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The Current State of Health Care System Reforms and Future Issues

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Key words: Health care reform; Medical care system; The elderly; Health care cost

Proposal by the Japan Medical Association (JMA)

1. Focus of the proposed reforms

Several years have passed since the public outcry for reforms of the health care system was first heard. As one of the forerunners who saw the need for such reforms much earlier, JMA first announced “A Proposal for Health Care Reforms” in July 1997.

Since then JMA has submitted specific proposals for structural reforms such as creating a medical care system for the elderly, reforms of the medical fee payment system, and structural reforms of the pharmaceutical related system. These reforms were compiled in an Interim Report in July 1999. Additionally, JMA’s “Grand Design for Health Care in 2015” was publicly announced in August 2000, wherein JMA’s medium-term vision of the health care system and the direction in which the reforms should ideally progress were presented.

In the pursuit of structural health care reforms, the JMA has advocated the policy dynamics approach to address the foremost issue of creating a medical care system for the

elderly. This approach promulgates the pursuit of focal and dynamic policies to realize overall policies and reforms.

The Japan Federation of Economic Organizations (Keidanren), the National Federation of Health Insurance Societies (Kemporen), and the Japanese Trade Union Confederation (Rengo) have generally agreed with the crux of the reforms, the creation of a medical care system for the elderly or radical reforms of the medical system for the elderly as advocated by the JMA. In truth, there was heated debate about this issue between these organizations until last year, which subsequently produced the general consensus to unite and dismiss minor differences.

However, in the face of unstable political circumstances, critical economic depression, and other negative factors, the administrative and legislative branches of the government have been unable to adopt concrete policies on this issue, and it has continued to be shelved.

2. Cause of the confusion behind the reform debate

Based on these circumstances, the course of

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the reform debate was clearly beginning to deviate in 2001, and the cause is due to the intervention of the Ministry of Finance (MOF).

The Basic Policy on structural reforms announced by the Council on Economic and Fiscal Policy (CEFP) in June 2001 and the Medium-Term Strategy of the Council for Regulatory Reform announced in July 2001 are reports that were compiled essentially under the control of the MOF, despite being touted as having been prepared under the supervision of the Prime Minister's Office.

It is common knowledge that the MOF is the ringleader that created the economic bubble, was directly involved in the frolic, and failed to soften the landing when it burst. It is an undeniable truth that their failure is one of the underlying causes for the deterioration in Japan's national finances. The series of proposed measures from the CEFP aim to shuffle off the bill of debts to health insurance finances and decrease the burden of the national treasury for health costs by shifting the financial obligation elsewhere and thereby, evade national responsibility.

The content of the draft plan of the Ministry of Health, Labor and Welfare (MHLW) that was announced in September 2001 reflected the inability of the MHLW to resist the overwhelming pressure of the MOF. Subsequently, the plan has been unable to escape the ruling precept that prioritizes financial concerns.

Furthermore, the Accounting Agency of the MOF announced its paper on "The Issues Debated in Structural Reforms of the Health Care System" one month later in October, as if in rebuke to the lukewarm stance of the draft plan submitted by the MHLW, which clearly outlined further health cost controls and an increased share of health costs to be borne by the patient. Such public intervention by the MOF authorities in the jurisdiction of other ministries and agencies is unprecedented.

The MHLW is in charge of improving the health and welfare of the nation. As one of the major ministries of the country, it should

strongly protest and oppose the MOF's act of overstepping its jurisdiction. The MOF's public intervention is just one in a series of acts aimed at controlling structural reforms.

The cabinet led by Prime Minister Koizumi has pursued structural reforms by utilizing its phenomenal public support, but in the area of health system reforms, the voice and interests of health and medical professionals and patients have been completely excluded — this is the crux of the problem.

If the government had taken a more firm and systematic approach when a medical care system for the elderly was being seriously debated, the MHLW would never have presented such a proposal on health reforms. It can be clearly stated that the government is seriously responsible for the consequences of having shelved these reforms for too long.

Problems in the Draft Plan Proposed by the Ministry of Health, Labor, and Welfare

I would like to comment on specific items in the bill on structural reforms of the health system proposed by the MHLW, as well as to touch upon the future steps to be taken for these reforms.

1. The implementation of a system to control the growth rate in health costs for the elderly

Measures to forcibly contain health costs for the elderly by implementing a system to control the growth rate of these costs have been proposed. Specifically, the elderly health cost amount for the following fiscal year is estimated and fixed by multiplying the elderly population and the per capita GDP growth rates. If the actual cost exceeds this fixed amount, the surplus amount is adjusted in the medical fee payment system in the following second fiscal year. Regional disparities in the elderly population or the individual characteristics of health and medical institutions have

been completely ignored, and health costs are controlled through penalization and legal authority.

The foremost controversy is that this system may be unconstitutional and in violation of Article 13 of the Constitution of Japan, which stipulates that all citizens are to be respected as individuals, and first paragraph of Article 14, which stipulates equal legal rights for all Japanese citizens.

A case in point, the bill for the social security finances act submitted to the French Parliament in 1998 to be enacted for the following fiscal year advocated a similar system. It was concluded to be unconstitutional and was discarded. Under this bill, physicians participating in the health insurance agreement were repaid the medical costs that exceeded the allocated fixed amount. It was this aspect of penalizing groups that was determined to be in violation of the principles of equality and respect for the individual under the Constitution of France.

The system to control the growth rate of health costs for the elderly suggested in the proposed reform bill in Japan contains several other major shortcomings. Firstly, the estimated GDP growth rate, that is used as the index to fix the standard amount of health costs for the elderly, is inaccurate. According to the data from January to March 2001 of the Economic and Social Research Institute, the primary preliminary value showed a 0.2 percent reduction in the annual growth rate of the previous fiscal year, in contrast to the GDP of the same period. But the secondary preliminary value showed a 0.1 percent increase — a disparity of 0.3 percent.

In view of the inaccuracy of past estimated GDP values, it would not be erroneous to state that accurate estimations for the following fiscal year can not be made. In addition, increased health costs due to unavoidable factors such as the onset of influenza have not been considered. Under the Medical Practitioners Law, physicians should not deny request for providing medical care, and health and medical institutions are required to provide medical treat-

ment under the health insurance program to all health insurance cardholders. If there is an influenza epidemic, this extremely irrational system greatly penalizes all medical institutions for providing reliable treatment that they are legally required to administer.

When health care is seen as an industry, objective data from the Input-Output Table show that it is a sector with an extremely high ripple effect in terms of employment and income.

2. What are the appropriate health cost controls for the elderly?

Forced health cost controls will unquestionably lower the quality of health care, and the public will be forced to bear the brunt of this consequence. Government officers should realize that this is a significant issue that is directly related to Article 24 of the Japanese Constitution, which stipulates that the government is entrusted with the social mission to protect the right to life of all its citizens.

With the marked aging of the population, increased health costs for the elderly will definitely rise. However, forced controls will only have a negative impact. Measures to moderate that growth should be based on a medium to long-term perspective, and should be approached systematically.

Specifically, these include such measures as introducing a reasonable medical fee payment system and a flat rate system based on the budgets of national and university hospitals. To moderate the growth in a short term, trials should be also made to set up an appropriate drug price table where the prices have been maintained high due to diminished efforts to lower the purchase price in a market, and an appropriate medical material/device price table where both the domestic and foreign price differences are given as a topic of discussion.

3. Reduced benefit ratio and the increased financial burden of the patient

One other important shortcoming of the proposed bill by the MHLW is the reduction in

the benefit ratio and the increased co-payment of the patient. It proposes to establish a fixed co-payment rate of 10 percent, to remove the existing ceiling, and with the exception of a designated segment of the population, the younger generation will be responsible for paying 30 percent of the cost. Additionally, it proposes to raise the minimum amount that will be paid by the patient for high health costs.

As can be corroborated by past case examples, the increased financial burden of the patient has simply been shifted to public expenses and family finances. What must be reviewed is the burden that family finances must bear as a financial source for health costs, i.e., the combined total health cost paid by the insured and the patient presently exceeds 45 percent.

The financial burden on the family finances of the elderly over the age of 70 is equivalent to 10 percent of the total health cost paid by family finances; this is equivalent to the population growth rate. The stance of the government council regarding the financial contribution of the elderly population should realize that the elderly are already contributing their fair share.

Basically, health costs should be covered by health insurance premiums. The government's role in terms of social security is to supplement the amount that is lacking from public expenditures to maintain stability and sustainability.

The bill of the MHLW has also proposed expanding the special health cost system. But such a move will produce disparities in the health services that are dispensed according to the economic condition of the patients. This is not only a denial of the element of equality in public insurance, but an increased burden on the patient's finances, i.e., their family finances.

It is imperative that we escape the unchanging government scheme to reduce health cost expenditures by increasing the patient's financial burden.

4. Proposed radical reforms of the system

One other problematic issue is that the min-

istry's bill is a distortion of JMA's proposal to establish a medical care system for the elderly. Thus, the proposed bill may end up being merely superficial reforms of the medical system for the elderly.

The medical system for the elderly according to this bill targets citizens over the age of 75 years, advocates increasing the investment ratio of public expenditures, and other components that at first glance appear to be similar to JMA's proposal; and this is what is problematic. However, the JMA proposal advocates creating a health insurance system that is designed for subscribers who are at high risk for disease, which in turn will strengthen the element of guarantee, invest 90 percent of public expenditures, and raise the participation awareness of subscribers through insurance premiums, which will also give them the opportunity to voice their opinions.

The JMA has also proposed eliminating payment from the general health insurance fund for the elderly, which will be managed according to financial sources comprised of an 80 percent health insurance coverage and a patient co-payment fee of 20 percent of the health cost. This system is also designed to help mobilize the general health insurance system to adequately reflect the costs of new medical technology and preventive medicine.

This will require establishing a strong system of financial adjustments between insurance companies, beginning with adjustments between the national health insurance and employees health insurance companies in each prefecture. The next step is to carry out financial adjustments between the national insurance and employees health insurance plans, and lastly, it is necessary to integrate the national insurance and employees health insurance as a regional insurance plan in each prefecture. The MHLW has also advocated reorganizing and integrating the insurance companies, but this is a task that can not be accomplished overnight and must be pursued in stages over the medium term.

Although an increase in the absolute number of subscribers in the medical system for the elderly is unavoidable, the JMA proposes fixing the unit growth of health costs of each patient per day at a low figure to control the burden as much as possible, on the premise that preventive medicine for the younger generation will become substantial, life-long health program will become systematized, an appropriate medical fee payment system will be developed and introduced, and the area covered by the newly developed technology will be relatively minimal in comparison to the younger generation because of differences in disease structure.

In contrast to this, the draft bill of the MHLW suggests simply to curtail the number of subscribers according to age (75 years and above) and to address the problem strictly from a financial standpoint only. In this sense, it is totally different from JMA's proposed plan.

