected during the 8-year period from 1993 to 2000. A diagnosis of post-transfusion GVHD was made in 61 cases based on the demonstrated presence of donor lymphocytes in the patients' peripheral blood using a microsatellite analysis technique developed by the Japanese Red Cross Society. Case distribution was analyzed according to patient background characteristics. In a majority of the cases examined, transfusion was made from a homozygous donor of a HLA haplotype to a heterozygous patient of the specific HLA haplotype. The analysis of data also revealed that patients aged ≥70 and those undergoing transfusion for the first time were more liable to develop post-transfusion GVHD. Cells cloned from patient peripheral blood lymphocytes were assessed for their immunological characteristics to delineate subsets involved in GVHD. Analysis of these clones has led to the discovery of a drug (Futhan®; Torii Pharmaceutical) which suppresses their cytotoxic activity of these clones. The drug has proven to be effective both *in vitro* and *in vivo*.

Key words: Postoperative erythrodermia; Microsatellite; Post-transfusion GVHD; Irradiation (of blood for transfusion)

Introduction

In 1955, a paper entitled "On postoperative erythrodermia" was published in *Geka* (Surgery) by Toshimaru Shimoda[1)] of the Department of Surgery, Chiba University School of Medicine. The term "postoperative erythrodermia" was applied to a clinical condition characterized by serious symptoms including fever, erythema, and hepatic dysfunction that developed postoperatively in the twelve cases reviewed therein. Although the etiology remained unclear, Shimoda believed it to be multi-organ failure due to bacterial toxins. Six of the 12 patients died and the other 6 recovered. Leukocytopenia was noted in 5 of the 6 fatally affected patients. In retrospect, the clinical manifestations observed in the 5 docu-

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mented cases were consistent with those of post-transfusion graft versus host disease (GVHD). Postoperative erythrodermia subsequently became the focus of growing concern as a serious adverse reaction of surgery, especially in the field of heart surgery.

Under such circumstances, Aoki *et al.*[2] from the Department of Internal Medicine, Tsukuba University Hospital, reported a valuable case in the Journal of the Japanese Society of Internal Medicine (1984). The patient underwent a massive blood transfusion due to a gastrointestinal hemorrhage following surgery for an abdominal aortic aneurysm. Six days after the final transfusion, the patient developed fever and erythematous macules accompanied by liver dysfunction and diarrhea, and subsequently pancytopenia. Pathologic examination of bone marrow aspirates disclosed lymphocytes containing large granules adhering around the injured hematopoietic stem cells. The report has demonstrated that GVHD may be etiologically implicated in some cases previously diagnosed as postoperative erythrodermia.

The report has generated momentum for a reassessment of postoperative erythrodermia as GVHD, and active research has commenced in this field. The widely accepted theory that GVHD occurs only in immunodeficient patients has thus become subject to reexamination.

Reexamining Postoperative Erythrodermia as a GVHD

In their study conducted to examine the human leukocyte antigen (HLA antigen) complex in peripheral blood lymphocytes collected from patients, Sakakibara and Juji (1986)[3] noted the existence of 2 patients bearing HLA antigens apparently distinct from those assumed to have been inherited, indicating that the patients' own lymphocytes had been replaced with those from the blood donor.

Matsushita *et al.* of the Department of Pathology, Toranomon Hospital, found that lymphocytes isolated from skin lesions in 2 female patients diagnosed as having postoperative erythrodermia contained Y chromatin of male origin. This indicated that lymphocytes from a male blood donor had proliferated and mounted attacks upon various organs in these female patients.

An in-depth study of a case conducted using HLA antigens was reported by Ito *et al.*[4] from the Department of Blood Transfusion, Kyoto University Hospital, in collaboration with Kyoto Blood Center of the Japanese Red Cross Society (JRC) (1988). They performed HLA typing of blood cell samples collected from the patient prior to and after the onset of postoperative erythrodermia. Two different HLA haplotypes assumed to be present from a genealogical examination were identified in the patient prior to onset. However, after the development of the disease, these two different HLA haplotypes were found to have been converted to homozygous with one of the haplotypes. Among this patient's blood donors, one donor had identical homozygote of the haplotype to the post-onset haplotype found in the patient (i.e., homozygous HLA haplotype). The blood donor (AA)-patient (AX) combination in the case was thus unidirectionally compatible in terms of the HLA haplotype.