5. Verifying the financial source for health insurance

Hence the ministry's proposed bill simply shifts the financial source for medical expenses from the national treasury to family finances. But the government has not taken any measure to corroborate and publicly circulate the facts about whether there is a real need for stringency in health insurance finances. There is a need to study Japan's health insurance finances from a broader perspective to conduct well-grounded and direct debate using objective data.

The following facts became clearly delineated when the settled account reports for FY1999 of each insurance company and their amount payables, as well as those of the All-Japan Federation of National Health Insurance Organizations were linked.

According to the profit and loss statement, overall health insurance generated a net profit of 196.6 billion yen (US\$ 1.49 billion) and net assets of 5.6 trillion yen (US\$ 42.42 billion). When seen separately, the Association-managed

Health Insurance had a separate reserve fund of 2.2 trillion yen (US\$ 16.67 billion), the National Health Insurance had uncollected insurance premiums of 800 billion yen, and the Government-managed Health Insurance had unsettled liquidation problems with the government's general accounting. As long as these are issues that concern public health insurance, it is the government's responsibility to actively resolve these problems, and the path to rebuilding health insurance finances begin by each insurance company executing their management responsibilities.

Assessing Japan's Health Care and Health Care Costs

Lastly, I would like to discuss the reforms of the health care system and what needs to be done in order to achieve these reforms.

Firstly, Japan's health care system should be evaluated by the third party organization. The public and the mass media have been influenced unknowingly by the government's propaganda that health care cost is the behemoth that will destroy Japan's finances. If Japan's health care costs are compared with international standards and objective data, we will find that they are not exorbitantly high as they are purported to be.

To the contrary, Japan's health care system has been given top objective ratings for its equality and impartiality, its health index, and the cost of its services, according to OECD data and WHO rankings. In other words, our health system is a success from a macro perspective.

The key to this success was the implementation of a universal national health insurance system, the design of a health insurance system that was focused on benefit in kind, the stance of nonprofit health care, and the provision of fair and equal access to health care for all citizens.

From a micro perspective, the aging of the population continues to progress rapidly as we enter the 21st century, and there are many issues under the present system that must be

reviewed. For example, there must be undeniably more active work in the area of information disclosure and improving the quality of health care.

Those elements that are outstanding in Japan's health system should be safeguarded, and those elements that need to be changed and kept must be reviewed impartially by relevant parties who are able to put their respective interests aside. Those elements that have a negative impact should be changed and replaced with elements that will produce positive benefits.

The nucleus of health care is a respect for life, and it is a humanitarian activity that is carried out by health professionals who utilize their knowledge and their technical expertise to relieve the primary pain and fear of patients suffering from a disease that has disrupted their health or threatened their life.

The health services that are rendered to the patient from the physician should not be transacted according to monetary values that repre-

sent health and life, but rather compensation for health services should be based on the principals of medical or bioethics. This concept is immutable and timeless, and the relationship between the health provider and receiver should be based on trust, specialized scientific knowledge, and ethical autonomy.

At the front line of health care, the patient will always want the best health services possible and the physician should constantly strive to provide such quality services. This may be called "optimum guiding principle".

Health care that truly represents the patient's best interests is achieved when this principle is implemented naturally.

Therefore, I strongly believe that reforms should not violate this principle. We must not overlook the fact that the crux of all health reforms is concerned with how institutional, environmental, and legal foundations can be concretely improved to develop and maintain the optimum guiding principle at a high standard.

Stress and Hypertension

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Abstract: Hypertension develops and progresses in people with hypertensive diathesis triggered by environmental factors such as stress and obesity. Granted that stress response in the cardiovascular system is induced by interactions between environmental stimuli and situational cognition of an individual, the development of hypertension depends on differences in situational cognition among individuals. This paper examines this issue by way of case study. A 53-year-old man with a 28-year history of labile and mild hypertension experienced abnormal elevation in blood pressure levels at ages 41 and 47 when he faced intractable problems. These abnormal blood pressure elevations did not respond to increase in antihypertensive drugs, but were able to be lower by changes in his life environment. However, severity of hypertension advanced following these two episodes. During his second hospitalization, physicians instructed the patient to confront problems with his wife that he had avoided, and he received treatment (autogenic training, fasting therapy, and group therapy) designed to help him become aware of his avoiding behavior. Although he has had white coat hypertension after the first abnormal BP elevation, his blood pressure has been stable for six years since discharge with no increase in dosage of antihypertensive drugs.

Key words: Hypertension; Autogenic training; Psychosomatic approach; Psychosocial stress

Introduction

There are three forms of stresses (or stressors to be precise), psychosocial stress, physical stress, and chemical stress. This paper focuses on the relationships between psychosocial stress and hypertension (essential hypertension).

Since we live in a competitive society filled with stresses, there is a heightened interest in

the relationship between health and stresses. In reference to the results of a nationwide survey conducted in Japan in patients with hypertension, gastritis, or gastric ulcers, Nakai reported that 78% of hypertensive patients were aware of the relationship between their disease and stresses.¹⁾ This information indicated that most of hypertensive patients believe the disease to be associated with stresses.

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The Framingham study, for example, demonstrated that, during 18–20 years of observation, middle-aged men with high levels of tension or anxiety were 2.19 times greater susceptible to hypertension than those without such stress factors.²⁾ According to Pickering, the extent of an increase in the blood pressure level is greater among men with a high workload and no discretionary powers.³⁾

These days, hypertension is considered a multifactorial genetic disease that is triggered by interactions between environmental and genetic factors.⁴⁾ In other words, hypertension is believed to develop as a result of a combination of predisposition to hypertension and environmental factors such as stresses, dietary habits, obesity, hyperlipidemia, smoking and alcohol consumption. It is easier to be understood that stress responses in the cardiovascular system result from interactions between environmental stimuli and individual situational cognition, as stated by Steptoe.⁵⁾

This paper examines the relationship between stresses and hypertension by way of case study. It suggests that the lack of individual situational cognition greatly contributes to the onset and progress of hypertension.

Case Report

The patient (“Patient A”) is a currently 53-year-old man and a high school teacher. His family history reveals that he has predisposition to hypertension, as his father had hypertension and died of acute myocardial infarction (at the age of 72), his grandfather also had hypertension and died of stroke, and his brother is also a hypertensive and is receiving treatment.

With reference to psychosocial backgrounds of the patient, he developed an inferiority complex about his skinny body when he was in a primary school and has ever since felt nervous when meeting people because he feels as if his skinny body was always stared at. In high school, wearing shorts for physical education lessons became an intolerable experience for

him. Since his school was an academic high school having many excellent students, school work as well as body image became a source of another inferiority complex. He then began to feel a strong physical stress whenever he faced situations that he had never experienced before. Eventually, he stopped attending physical education lessons when he did not feel well.

The onset of the present illness dates back to his high school days. When Patient A was a junior in high school, he visited the department of internal medicine at our hospital, complaining of unwell feeling and malaise. Although a high blood pressure (150/80 mmHg) was pointed out, he kept it untreated. When he became a high school teacher at the age of 25, hypertension (170/90 mmHg) was pointed out at every annual health check-up, but it remained untreated. At around the age 34, he was under a lot of stresses at work and experiencing anxiety and dizziness. His home doctor referred him to the department of internal medicine at our hospital for psychosomatic approaches. He was given a diagnosis of borderline hypertension and anxiety neurosis, and received autogenic training in addition to an antianxiety drug and a beta-blocker for tachycardia.

The subsequent clinical course had been favorable until Patient A, at ages 41 and 47, confronted intractable stresses, which led to abnormally high levels of blood pressure. Changing living environment (e.g. hospitalization) improved his hypertension in both incidences, and during the second hospitalization, he for the first time had an opportunity to learn stress coping skills to face his unsolved problems squarely. Since then, he has been able to lead a full life to date.

Psychophysical Responses, Continuous Elevation in Blood Pressure in Particular, under Intractable Stresses

1. More than 25 years had passed since hypertension was pointed out in Patient A. Until recently, he was living in fear of hyper-

tension and a cerebral stroke. In July of 1990, when he was 41, he distressed himself with intractable marital problems on top of stresses at work. Before this incident, his blood pressure had been around 130/85 mmHg, but it rose to 150–160/90–110 mmHg and he began to experience general malaise, easy fatigability, and stiff neck. Since the blood pressure did not fall despite an increase in the daily dosage of nifedipine from 20 mg to 40 mg, he was admitted to our department in October 1990. On admission, although the level of noradrenaline in the urine was high at 209 $\mu\text{g}/\text{day}$, no other evidences indicative of secondary hypertension were observed.

The blood pressure began to fall on the third day of admission due partly to the fact that he was able to feel relaxed, and he was discharged on the 20th day. He returned to work after some rest, and he began to exhibit the blood pressure levels over 160/90 mmHg in periodical outpatient check-ups. In addition to tranquilizers and beta-blockers, 10 mg of nitredipine was administered and treatment response was favorable. However, at around this time he started to present signs of white coat hypertension with the blood pressure of 200/110 mmHg in periodical check-ups.

2. The condition of Patient A had been under control for five years following the discharge. However, he led a stirring life for half a year in 1994, marital problems surfaced again, and he developed feelings of exhaustion and malaise, which interfered with his job performance. When he visited a local hospital in May 1995, his blood pressure was abnormally higher at 230/130 mmHg than the levels from five years earlier. He was immediately admitted to a hospital specialized in cardiology ("Hospital A"), where he underwent a detailed examination for secondary hypertension, but the result turned out to be negative.

Although the blood pressure dropped as a result of increased dosage of antihypertensive drugs, the level of 230/130 mmHg was continuously observed after he returned to work, and

he was once again admitted to Hospital A in July 1995. Since headaches and tinnitus persisted, he was transferred to our hospital in August 1995. Drugs prescribed on August 31 were as follows: one 10 mg tablet of nitrendipine, one tablet of beta blocker, tranquilizer, and sleeping pills. The average blood pressure based on ambulatory blood pressure monitoring (ABPM; 24-hour measurement of the blood pressure) was 152/94 mmHg.

Psychosomatic Approach and His Clinical Course

Patient A is by nature a serious and hypersensitive person. High blood pressure was pointed out when he was 16, and it further worsened the inferiority complex that he had had about his body. Ever since he stopped attending physical education lessons using his high blood pressure as an excuse, he had begun to avoid situations that arouse anxiety.

On the first hospitalization, he was discharged without realizing the relationship between stressors and high blood pressure. Although guidance should have been given at that time, it was difficult to intervene in marital disputes, resulting in postponement of essential problems. However, the disease progressed when the high blood pressure persisted for three months, and there was no other choice but to initiate treatment with antihypertensive drugs after he was discharged from the hospital.

Despite the fact that his second admission resulted from stress at work and marital problems just like the first admission, Patient A was not fully aware of it. Unlike the first admission, his blood pressure was abnormally high and he found himself seized with the fear of a cerebral stroke. After he was admitted to our hospital, the blood pressure began to fall in a few days after appropriate treatment with tranquilizers, etc. As a preventive measure, counseling was subsequently initiated in an attempt to help him understand the relationship between stress and elevation in blood pressure. The emphasis

of the counseling was not on how to evade stressful situations using high blood pressure as an excuse, but on how to recognize and deal with the stressors.

Treatment included autogenic training to facilitate relaxation of mind and body, and participation in group therapy twice weekly. In addition, fasting therapy was also proposed to provide him with an opportunity to experience how to overcome stressful situations by himself. He accepted the proposal, started 10-day fasting therapy starting on the 33rd day of admission, and completed it despite sufferings.

ABPM was performed on August 31, which was the day for group therapy, and the blood pressure levels in the resting state at 16:00 and 16:30 were 144/95 and 149/91 mmHg, respectively, and they were 193/114 and 190/113 at 17:30 and 18:00, respectively, during group therapy. These data positively influenced the way for him to perceive blood pressure. The following remarks were made by him prior to his discharge from the hospital.

“Listening to speeches and thoughts of others in group therapy, I came to realize that I fell short of confronting with my own problems and I was too dependent on people around me.”

“It came to my mind when I was awakening in the morning that ever since I was found to have hypertension 30 years ago, I have always run away from dealing with every stressful situations, such as agonizing, troublesome, unfavorable, or scabrous situations, on the excuse of hypertension. To make things worse, I developed fear of death from a cerebral stroke whenever my blood pressure went up, and I pictured this scenario in my mind again and again. I have now realized that my body came to respond such a way over these long years.”

Although the outcome of fasting therapy fell short of our expectations, the second hospitalization, unlike the first one, gave him opportunities to reflect on his inner self, talk about the relationship with his wife, and think deeply about his family. He returned to work two

months after discharge. Six years have passed since then, and he is now able to put his blood pressure under control even when facing stressful situations, and is leading a fullhearted life, although he still has white coat hypertension and hypertension. For six years, there has been no dosage increase in medication, or 50mg of atenolol and 20mg of nifedipine per day, and no changes have been observed in the ocular fundi or the heart.

Conclusion

Those who are living in modern society are frequently exposed to unexpected stress. The ability to control and manage stress is a determining factor in the development and progression of hypertension. It should be noted that blood pressure response to an abnormally high and uncontrollable level of stresses can be life-threatening and can even exhibit resistance to drug therapy.

Ignorance or false knowledge often leads people to taking inappropriate reactions to stressors. The key for treatment of hypertension lies in physicians' instructions and social support systems (which allows a temporal retreat from the stressful situations) for patients to correctly change or modify inappropriate coping behaviors.

REFERENCES

- 1) Nakai, Y.: Discussion on the results of a survey on health and stress. *Nihon Iji Shinpo* 1998; 3895: 43–49. (in Japanese)
- 2) Markovits, J.H. *et al.* Psychological predictors of hypertension in the Framingham study. Is there tension in hypertension? *JAMA* 1993; 270: 2439–2443.
- 3) Pikerling, T.G.: The effect of environmental and lifestyle factors on blood pressure and the intermediary role of the sympathetic nervous system. *J Human Hypertens* 1997; II (Suppl I): S9–S18.
- 4) Ward, R.: *Familial Aggregation and Genetic Epidemiology of Blood Pressure*. ed. Laragh,

J.H., Brenner, B.M., In *Hypertension: Pathophysiology, Diagnosis, and Management*. Raven Press Ltd., NY, 1990; 81–125.

5) Juhnston, D. and Steptoe, A.: Hypertension.

In: Pearce, S. and Wardle, J. (eds.); The practice of behavioral medicine. Oxford University Press, Oxford, 1989.

Ischemic Heart Disease

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Abstract: The cardiovascular system is particularly susceptible to influence of emotional stresses, and it has long been thought that the location of emotions was in the heart. In recent years, it became known that stresses promote abnormalities in circulation kinetics and aggravate arteriosclerosis via the nerve and endocrine systems. Autonomic nerves, in particular, mediate the onset of coronary vasospasm, a disease prevalent in Japan. Stresses are known to directly trigger attacks of angina pectoris and myocardial infarction, particularly emotions of anger (or hostility) increasing the risk. Depression is also reported to be involved with the onset of this disease. One of the risk factors for ischemic heart diseases noted recently is Type A behavior pattern—so-called workaholic type personality—, and the emphasis in recent years is on anger and quick temper as their causes. The result of our studies on Japanese revealed the same tendency as that of westerners of pronounced psychological traits of anger and quick temper, particularly in patients aged 50 or younger.

Key words: Anger and anxiety; Coronary vasospasm;
Type A behavior pattern; Japan Mental Health Inventory (JMI)

Introduction

It is known since old times that angina pectoris and myocardial infarction are triggered by emotional stresses as described by Heberden (1768) who first recorded angina pectoris accurately. There is a report that many people in Japan suffered attacks of angina pectoris while watching sports programs on TV such as those of professional wrestling.

Meanwhile, the personality or behavior pattern peculiar to patients of ischemic heart dis-

ease is known as a risk factor. In this case, what may be described as chronic stresses must be involved.

The cardiovascular system is particularly susceptible to influence of emotional stresses, as it has long been described that emotions are located in the heart. Emotional heart (mind) and organic heart are thus regarded as identical. Cannon *et al.* (1915) found that changes in the cardiovascular system occur by stresses via the nerve and the endocrine systems, and cause psychosomatic disorders such as ischemic heart

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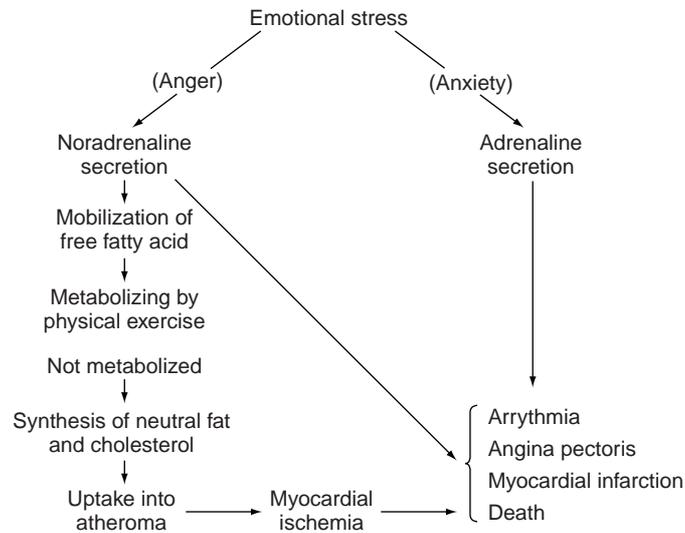


Fig. 1 Hypothesis by Carruthers *et al.*
(Source: Tagart & Carruthers: *Stress and the Heart*. Raven Press, New York, 1981; 25)

diseases, hypertension, arrhythmia, etc.

Stresses and Changes in Cardiovascular System

As mentioned above, Cannon reported that when the biological body encounters an emergency, it manifests a series of reactions called “emergency reactions” in the sympathetic nerve-adrenaline gland system and demonstrated by animal experiments that the heart rate increases, the small arteries contract and blood pressure becomes elevated. However, anxiety and anger are said to affect the cardiovascular system in slightly different ways even though both are emotional stresses.

Carruthers *et al.* hypothesized the relation between catecholamines and heart diseases as shown in Fig. 1 (1981).¹⁾ According to them, noradrenaline is mainly related to aggressive emotions (anger) and mobilizes lipid (free fatty acid) more intensely. If this lipid increase in blood is not metabolized by physical exercises, it is synthesized into neutral fats and cholesterol, causing arteriosclerosis and inducing myocardial ischemia. On the other hand, adrena-

line is related to intense anxiety, and directly causes arrhythmia, angina pectoris, myocardial infarction, etc. along with noradrenaline.

More recently, Henry *et al.* (1990) reported a route of stimulating hypothalamus—hypophysis—adrenal cortex system by depressive reaction in addition to activating the route of amygdala—sympathetic nerves—adrenal medulla by the fight-flight reaction to stresses.

Erbel *et al.* (1981)²⁾ presented a schematic drawing regarding coronary vasospasm, a disease said to be widely prevailing in Japan, as shown in Fig. 2. Alpha-receptors of the sympathetic nerves are assumed to be mainly related to coronary vasospasms, but involvement of parasympathetic nerves is also suspected. Other factors as causes for vasospasms include localized vascular factors (thromboxane, etc.) and alkalosis of blood. Hyperventilation syndrome due to anxiety and strain is suggested to induce coronary spasms by generating alkalosis.

Stress and Ischemic Heart Diseases

1. Stress and heart attacks

Ishikawa *et al.* reported that occupational

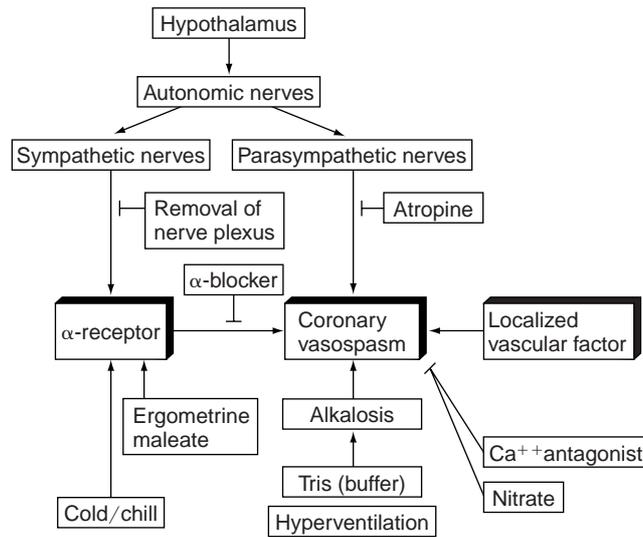


Fig. 2 Conceptual diagram of pathological mechanism inducing coronary spasms
(Source: Erbel & Effert; Dtsch Med Wschr (Translation) 1981; 3 (18); 613)

stressful interviews induced attacks of angina pectoris. According to Shinoda,³⁾ 36 (15%) out of 240 angina pectoris attacks were deemed to have been induced only by psychological factors, and 117 (48.8%) were attributed to combination of psychological and physical factors. Further examination revealed that many attacks occurred while the patients were watching sports programs on TV. Strain, anxiety, frustration, and anger were also cited as psychological factors.

The onset of myocardial infarction in 16 out of 43 patients was described by Weiss⁴⁾ as related to acute emotional stresses. He recognized chronic stresses in 21 others. In the latter case, patients were not clearly aware of the stressor and therefore information (such as recent increase in alcohol intake or insomnia) provided by spouses or family members is important.

As hypothesized by Carruthers *et al.*, the relation between ischemic heart diseases and emotional stresses, particularly anger (or hostility), is attracting attention in recent years.