Thus, several studies in Japan have led to the formation of a consensus that some postoperative erythrodermia, if not all, are considered to be a post-transfusion GVHD.

Pathogenetic Mechanism of Post-Transfusion GVHD

Researchers in basic immunology discovered a new immunological phenomenon around the time when postoperative erythrodermia was reported by Shimoda in 1955. In an animal with radiation disorder, injection of splenocytes from another animal of the same species may be effective in treating the disorder, however, another disorder may develop after a period of time. This is a so-called secondary disease and is attributed to immune reactions against the

host caused by immunocompetent cells among the injected spleen cells, thereby mounting an attack on the host. Occurrence of acute GVHD after bone marrow allotransplantation was documented by Mathé *et al.* (1959) and after blood transfusion in immunologically deficient children by Hathaway *et al.*[5] (1965).

The following two conditions are noted in the development of GVHD: (1) Immunocompetent cells (chiefly, lymphocytes) injected extraneously are not precluded by the host, and (2) host tissue is recognized as a foreign body (i.e., possessing different histocompatibility antigens) by the injected immunocompetent cells.

Blood transfusion into immunodeficient (deficient in cell-mediated immunity) patients would fulfill the above conditions. In such case, immunocompetent cells contained in transfused donor blood are incapable of excluding any HLA types; hence the patients are vulnerable to immunologic attacks. When blood from an HLA haplotype homozygous donor (A24, B52 and DR15 is the commonest haplotype among Japanese) is transfused into a heterozygous patient of the haplotype and other haplotypes than the haplotype, the patient is unable to recognize immunocompetent cells contained in the transfused donor blood as foreign bodies and is competent for those cells even if the patient is not immunologically deficient. These cells recognize HLA antigens of the non-public haplotype distributed in patient tissues as foreign bodies and may eventually launch an attack.

Nationwide Survey on Incidence of Post-Transfusion GVHD

In view of the high frequency of suspected post-transfusion GVHD events reported among heart surgery cases, in 1986 the Japanese Society of Blood Transfusion in cooperation with the Japanese Society of Thoracic Surgery collected clinical data on suspected cases of post-transfusion GVHD encountered among 63,257 cases treated by open heart surgery at 137 hospitals nationwide during the 6-year period from 1981 to 1986. An analysis of the data revealed that post-transfusion GVHD was diagnosed in 96 patients; i.e. an incidence rate of 1 per 658.9 patients with open heart surgery.[6] A nationwide survey conducted by the JRC Research Group in 1991 revealed the frequent occurrence of post-transfusion GVHD not only among cases of cardiovascular surgery but among cases of surgery for malignancies as well.

Method for Definite Diagnosis of Post-Transfusion GVHD

It is essential to demonstrate the presence of donor-derived lymphocytes in the patient peripheral blood at a certain level, using a small quantity of blood sampled from the patient. In general, it is considered risky to unduly raise sensitivity levels in terminal-stage patients with pancytopenia because they are receiving blood transfusions on consecutive days. As far as the cases we have examined are concerned, replacement of peripheral blood lymphocytes with lymphocytes of donor origin was evident in the majority of patients with post-transfusion GVHD. We have established and reported a laboratory testing method which utilizes the fact that the number of repetitions of the gene base sequence for microsatellite markers varies among individuals (1994).[7]

This test requires the use of a nail specimen and a small volume of blood sampled from the patients. Lymphocytes from a donor do not infiltrate the nails even if post-transfusion GVHD has developed. The electrophoretic pattern of DNA extracted from the nail, being taken as patient-derived DNA, is compared with that of DNA from circulating blood lymphocytes. Care is taken to avoid incidental concordance by selecting five highly polymorphic microsatellite sites for the assay.