Mittleman *et al.* (1995)⁵⁾ reported that the risk for attack increased by anger within two hours preceding the onset (relative risk, 2.3).

A report from Sweden (1999)⁶⁾ also described that the risk of attack of myocardial infarction was high within one hour of violent anger.

On the other hand, it is reported that depression is very much related to the onset of the present disease and also that the depressed state worsens prognosis.

Appels *et al.* (2000)⁷⁾ divided the subjects with severe angina pectoris who had undergone coronary artery plasty into those with depressed mood and those without, measured cytokines and virus antibodies, and reported that the former group showed respectively higher values. This indicates that inflammatory diseases and depressed mood may be involved with the onset.

2. Personality traits and ischemic heart diseases

A risk factor for ischemic heart diseases which is reported in recent years is specific personality traits or Type A behavioral pattern. Friedman *et al.* (1959) named the behavioral pattern that is susceptible to ischemic heart diseases as "Type A" based on their clinical experience, and the pattern subsequently became known widely. Type A pattern means the personality who sustained and passionately drives

the self for achievement, is competitive with his/her peers both at work and in avocation and is driven by time. Their follow-up study for 8.5 years from 1960 revealed that the incidence of ischemic heart diseases was higher by two times in Type A personality than in Type B (contrastingly gentle and mild personality).

Recently, Friedman⁸⁾ emphasized “impatience” and “free-floating hostility” as expressive factors of Type A behaviors and pointed out that it was a medical disorder. Many other subsequent studies reported that personality traits of hostility or anger were particularly related to the present disease.

“Anger” may be expressed as “anger-out” and “anger-in”, and suppressed anger such as “anger in a different form as cynical or slander” is also considered problematic.

The author and his colleagues conducted a study (1994)⁹⁾ on ischemic heart diseases among working men using Japan Mental Health Inventory (JMI) developed for mental health surveys of industrialists by Japan Productivity Center (currently Social Economic Productivity Center). The result is discussed below.

Compared to controls, ischemic heart disease patients have many complaints about other parts of their body beside the cardiovascular system, have strong sense of fatigue, are quick tempered and easily angered, but at the same time they are concerned about others, and have neurotic emotions such as anxiety, etc. Compared to the controls of the same age group, they were more active, less tenacious but had the superior complex.

As for their personality traits, they were highly flexible, spontaneous, and future-oriented, but had less control over emotions. In other words, they were highly sociable and positive, motivated, had a tendency to do things in haste, and were emotional. These personality traits seem to coincide with those of Type A behavioral pattern as described by Friedman *et al.* In their workplace, their relationship with co-workers was not good and they did not have the sense of belonging.

Subsequent studies conducted by us revealed that 72% of comparatively young ischemic heart disease patients whose onset occurred at an age below 50 had higher scores for anger and quick temper.

Psychological and social factors influencing the onset of ischemic heart diseases are also reported.¹⁰⁾ A study on Japanese-Americans in California revealed a higher incidence of this disease in those who grew up in completely westernized surroundings than those who grew up in surroundings retaining more Japanese traits as disciplines. There were no differences in the contents of meals, and the author assumed that this was due to the difference in social support by families.

Conclusion

Stress not only induces the attack of ischemic heart diseases directly, but also aggravates on chronic basis arteriosclerosis through daily habits. The important thing is to understand their personality traits, particularly psychology of anger and quick temper, and to offer optimum countermeasures for emotional stresses as primary and secondary preventions. Psychosomatic approaches are always recommendable for ischemic heart diseases.

REFERENCES

- 1) Taggart, P. and Carruthers, M.: Behaviour pattern and emotional stress in the etiology of coronary heart disease: cardiological and biochemical correlates. *Stress and the Heart*. 2nd ed., Raven Press, New York, 1981; 25–37.
- 2) Erbel, R. and Effert, S.: Koronar-spasmen. *Dtsch Med Wschr* 1981; 106: 586–592.
- 3) Shinoda, T.: Various psychosomatic factors of ischemic heart diseases. *Jap J Psychosomatic Med* 1976; 16: 14–17. (in Japanese)
- 4) Weiss, E.: *Don't worry about your heart*. (translated by H. Ishikawa *et al.*) Shindan To Chiryosha, Tokyo, 1973. (in Japanese)
- 5) Mittleman, A.M., Maclure, M., Sherwood, J.B., *et al.*: Triggering of acute myocardial infarction

- onset by episodes of anger. *Circulation* 1995; 92: 1720–1725.
- 6) Möller, J., Hallovist, J., Didrichsen, F. *et al.*: Do episodes of anger trigger myocardial infarction? A case-crossover analysis in the Stockholm Heart Epidemiology Program (SHEEP). *Psychosom Med* 1999; 61: 842–849.
 - 7) Appels, A., Bär, W., Bruggeman, C. *et al.*: Inflammation, depressive symptomatology, and coronary artery disease, *Psychosom Med* 2000; 62: 601–605.
 - 8) Friedman, M.: Type A behavior: Its diagnosis, cardiovascular relation and the effect of its modification on recurrence of coronary artery disease. *Am J Cardiol* 1989; 64: 12c–19c.
 - 9) Kikuchi, T., Takimoto, H., Nakagawa, M. *et al.*: Psychosomatic study of ischemic heart diseases using a Broad Spectrum Inventory System (JMI). *Jap J Psychosomatic M* 1994; 34: 395–400. (in Japanese)
 - 10) Marmot, M.G. and Syme, S.L.: Acculturation and coronary heart disease in Japanese-Americans. *Am J Epidemiol* 1976; 104: 225–247.

Diabetes Mellitus

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Abstract: Diabetes mellitus is not a simple physical disease because genetic and environmental factors are regarded as being involved in its development. Recently, a hypothesis has been suggested concerning the psychological influence on genetic factors. This indicates the possibility that the prevention of diabetes mellitus and blood sugar control can be successfully achieved by lifestyle improvements. The author has obtained results suggesting the impairment of glucose tolerance and inhibition of blood insulin response under psychological stress. Furthermore, the diurnal blood sugar rhythm is often adversely affected by stress. These phenomena are regarded as evidence indicating the mind-body correlation in diabetes mellitus. In general, diabetic patients with overadaptation characterized by abnormal eating behavior show higher blood sugar levels than those with maladaptation characterized by higher levels of anxiety. This finding demonstrates that the patient education program plays an important role in improving lifestyle and controlling diabetes mellitus. Regarding the treatment of diabetes mellitus, an approach based on behavioral medicine can be adopted to control stress-related abnormal overeating behavior and physical exercises and sport can be introduced into daily life. According to the results obtained from an analysis of eating behavior, patients are encouraged to participate in dietetic therapy and therapeutic exercise to control their body weight. It is necessary for diabetic patients to continue to actively participate in the educational program. The hospitalization system for educational purposes and small group therapy are useful for promoting understanding among diabetic patients of how to deal with stress and fully correct their lifestyles.

Key words: Life stress; Mind-body correlation; Lifestyle-related disease; Behavioral modification; Group therapy

Introduction

Diabetes mellitus including type 1 and type 2 diabetes is regarded as a multifactorial disease caused by multiple genetic predispositions and

environmental factors.¹⁾ Type 2 diabetes in particular, is strongly associated with problems in daily life including obesity, insufficient physical exercise, and psychosocial stress. Effective treatment of diabetes mellitus can not therefore be

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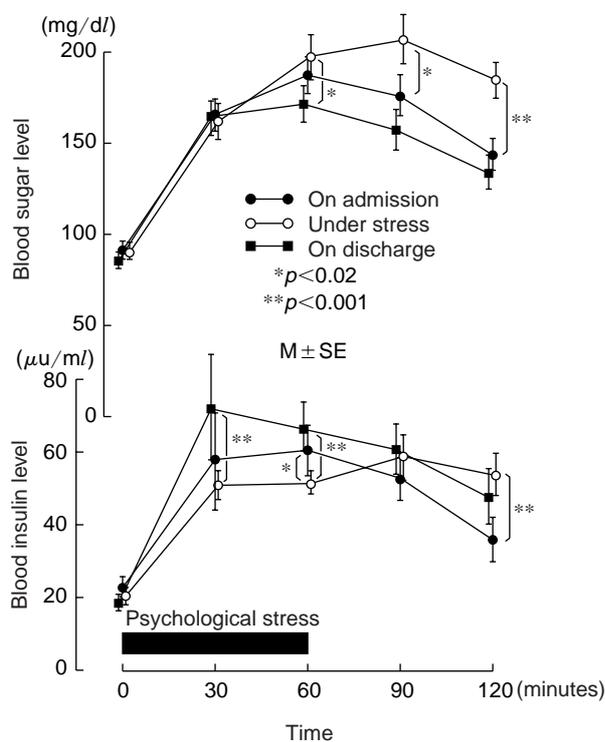


Fig. 1 Glucose tolerance curve and blood insulin response during the interview under stress

The subjects were 11 patients with mild diabetes mellitus or impaired glucose tolerance (IGT).

The data obtained demonstrate the impairment of glucose tolerance and inhibition of blood insulin response under psychological stress.

established only via the promotion of a genome project to seek out responsible genes. Recently, an interesting hypothesis has been proposed concerning the psychological influence on genes.²⁾ According to this hypothesis, the primary prevention of type 2 diabetes, the incidence of which is said to be high in Japan, can also be achieved by improving lifestyles,³⁾ which is why diabetes mellitus is considered to be a lifestyle-related disease. The possibility has been suggested that diabetic patients and candidates for the disease can be effectively treated using behavior therapy.

The latest study of psychoneuroimmunology has demonstrated that cytokines play important roles in controlling blood sugar in patients with type 1 diabetes.^{4,5)}

Accordingly, a psychosomatic approach is indispensable for establishing effective treatment

for diabetes mellitus because this disease is not a simple physical disease but is a pathological condition which is markedly affected by the lifestyle of an individual. The present study discusses diabetes mellitus from the aspect of psychosomatic medicine and behavior medicine.

Psychosomatic Aspect of Diabetes Mellitus

The author investigated diabetic patients and obtained results demonstrating that lifestyle-related stress was more frequently involved in the development of type 2 diabetes than family history of obesity or diabetes.⁶⁾ Consequently, it is possible to suggest a hypothesis that overeating behavior caused by lifestyle-related stress accelerates the development of type 2 diabetes. According to the results obtained from close observation of diabetic patients, blood sugar levels are aggravated when such patients are busy or under intense environmental stress. On the other hand, blood sugar levels decrease when patients are relaxed.

These phenomena can be reproduced in a psychophysiological loading test in the laboratory. The results obtained in the test are summarized in Fig. 1.

Patients suffering from mild diabetes mellitus or impaired glucose tolerance (IGT) with psychosocial stress were selected as subjects for the study. They underwent tests comprising an interview under stress and a glucose tolerance test. Individual stress items were investigated in advance and were recorded on tapes to be used as ca. 60 minute acoustic stimulation. The glucose tolerance curve and blood insulin responses for individual patients were recorded on admission, under stress during their hospital stay and on discharge. The results obtained were compared. Although no significant differences in fasting blood sugar levels were observed, glucose tolerance under stress showed a delayed pattern indicating definite aggravation. Favorable findings were obtained after psychosomatic therapy performed during short duration hospi-

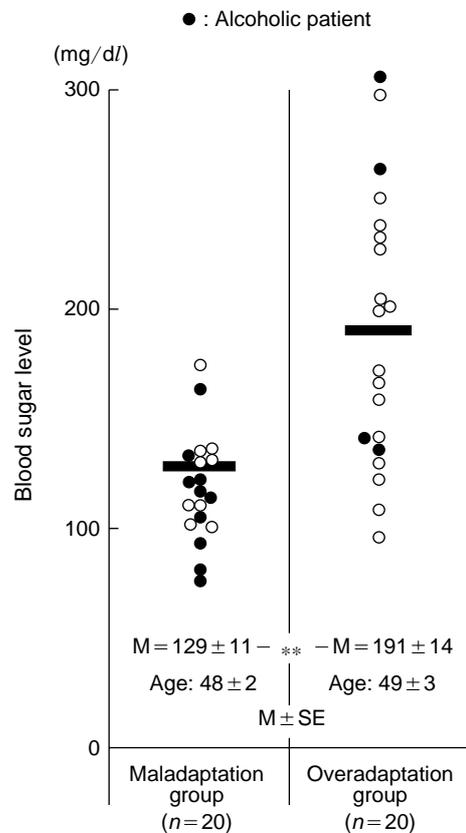


Fig. 2 Distribution of fasting blood sugar levels before the therapy: a comparative study from the aspect of social adaptability

Fasting blood sugar (FBS) levels are distributed more extensively in the overadaptation group than in the maladaptation group. The mean FBS of the overadaptation group was significantly higher than that of the maladaptation group ($p < 0.01$). The fact that the overadaptation group included more obese patients suggests a higher incidence of stress-related overeating behavior in this group. (○: Obese diabetic patients)

In the maladaptation group, an alcoholic patient showed abnormally high FBS level. This datum was stochastically evaluated and proved to be exceptional value and this was accordingly excluded from this statistical analysis.

tal stays.

A comparative study was conducted using Pima Indians with type 2 diabetes and Caucasian controls. According to the results obtained from the mental calculation test, the delayed elevation of blood sugar levels due to environmental stress was noted with higher frequency in the Pima Indian group.⁷ This finding supports the author's results. On the basis of these experimental results, it is possible to propose a

hypothesis that environmental stress may adversely affect the sympathetic nervous system of individual patients.

Disturbance to the diurnal blood sugar rhythm may also be attributed to psychosomatic stress.⁸

Psychology, Personality, and Behavior of Diabetic Patients

The author does not believe that diabetic patients have typical premorbid characters. However, this disease, which requires lifelong therapeutic intervention, is often accompanied by anxiety, depression, hypochondria, and obsessive symptoms. Among these psychiatric symptoms, a depressive state is often recognized concomitantly.⁹

In general, hyperfunction of the hypothalamo-pituitary-adrenal axis (HPAA) and increased insulin resistance, which accompany a depressive state, in either order, trigger off diabetes mellitus. Overadaptation type individuals who work obsessively hard, usually adopt a behavioral pattern characterized by alexithymia and alexisomia resulting in burnout and loss of blood sugar control. Diabetic patients, therefore, require therapeutic intervention including effective behavior therapy to deal with stress, and social support is also desirable.

Patients with diabetes mellitus complicated by neurosis type maladaptation characterized by hypochondriacal anxiety, can usually control their underlying disease effectively by themselves. The author obtained results demonstrating that the symptoms of diabetes mellitus were milder in the maladaptation group than in the overadaptation group (Fig. 2). This finding suggests that diabetic education programs should be modified according to the social adaptability of individual patients.

Methods of Behavior Therapy

The goal of behavior therapy is to maintain self-care activities by overcoming various types

Table 1 Behavior Therapy for Diabetes Mellitus

1. Analysis of eating behavior and its correction based on the results obtained
2. Control of body weight
3. Educational programs including short duration hospital stays and group therapy
4. Relaxation
5. Physical exercises and sport
6. Self measurement of blood sugar level and utilization of measurement results as feedback on the control of diabetes mellitus
7. Keeping a diary of daily lifestyle habits and its visualization
8. Group balneotherapy

of psychological stress, including the restriction of food intake. In general, the diabetic patients who are not adherent to dietetic therapy have unstable and opportunistic personalities.¹⁰⁾ However, personality traits can not be easily corrected.

In cooperation with a treating physician, it is necessary for a diabetic patient to analyze his/her own eating behavior and correct it. This procedure is regarded as a treatment contract between the therapist and the patient. The treating physician emphasizes the importance of preventing obesity and encourages the patient to control his/her body weight. Using a pedometer when walking and recording body weight daily are recommended as useful methods, since patients get feedback from such behavior therapy. Diabetic patients can undergo group therapy during short duration hospital stays as part of the patient education program.¹¹⁾ This type of group therapy, which includes relaxation, physical exercises, and sport as part of daily life, is effective for improving blood sugar control. Diabetic patients need to consider blood sugar measurement as one of their routine activities. The introduction of feedback techniques is highly recommended.

It is necessary for diabetic patients to improve all aspects of their lives so that their days may be filled with comfortable and flexible schedules.¹²⁾ In addition to bathing in hot springs and

relaxing in natural surroundings, visualizing the behavioral pattern by keeping a diary appears to contribute to lifestyle improvements (Table 1).¹³⁾

Conclusion

The author has pointed out the close relationship between life stress and blood sugar control. It is necessary for clinicians to recognize the existence of psychosomatic correlation and to provide both treatment for physical symptoms and appropriate lifestyle advice. Diabetic patients, who need individualized counseling on their way of life, receive only routine treatment at outpatient clinic visits. The establishment of education programs for diabetic patients comprising short duration hospital stays and practical training including group therapy is eagerly anticipated.

REFERENCES

- 1) Kasuga, M.: Study on diabetes. *Nihonijishinpō* 2001; 4009: 1–7. (in Japanese)
- 2) Murakami, K.: Decoding Your Genes as Life Codes. *Sun Mark Publishing Co., Ltd.*, 2000; pp.16–19. (in Japanese)
- 3) Sakamoto, Y. and Ikeda, Y.: Candidates for diabetes. *Sōgōrinshō* 2000; 49: 2779–2783. (in Japanese)
- 4) Hirano, T. ed.: Cytokines and Diseases. *Yodo Publishing Co., Ltd.*, 1993; pp.56–68. (in Japanese)
- 5) Moynihan, J.A. and Ader, R.A.: Psychoimmunology: Animal models of disease. *Psychosom Med* 1996; 58: 546–558.
- 6) Yamauchi, Y., Taguchi, F. and Kawakami, K.: Diabetes mellitus and psychosomatic medicine. *Diabetes Frontier* 1994; 5: 7–18. (in Japanese)
- 7) Surwitt, R.S. and Williams, P.G.: Animal models provide insight into psychosomatic factors in diabetes. *Psychosom Med* 1996; 58: 582–589.
- 8) Yamauchi, Y., Taguchi, F. and Kawakami, K.: Diabetes mellitus as a psychosomatic disease. *Psychosomatic Therapy* 1993; 5: 905–911. (in Japanese)
- 9) Talbot, F. and Nouwen, A.: A review of the relationship between depression and diabetes

- in adults. *Diabetes Care* 2000; 23: 1556–1562.
- 10) Lustman, P.J., Frank, B.L. and McGill, J.B.: Relationship of personality characteristics of glucose regulation in adults with diabetes. *Psychosom Med* 1991; 53: 305–312.
- 11) Yamauchi, Y.: Diabetes and behavior medicine, *Jpn J Psychosom Med* 2000; 40: 11–22. (in Japanese)
- 12) Yamauchi, Y.: Advice on lifestyles. *Jpn J Psychosom Med* 2000; 40: 483–487. (in Japanese)
- 13) Ohkuma, K. and Sakata, T.: Established dietetic therapy as behavioral approach to obesity. *Rinshōeiyo* 1991; 78 (extra issue): 668–676. (in Japanese)

Tension-type Headaches

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Abstract: Tension-type headaches are generally regarded as head pain caused by excessive contraction of the pericranial muscles, and since approximately 10 to 20% of the general population complain of tension-type headaches, they are considered to be one of the symptoms most frequently recognized in daily life. Although tension-type headaches are not life-threatening, the severest symptoms of this disorder may adversely affect daily life and social activities. Although tension-type headaches are often triggered by stress, they are more frequently reported as a physical symptom of depression, anxiety disorder, and somatoform disorder. Some patients with tension-type headaches may require treatment for chronic pain disorder. From a prophylactic and therapeutic standpoint, clinicians need to direct particular attention to effective control of stress. Physical symptoms and related problems can usually be ameliorated by making improvements to a patient's daily life and by the introduction of exercise and drug therapies. Various therapeutic approaches, including drug therapy using anxiolytic or antidepressant agents, should be considered to remove psychological factors.

Key words: Psychosomatic disorder; Psychological factors;
Depressive state; Somatoform disorder

Introduction

Headaches are one of the symptoms most frequently recognized in daily life. Most headaches that are usually encountered are classified as functional headaches including migraine and tension-type headaches (tension headaches, muscle contraction headaches).

Regarding functional headaches, the morbidity of the general population in Europe and America is said to range from 10 to 20%.

The morbidity is also high in Japan. Although functional headaches rarely cause directly life-threatening effects, the severest symptoms may adversely affect daily life and social activities.