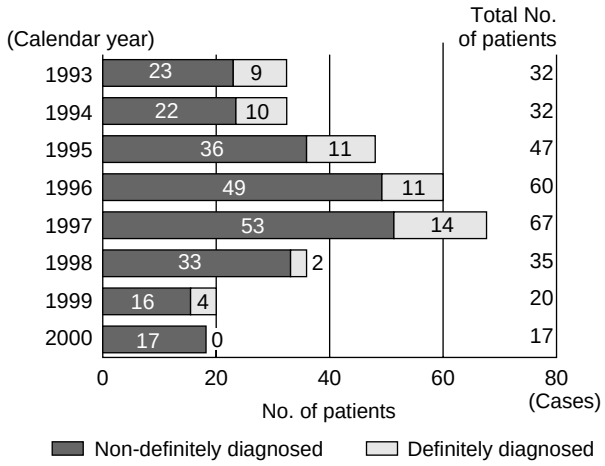

Fig. 1 Polymorphic microsatellite analysis data on suspected cases of post-transfusion GVHD

Drug Information Activities of the Japanese Red Cross Society

Beginning in 1993, the Japanese Red Cross Society has been appointing drug information officers to Blood Centers nationwide to collect information on adverse reactions to blood transfusion, and has analyzed the information collected. Accordingly, any data considered to be of significance has been reported to the Ministry of Health, Labor and Welfare.

Cases of suspected post-transfusion GVHD found have been subjected to the above microsatellite test since 1993 (Fig. 1). A definite diagnosis of post-transfusion GVHD was made in 9 of the 32 cases with relevant specimens reported in 1993. During the period from 1993 to 2000, 310 cases with relevant specimens were reported as suspected cases of post-transfusion GVHD to the JRC Central Blood Center from medical institutions across the country, with a diagnosis of post-transfusion GVHD being established in 61 cases based on microsatellite test data.

Analysis of Background Factors in 61 Definitely Diagnosed Cases

Gender difference: Thirty-eight male and 23 female cases were definitely diagnosed with GVHD; there was no statistically significant difference between the sexes.

Aging: Of the 61 patients, 31 were aged ≥70 years while patients at 59 years or younger numbered fewer than 6. When age distribution is compared with the number of blood transfusion units used in the Tokyo Metropolitan Area, nationwide data revealed a significant difference for the ≥70 years age group at $p<0.01$, indicating that aging constitutes a risk factor for post-transfusion GVHD.

Blood transfusion history: Fifty-one of the 53 patients, excluding 8 cases with no documented blood transfusion history, experienced GVHD following the first transfusion. It has been suggested that resistance to post-transfusion GVHD may be induced in patients undergoing repeated blood transfusions. Laboratory animal study data supporting this hypothesis have also been reported. The primary disorders for which surgery was performed included malignant tumors in 25 cases, cardiovascular disorders in 13 cases, and traumas in 9 cases. In 2 patients who received blood transfusion for massive hemorrhage from a gastric ulcer, GVHD developed after the transfusion alone without surgical intervention.

Patient-Donor Combination of HLA Antigens

In a majority of the cases examined, the donor was homozygous with a haplotype: HLA-A24, B52 and DR15 while the patient was heterozygous with the said haplotype plus a different haplotype. Cases also included a combination of a haplotype homozygous donor (A33, B44 and DR13), ranking in second place in terms of frequency, and a heterozygous patient. There were a donor-patient combination where the HLA-A and HLA-DP antigen series were homo-/heterologous and 2 combinations where only the HLA-DR antigen series was homo-/heterologous. In cases of severe combined immunodeficiency, the condition has no specific relationship with patient

and donor HLA antigens, hence transfusion of blood from any other individual may lead to the development of GVHD.

Establishment of Cell Clones from Peripheral Blood Lymphocytes

As it is inferred that donor-derived immunocompetent cells in the blood of a patient mount an attack on host tissues, we attempted to clone such cells to analyze their characteristics. Cell clones were prepared from lymphocytes of a total of 5 patients. The target antigens for the $CD8^+$ cytotoxic T cell clones were found to be class I antigens such as HLA-B46 and B52. The target antigens for the $CD4^+$ cytotoxic T cell clones were noted to be class II antigens such as HLA-DR4, DR13, DR15, and DP4. Another $CD4^+$ clone obtained had no direct cytotoxic activity, responded with proliferation to antigen stimulation and produced tumor necrosis factor (TNF). A B cell clone elaborating an antibody which reacts with HLA-DR4 antigen was also obtained.[8)]

Treatment of Post-Transfusion GVHD

An attempt was made to seek drugs for treatment of post-transplantation GVHD using the cytotoxic cell clones proven to react with target antigens *in vitro*. The exploration was conducted using commercially available drugs insomuch as it was impracticable to try new drugs in patients with post-transplantation GVHD where death usually follows within 1–2 weeks of the onset of clinical symptoms.