Among individuals who present with the chief complaint of such headache symptoms, some show chronic or intractable symptoms which are resistant to treatment. Tension-type headaches are frequently observed as a physical symptom of depression, anxiety disorder or somatoform disorder. Therefore, the success

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Table 1 Classification of Tension-type Headaches⁴⁾

2.1 Episodic tension-type headaches (≤ 180 days/year, ≤ 15 days/month)
2.1.1 Episodic tension-type headaches associated with pericranial muscle disorders
2.1.2 Episodic tension-type headaches not associated with pericranial muscle disorders
2.2 Chronic tension-type headaches (≥ 180 days/year, ≥ 15 days/month)
2.2.1 Chronic tension-type headaches associated with pericranial muscle disorders
2.2.2 Chronic tension-type headaches not associated with pericranial muscle disorders
2.3 Tension-type headaches not fulfilling any of the above criteria

Table 2 Diagnostic Criteria for Episodic Tension-type Headaches⁴⁾

A. At least 10 previous headache episodes fulfilling criteria B–E listed below. Number of days with such headache ≤ 15 days/month.
B. Headache lasting from 30 minutes to 7 days
C. At least 2 of the following pain characteristics:
1. Pressure/tightening (non-pulsating) quality
2. Mild or moderate intensity (may inhibit, but does not prohibit daily activity)
3. Bilateral location
D. Both of the following:
1. No nausea or vomiting (anorexia may occur)
2. Photophobia and phonophobia are absent, or one but not the other is present
E. At least one of the following:
1. History, physical- and/or neurological examinations do not suggest any of the disorders listed in groups 5–11
2. History, physical- and/or neurological examinations suggest the presence of such disorder, but it is ruled out by appropriate investigations
3. Such disorder is present, but tension-type headaches do not occur in close temporal relation to the disorder

Table 3 Diagnostic Criteria for Chronic Tension-type Headaches⁴⁾

A. Average headache frequency ≥ 15 days/month for the previous 6 months fulfilling criteria B–D listed below.
B. At least 2 of the following pain characteristics:
1. Pressure/tightening (non-pulsating) quality
2. Mild or moderate severity (may inhibit, but not prohibit daily activity)
3. Bilateral location
4. No aggravation when climbing stairs or undertaking similar routine physical activity
C. Both of the following:
1. No vomiting
2. No more than one of the following: Nausea, photophobia or phonophobia
D. At least one of the following:
1. History, physical- and/or neurological examinations do not suggest any of the disorders listed in groups 5–11
2. History, physical- and/or neurological examinations suggest the presence of such disorder, but it is ruled out by appropriate investigations
3. Such disorder is present, but tension-type headaches do not occur in close temporal relation to the disorder

in treating tension-type headaches is largely dependent on accurate diagnosis.

Classification of Headaches

In recent years, researchers use the headache classification established by the International Headache Society (IHS).⁴⁾ According to the IHS Guidelines, headaches are divided into func-

tional headaches and organic headaches, and diagnostic criteria for both types of headache are established. Among tension-type headaches, those whose association with excessive muscular contraction can be demonstrated by muscular induration or increased electrical activity in electromyography (EMG) are defined as muscle contraction headaches (Table 1, 2, 3).

This type of headache is characterized by a pressure or bandlike sensation around the head and unbearable dull pain which is obtuse, tormenting and builds steadily. Although headaches develop gradually and persistently, the symptoms appear to recede as a result of physical exercise and bathing. Therefore, the absence of aggravation of the symptoms after physical exercise is regarded as a diagnostic criteria.

Individuals who are nervous, have a tendency to become tense and find difficulty in relaxing and resting effectively frequently complain of muscle contraction headaches. Continuous muscle contraction due to mental stress and maintaining the same posture results in the disturbance of muscle blood flow leading to the accu-

Table 4 Items Related to the Causative Factors of Tension-type Headaches⁴⁾

0. No identifiable causative factor
1. More than one of the factors 2–9 (list in order of importance)
2. Oromandibular dysfunction
3. Psychosocial stress DSM-III-R criteria: Associated with psychosocial stressors rated 4–6 on a 1–6 scale (1. no stress, 2. mild, 3. moderate, 4. severe, 5. extreme, 6. catastrophic).
4. Anxiety Fulfilling DSM-III-R criteria for one of the anxiety disorders
5. Depression Fulfilling DSM-III-R criteria for one of the depressive disorders
6. Headache as a delusion or an idea (psychogenic headache, conversion cephalalgia) Fulfilling DSM-III-R criteria for the somatic delusion and somatoform disorders
7. Muscular stress
8. Drug abuse for tension-type headaches
9. One of the disorders listed in groups 5–11 of this classification (specify).

mulation of lactic acid and the release of pain producing substances. These substances not only cause pain but also induce muscle contraction. This phenomenon starts a vicious circle and accelerates the development of persistent headaches. Recently, Lance¹⁾ pointed out a lower threshold to pain resistance as the essential cause of such headaches.

Tension-type headaches are often accompanied by psychological symptoms such as anxiety and depressive state. Psychological regulation of secondary gain from illness is often recognized in individuals suffering from tension-type headaches. Patients with depression or anxiety neurosis frequently complain of this type of headache.²⁾

Users of the IHS Guidelines can evaluate psychosocial stress, the load on muscles and psychological symptoms and record the results obtained. If an individual satisfies the criteria of Diagnostic and Statistical Manual of Mental Disorders III Revised (DSM-III-R), the appli-

cable mental disorders including anxiety disorder, depression, and others are to be reported after the classification of tension headache (Table 4). Of these, headaches due to hysterical conversion regulation or delusion are defined as so-called psychogenic headaches.

Headaches Resistant to Treatment: Headaches as So-called Psychosomatic Disorder

Clinical problems arise in treating headaches because there are intractable headaches such as persistent headaches whose symptoms can not be alleviated by routine diagnostic procedures and appropriate drug therapy, headaches followed by new symptoms, and headaches which can not be successfully treated using drugs.

Psychological factors are generally involved in the development of this type of symptoms. Patients suffering from such symptoms make more favorable progress when they are placed on treatment for psychosomatic disorder rather than that for chronic headache. According to the criteria of Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) established by the American Psychiatric Association, these types of headaches are categorized as “Psychological Factors Affecting Medical Condition.”

Psychological factors adversely affect the general medical condition of patients in one of the following ways:

- (1) The factors have influenced the course of the general medical condition
- (2) The factors interfere with the treatment of the general medical condition
- (3) The factors constitute additional health risks for the individual
- (4) Stress-related physiological responses precipitate or exacerbate symptoms of the general medical condition

In addition, the following have been cited as the psychological factors:

- (a) Mental disorder
- (b) Psychological symptoms
- (c) Personality traits or coping patterns

- (d) Inappropriate health behavior
- (e) Stress-related physiological response (e.g, stress-related exacerbation of tension-type headaches etc.)
- (f) Other unspecified psychological factors (e.g, interpersonal, cultural, or religious factors)

In the case of tension-type headaches, various stresses can cause pain in the head and the complication of depressive state and anxiety state usually results in further exacerbation and chronicity.

Mental Disorders to be Considered in the Treatment of Headaches

As mentioned above, we encounter individuals who develop headaches complicated by psychological factors or a mental disorder. However, clinicians need to direct particular attention to cases of mental disorder complicated by headaches.³⁾

1. Depressive state, depression

Headaches and lumbago are regarded as the physical symptoms of a depressive state. Hypermyotonia is known to be a symptom of depressive state and tension-type headaches which produce a bandlike sensation, as if one is being forced to wear an extremely tight band, is also recognized as a typical symptom. Furthermore, the threshold of resistance to pain is said to be lowered.

Patients occasionally develop no clear psychiatric symptoms such as depressive mood, hypobulia or decreased concentration. Moreover, some patients are so conscious of their headaches that they deny the existence of a depressive state or depression. These symptoms often introduce confusion into the formation of a definite diagnosis.

2. Somatoform disorder (somatization disorder)

The process of psychological regulation by which psychological conflicts are settled by expressing physical symptoms is defined as

somatization. Somatoform disorder (somatization disorder) is a disease resulting from such psychological regulation. Headaches may develop as a symptom of somatoform disorder. Such patients frequently complain of multiple organ disorder. They repeat superficially meaningless words and emphasize their trouble and unhappiness because there is no one to help them. They often make reference to doctors and medical terms while in conversation. They frequently visit clinics although they do not appear to be seeking medical advice, and appear to visit clinics only to insist that no physicians can improve their symptoms, which occasionally causes disappointment to clinicians.

It is often difficult to make a symptom-based diagnosis of somatoform disorder. An accurate diagnosis can be made by directing particular attention to their typical patterns of behavior and complaint.

3. Psychogenic pain disorder

Somatoform disorder includes psychogenic pain disorder although patients with psychogenic pain disorder frequently complain of atypical facial pain rather than headache. Unlike pain due to a conversion reaction which appears anatomically, pain caused by psychogenic pain disorder assumes a more symbolic form. According to Kolb, the symptoms of psychogenic pain disorder are typically manifested after a psychologically important episode which causes the sensation of receiving a blow to the face. An individual may recognize pain following an experience which causes psychological confusion. Pain develops whenever that experience is repeated. The personality structure is characterized by masochism. Patients with this disorder tend to adopt a behavioral pattern that emphasizes their pain as if they wanted to flaunt their painful state.

4. Schizophrenia

Schizophrenics are often said to be in a state characterized by lower threshold of resistance to pain. In such patients, the threshold of resis-

tance to pain is so low that it is below the level which can be regarded as the byproduct of disability to communicate pain. Even if pain is reported, the reported pain can not be properly evaluated. Although some schizophrenics develop typical muscle contraction headaches, the description of symptoms is distorted by their delusional words, inappropriate emotions, and associated disorders. They fall into a state characterized by hallucinations or a delusion of headaches. The finding that the nature of headaches is bizarre and fixed is characteristic of patients with schizophrenia complicated by headache delusions.

Treatment

Although most tension-type headaches are classified as pain caused by the excessive contraction of the pericranial muscles (muscle contraction headaches), increased electrical activity in EMG of the pericranial muscles is not always recognized and a mixture of the above-mentioned pathological conditions is observed in some cases.

Generally, the psychosocial factors including stress are heavily involved in the development of headaches. Some patients may complain of recurrent headaches due to minor stress. In such cases, ways of dealing with stress should be considered in terms of headache prevention.⁵⁾

The improvement of the pattern of physical activities in daily life and the introduction of therapeutic exercise and drug therapy are often effective in solving problems. If this approach proves ineffective, appropriate use of anxiolytic or antidepressant agents should be considered as a therapeutic approach to ameliorate psychological factors.⁶⁾ Some researchers reported the beneficial effects of topical injection of botulinus toxin.⁷⁾

Patients who chiefly complain of physical symptoms including headache are usually reluctant to receive psychological intervention such as counseling. Some patients may regard aggressive psychological intervention as an experience of psychic trauma. In such cases, increased emphasis on adopting a therapeutic approach that takes into consideration the psychological state of the patient is deemed to be the most effective psychological support a physician can provide. The more widespread use of psychosomatic approaches in routine therapy is eagerly anticipated.

REFERENCES

- 1) Lance, J.W.: A concept of migraine and the search for the ideal headache drug. *Headache* 1990; 30(Suppl. 1): 17–23.
- 2) Tsutsui, S.: Headache. *Modern Medicine* 1983; 38: 442–447. (in Japanese)
- 3) Tsuboi, K. and Tsutsui, S.: Headache as psychosomatic disorder. *General Clinical Medicine* 1983; 32: 2913–2917. (in Japanese)
- 4) Headache Classification Committee of the International Headache Society: Classification and diagnostic criteria for headache disorders cranial neuralgias and facial pain. *Cephalalgia* 1988; 8(Suppl. 7): 1–96.
- 5) Jensen, R. and Olesen, J.: Initiating mechanisms of experimentally induced tension-type headache. *Cephalalgia* 1996 May; 16(3): 176–182, discussion 138–139.
- 6) Holroyd, K.A., O'Donnell, F.J., Stensland, M. et al.: Management of chronic tension-type headache with tricyclic antidepressant medication, stress management therapy, and their combination: A randomized controlled trial. *JAMA* 2001 May 2; 285(17): 2208–2215.
- 7) Gobel, H., Heinze, A., Heinze-Kuhn, K., et al.: Botulinum toxin A for the treatment of headache disorders and pericranial pain syndromes. *Nervenarzt* 2001 Apr; 72(4): 261–274.

Current Review of the Etiology of Kawasaki Disease

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Abstract: The etiology of Kawasaki disease remains unknown. Since Kawasaki disease shares many clinical features with scarlet fever and toxic shock syndrome, it was once suggested that superantigens, especially TSST-1, SPEA or SPEB, might be involved in the pathogenesis of Kawasaki disease. This paper focuses on the SPEC hypothesis of Kawasaki disease, which today appears to be the most persuasive.

Key words: Kawasaki disease; Superantigen; Streptococcal pyrogenic exotoxin C (SPEC)

Introduction

Kawasaki disease (KD) is an acute, febrile, exanthematous disease that generally occurs in children under the age of 5 years. Although it is usually benign, in 20–25% of the cases, it is complicated by coronary aneurysm or ectasia. Giant aneurysms may lead to thromboembolism or vascular stenosis, sometimes associated with cardiac infarction and sudden death. KD has now surpassed rheumatic fever as the leading cause of acquired cardiac diseases in Japan and the United States.

Changes in the Incidence of KD and the Current Morbidity

The incidence of KD is overwhelmingly high

in Japan, but the reason still remains unclear. The National survey conducted every 2 years by the Kawasaki Disease Research Team constituted by the Ministry of Health and Welfare (now renamed Ministry of Health, Labor and Welfare) revealed that the total number of patients with KD in Japan was 153,803 in December 1998 (Fig. 1).¹⁾

As shown in Fig. 1, the number of KD patients has been increasing yearly from 1968 onward throughout Japan, and reached its first peak in 1979, second peak in 1982, and third peak in 1986, which is indicative of an epidemic pattern every 3 to 4 years. Although no countrywide outbreak has occurred since 1987, about five thousand people developed the disease yearly from 1987 to 1993, and about six thousand developed the disease yearly from 1994 to 1998. The

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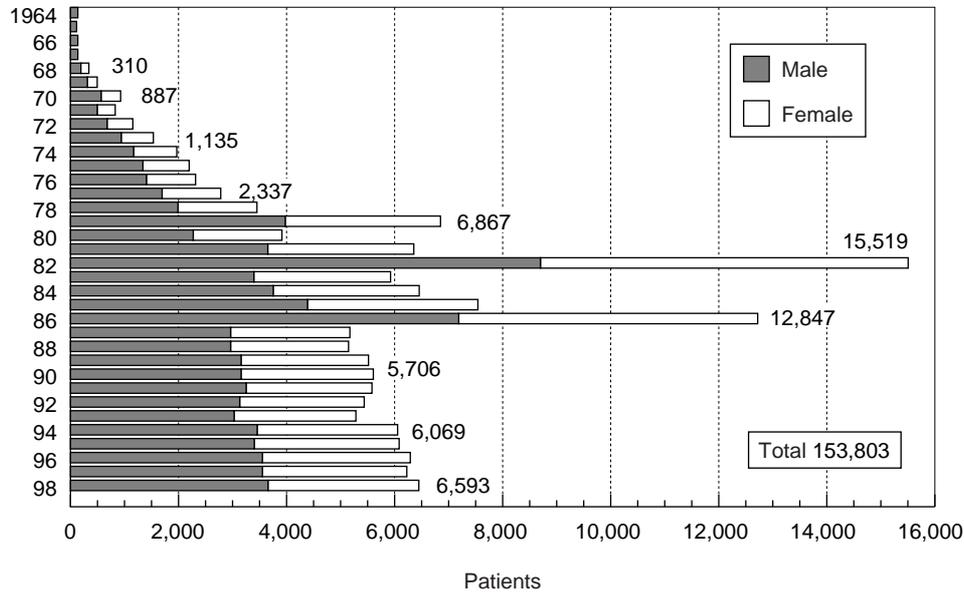


Fig. 1 Yearly number of patients developing Kawasaki disease according to the National Survey of Kawasaki Disease (15 surveys, 1970 to 1998)¹⁾

Table 1 Comparison of Clinical Features of Kawasaki Disease, Scarlet Fever, and Toxic Shock Syndrome²⁾

	Kawasaki disease	Scarlet fever	Toxic shock syndrome
Features of rash	Erythema varying morphologically	Diffuse erythema with spotted papules	Diffuse erythroderma
Conjunctival injection	+	-	+
Labial and oral hyperemia	Whole area +	Localized to pharynx, soft palate	Whole area +
Swollen cervical node	+	+	-
Strawberry tongue	+	+	+
Erythema of the palms and soles	+	+	+
Palmar desquamation	+	+	+
Recurrence	3-4%	Rare	30%
Shock or hypotension	-	-	+
Coronary arteritis (aneurysm)	+	-	-
Age at onset	≤4 years of age	≥3 years of age	90% comprising girls reaching the menstrual age
Epidemic	+	+	-
Cause	?	A streptococcal pyrogenic exotoxin (SPE-A, B, C)	Staphylococcus enterotoxin (TSST-1)

Table 2 Biological Features of Bacterial Pyrogenic Exotoxins Acting as Superantigens

1. Bacterial exotoxins acting as superantigens are proteins secreted by certain bacteria, which stimulate large numbers of T cells.
2. They bind to MHC class II molecules in the host.
3. They require binding to MHC class II molecules on accessory cells to activate T cells.
4. T cells recognize superantigens through T cell receptors (TCR), in the same way they recognize conventional antigens.
5. T cells recognize superantigens through TCR β chain-variable V β segments. Superantigens directly bind to V β segments and selectively stimulate V β gene segments in vast numbers.
6. Bacterial exotoxins do not exert any direct cytotoxicity, such as cytolysis and cell dysfunction.

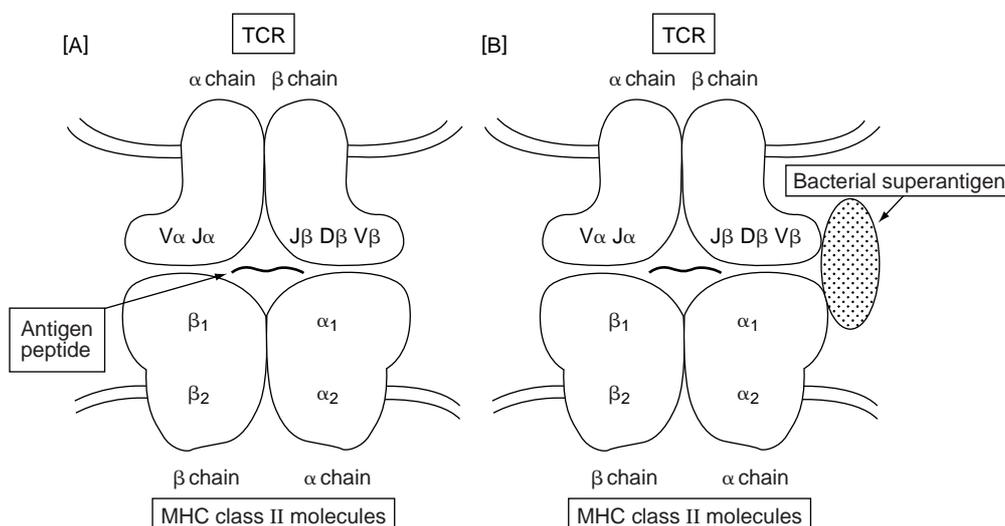


Fig. 2 Antigen-binding complex models; one consisting of antigen peptide, MHC class II molecules and T cell receptor (TCR)(A), and the other consisting of bacterial superantigen, MHC class II molecules and TCR (B)³⁾

incidence of KD appears to be on the rise in parallel with the declining birth rate.

Recent epidemiological studies have shown that although no nationwide outbreak has occurred since 1987, small-scale outbreaks of KD have occurred across the country every year. These findings suggest that some infectious factors may be involved in the pathogenesis of KD. However, the precise cause of KD remains unknown despite extensive effort by scientists worldwide.

Clinical Features of KD and Hypotheses Regarding its Pathogenesis

It has been pointed out that KD shares many clinical features with scarlet fever and the toxic shock syndrome (TSS).²⁾ Table 1 shows a comparison of the three conditions. Scarlet fever is caused by group A streptococcal pyrogenic exotoxins (SPEs), or SPEA, SPEB, and SPEC. As for TSS, the toxic shock syndrome toxin-1 (TSST-1) produced by exotoxin-producing strains of

Staphylococcus aureus was initially identified as the causative agent. Subsequently, *staphylococcal enterotoxin* (SE) A to H have also been demonstrated to be toxins that can cause TSS. Furthermore, SPEs were also found to cause TSS. All these toxins have the characteristics of superantigens (Table 2).³ As shown in Table 1, TSS and scarlet fever share many clinical features with KD, although there are a few differences. Therefore, it may not be unreasonable to suppose that superantigens may contribute to the pathogenesis of KD. Figure 2 shows a comparison of two antigen-binding complex models; one consisting of the superantigen-antigen-presenting cell (APC) MHC class II molecules and T cell antigen receptor (TCR), and the other consisting of a conventional antigen peptide, APC MHC class II molecules and TCR.³

Review of the Superantigen Hypothesis for the Etiology of Kawasaki Disease

Uchiyama *et al.* first demonstrated the superantigenicity of TSST-1, SPEA, and SPEB, using mouse T cells.^{3,4} Thereafter, it was suggested for the first time by Abe *et al.* that SPEA and SPEB might be involved in the pathogenesis of KD.⁵ Abe and his colleagues showed in 1991 that SPEA and SPEB are superantigens, based on the finding that the addition of SPEA to human peripheral blood lymphocytes *in vitro* could selectively activate TCR V β 8+, 12+, 14+ T cells, and that SPEB could activate TCR V β 2+, 8+ T cells.

In 1992, they conducted a further analysis of the TCR V β repertoire of T cells using anti-V β monoclonal antibodies in peripheral blood samples obtained from KD patients, by PCR assay and cytofluography.⁶ The results revealed a significant increase in the percentage of V β 2+ and V β 8.1+ T cells in the population of T cells in the peripheral blood, while the percentage of two V β subpopulation-positive T cells was markedly decreased in convalescent specimens of KD patients. In contrast, none of

the other 20 TCR V β subpopulations showed any expansion.

Furthermore, Abe and his colleagues examined serum samples of patients with acute KD, and found that more than half of the samples were positive for anti-SPEA antibody and 15% were positive for anti-SPEB antibody. Based on these results, they suggested that the two SPEs might function as superantigens and contribute to the pathogenesis of KD. Subsequent studies performed to verify the hypotheses of Abe and his colleagues have remained inconclusive.