Involvement of perforin and granzymes constitutes, at least in part, a mechanism whereby cytotoxic T cells mount an attack on target cells. Perforin makes a hole in the cell membrane of target cells, and granzyme injected by the T cell injures the target cells via its enzymatic activity. The granzyme exhibits serine protease activity during the cytotoxic process. Futhan® (nafamostat mesilate), which inhibits the serine protease activity and has been used

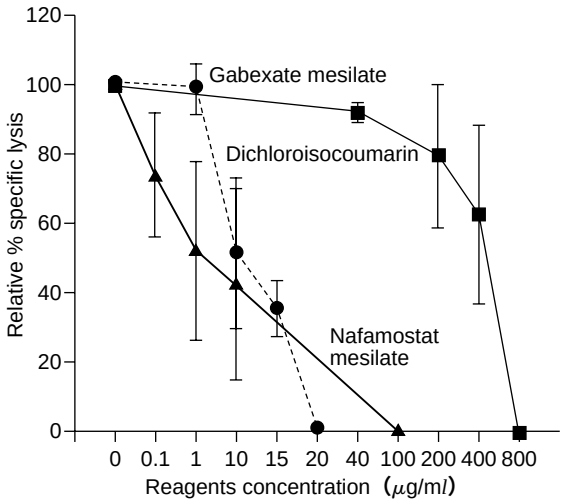

Fig. 2 Suppressive effects of drugs on cytotoxic activity

to treat disseminated intravascular coagulation syndrome (DIC) was discovered to markedly suppress the activity of a cytotoxic T cell clone.[9)] FOY® (gabexate mesilate), another drug used for the treatment of DIC, was demonstrated to be entirely ineffective in this respect (Fig. 2).

Futhan® was administered to 4 patients with post-transplantation GVHD, all of whom responded with symptomatic amelioration. Analyses by the microsatellite method revealed that peripheral blood lymphocytes returned from donor-predominant to the patient's intrinsic population.[10)] Nevertheless, plasma potassium elevation may occur as an adverse reaction inherent to the use of Futhan®. In the first 3 cases, the Futhan® medication was discontinued as plasma potassium increased to $>6\,\mathrm{mEq}/l$, and subsequently GVHD recrudesced, fatally affecting the patients. In the fourth case, the treatment with Futhan® was continued while appropriate measures were adopted to control the plasma potassium level, to effectively suppress the recurrence of GVHD over an extended period. This patient died due to a cause other than GVHD. The results in these cases, and *in vivo* experiments, have demonstrated that Futhan® effectively suppresses the activity of cytotoxic T cells. A

more effective treatment will be established if any measures to eliminate activated cytotoxic T cells are introduced in line with the above suppressing effect of Futhan®.

Prevention of Post-Transfusion GVHD

Blood products supplied by JRC Blood Centers are pretreated with radiation when directed to do so by the medical institution requesting such products. Non-irradiated blood products are supplied to medical institutions furnished with radiation units. However, the use of non-irradiated blood for transfusion has fallen dramatically in line with increasing concern about GVHD associated with blood transfusions. Consequently, to our delight, there were no definitely diagnosed cases of post-transfusion GVHD among the suspected cases collected by the Japanese Red Cross Society in 2000 (Fig. 1), and also none among the suspected cases collected up to October 2001.

Conclusion

Japanese researchers have demonstrated that post-transfusion GVHD, which had been diagnosed as postoperative erythrodermia and regarded as a symptom of unknown etiology since 1955, occurs even in the absence of immunodeficiency. Furthermore, the studies have indicated that the relatively high incidence of post-transfusion GVHD in Japan was at least partially attributable to the high uniformity of HLA antigen complex and the high proportion of homozygous HLA haplotypes among indigenous blood donors.

The advent of the microsatellite method contributing to the feasibility of definite diagnosis is also a noticeable progress. The etiology accounting for the failure to detect donor lymphocytes in the peripheral blood of patients suspected to have post-transfusion GVHD is yet to be clarified.

Long-term observation is to be pursued to ascertain whether irradiated blood transfusions are truly safe or not.

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