Five years after the proposition by Abe *et al.*, Suzuki and his collaborators⁷ belonging to a cooperative research project of Wakayama Medical College and Shionogi Central Institute for Medical Science, Shionogi & Co., Ltd., presented a paper entitled "Analysis of TCR V α and TCR V β repertoires in children with KD" at the 17th Japan Kawasaki Disease Research Meeting (Chairman: Professor Shunzo Chiba of Sapporo Medical University) held in Sapporo in October 1997. They found a significant expansion of V β 2.1 and V β 6.5 of the TCR V β repertoire in the peripheral blood T cells of KD patients in the acute phase as compared with that in the convalescent phase, based on an analysis of blood samples conducted from September 1994 to July 1995 using the adaptor-ligation PCR (AL-PCR) method and reverse dot-blotting (RDB). No marked change was found in the V α populations during the observation period.

The collaborative research project team conducted further studies and presented two proposals at the 19th Japan Kawasaki Disease Research Meeting held in Hiroshima in November 1999. The first was a fundamental research entitled "Involvement of SPEC in the pathogenesis of Kawasaki disease" by Yoshioka *et al.*⁸ of Shionogi Institute for Medical Science, and the second was, "Anti-SPEC and anti-SPEA antibody titers in acute Kawasaki disease", a study conducted from a clinical viewpoint by Suzuki and his coworkers of Wakayama Medi-

cal College. In the former proposal, Yoshioka and his collaborator, using a new method of assay, demonstrated a significant expansion of V β 2+ and V β 6.5+ T cells in the peripheral blood of acute KD patients in 1999 as compared with that in specimens obtained in the convalescent phase. These findings were consistent with the results of previous studies. They performed an additional stimulation test *in vitro* to confirm their findings, using purified recombinant SPEA (r-SPEA) and r-SPEC. The results showed that SPEC induced a selective expansion of TCR V β 2 and TCR V β 6.5, which led them to propose that SPEC probably plays an important role in the pathogenesis of KD.

The latter proposal presented by Suzuki *et al.*⁹⁾ was based on a study of about 17 children and 207 age-matched healthy children, which revealed that the serum titers of antibodies to SPEA and SPEC tended to be higher in acute KD patients than in healthy controls, as measured by the enzyme-linked immunosorbent assay (ELISA), after the stimulation by r-SPEA and r-SPEC proteins. These proposals at the Hiroshima meeting were widely reported by newspaper and television media. Many people believed that SPEC had finally been identified as the cause of KD.

In April 2000, at the 103rd Japan Pediatric Society meeting, Professor Michio Koike of Wakayama Medical College, President of the meeting, presented a review entitled "Etiology of Kawasaki disease,"¹⁰⁾ summarizing the collaborative study conducted by the Department of Pediatrics of Wakayama Medical College and the Shionogi Institute for Medical Science.¹¹⁾ Professor Koike of the Kawasaki Disease Research Team has contributed substantially to elucidation of the pathogenesis of KD. He and his collaborator, Professor Yorio Konuma, of the Shionogi Institute for Medical Science, along with the staff of the institute, assessed the validity of the superantigen hypotheses for KD, while rejecting many other hypotheses.

They focused on the superantigens, SPEA

and SPEC, and transferred the genes encoding the two superantigens into *E. coli* to induce the production of the toxins. Then, they employed purified r-SPEA and r-SPEC *in vitro* to evaluate the role of these superantigens in the pathogenesis of KD by comparing blood samples between KD children and healthy adults using the adaptor-ligation PCR and microplate hybridization assay developed by Ryuji Suzuki and coworkers of the Shionogi Institute for Medical Science. This technique allowed Koike and his collaborators to measure 38 different TCR V β repertoires activated by superantigens in a single step.

The results showed that TCR V β 2-positive cells were noted among peripheral blood T cells in 8/9 healthy subjects after stimulation with r-SPEA *in vitro*, and TCR V β 6.5-positive cells were present in 4/9 patients. All healthy subjects (9/9) were TCR V β 2- and/or TCR V β 6.5-positive, however, none were TCR V β 2- or TCR V β 6.5-positive after the stimulation with r-SPEA; several subjects responded for TCR V β 12, V β 13.1, V β 14, and V β 15.

On the other hand, TCR V β 2-positive peripheral blood T cells were detected without any exogenous stimulation in 41% of 22 acute KD children in 1995–1996, and in 38% of 16 acute KD children in 1999, while TCR V β 6.5-positive cells were found in 59% of 22 acute KD patients in 1995–1996, and in 56% of 16 patients in 1999. TCR V β 2- and/or TCR V β 6.5-positive cells were found in 77% of acute KD children in 1995–1996, and in 81% in 1999. There were no marked differences in the positivity rates between the two periods (1995–1996 and 1999). The expansion of TCR V β 2 and TCR V β 6.5 in KD patients continued until the third week after the onset of the disease, and thereafter gradually declined in all patients during the convalescent phase, that is, 90 to 140 days after the onset. The measurement results of the two TCR V β segments in the convalescent KD phase were similar to those in age-matched healthy controls.

In addition, the serum tested positive for

antibodies to SPEA and SPEC in 24/28 and 25/28 children, respectively, revealing that the serum titers of the anti-SPEA and anti-SPEC antibodies markedly increased in patients with KD even earlier in the acute phase.

Professor Koike stated that these findings strongly suggested a relationship between group A streptococcal infection and KD. He concluded that the strong relationship between group A *streptococci* and KD might indicate the involvement of streptococcal pyrogenic exotoxin C (SPEC), a superantigen, in the pathogenesis of KD, based on analysis of the TCR V β repertoire.

If Professor Koike's proposition were right, it will mark a milestone in the elucidation of the pathogenesis of KD. However, until now, many hypotheses for the pathogenesis of KD have made a promising debut but disappeared in the course of time. Further studies would be required to validate the SPEC hypothesis and to detect SPEC antigen peptides in the serum of patients with KD.

From a standpoint different from the Wakayama/Shionogi research team's, the Kagoshima University Medical School Pediatric Research Team also suggested, in 1997, the involvement of SPEC in the pathogenesis of KD,¹²⁾ and published a related paper in a journal in 1998.¹³⁾ They stimulated peripheral blood T cells derived from 43 KD patients in different phases with SPEA, SPEC, and TSST-1. They observed that the peripheral blood T lymphocytes showed a transient lowering of response to SPEC up to 2 months after the onset of the disease, while no change in response of the peripheral blood T cells was observed after stimulation with SPEA and TSST-1. This transiently decreased response to SPEC by the peripheral blood T cells of KD patients recovered to normal within one year after the onset of the disease. The Kagoshima University investigators proposed that the decrease in response to SPEC might be attributable to anergy, or the absence of T cells responsive to SPEC as a result of migration of the cells to the sites of inflammation. No

decrease in response was observed after stimulation with SPEA or TSST-1. They concluded that these findings suggested the involvement of SPEC in the pathogenesis of KD.

In summary, one study showed the activation of peripheral blood T cells by SPEC, and the other revealed a transient decrease in the peripheral blood T cell response to SPEC. It should be noted that both the different proposals for the pathogenesis of KD implicate SPEC, a group-A streptococcal pyrogenic exotoxin. Further studies will be required to validate this hypothesis.

REFERENCES

- 1) Yanagawa, H., Nakamura, K. and Yashiro, M.: The 15th National Survey Research Results of Kawasaki disease by the MHW Japan Kawasaki Disease Research Team. *Shonika Shinryo (Journal of Pediatric Practice)* 2000; 63: 121–132.
- 2) Kawasaki, T.: Kawasaki disease. *Junkanki Senmoni* 1994; 2: 211–214.
- 3) Uchiyama, T.: Relationship between superantigen and a disease — Kawasaki disease. *Pro Med* 1995; 15: 1191–1201.
- 4) Uchiyama, T., Yan, X.J., Imanishi, K. *et al.*: Bacterial Superantigens — Mechanism of T cell activation by the superantigens and their role in the pathogenesis of infectious diseases. *Microbiol Immunol* 1994; 38: 245–256.
- 5) Abe, J., Forrester, J., Nakahara, T. *et al.*: Selective stimulation of human T cells with streptococcal erythrogenic toxins A and B. *J Immunol* 1991; 146: 3747–3750.
- 6) Abe, J., Kotzin, B.L., Jujo, K. *et al.*: Selective expansion of T cells expressing T-cell receptor variable region V β 2 and V β 8 in Kawasaki disease. *Proc Natl Acad Sci USA* 1992; 89: 4066–4070.
- 7) Suzuki, T., Uemura, S., Koike, M. *et al.*: Analysis of TCR V α and TCR V β repertoires in children with Kawasaki disease. *Prog Med* 1998; 18: 399.
- 8) Yoshioka, K., Matsutani, R., Maeda, T. *et al.*: Involvement of SPEC in the pathogenesis of Kawasaki disease. *Prog Med* 2000; 20: 400.
- 9) Suzuki, K., Koike, M., Uemura, S. *et al.*: Evi-

- dence of antibodies to SPEC and SPEA during acute Kawasaki disease. *Prog Med* 2000; 30: 401.
- 10) Koike, M.: Keynote lecture of the 103rd Japan Pediatrics Society Meeting: Hypothesis about the pathogenesis of Kawasaki disease. *Nippon Shonika Gakkai Zasshi (Acta Paediatrics Japonica)* 2000; 104: 113.
 - 11) Yoshioka, T., Matsutani, T., Iwagami, S. *et al.*: Polyclonal expansion of TCR V β 2- and TCR V β 6-bearing T cells in patients with Kawasaki disease. *Immunology* 1999; 96: 465–472.
 - 12) Nomura, Y., Masuda, K., Oku, S. *et al.*: Selective depletion of peripheral blood TCR V β subfamilies in acute KD children. *Prog Med* 1997; 17: 2786.
 - 13) Masuda, K., Takei, S., Nomura, Y. *et al.*: Transient low T cell response to streptococcal pyrogenic exotoxin-C in patients with Kawasaki disease. *Pediatr Res* 1998; 44: 27–31.

Pregnancy, Delivery and Mental Health

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Abstract: Pregnancy and delivery have a major impact on the mental health of women, and give rise to many conditions mainly including maternity blues, postpartum depression, and puerperal psychosis, and also including psychiatric symptoms, neurosis, personality disorders and alcohol or drug dependence. While the incidence of maternity blues among postpartum women is high, the symptoms are improved spontaneously with no sequelae. On the other hand, postpartum depression persists for longer periods, leading to insufficient mother-infant interaction and further to the developmental disturbance of infants. Although puerperal psychosis is infrequent, it is commonly associated with delusion and the risk of infanticide. When mothers have this type of mental health problem, they cannot adequately take care of their children and develop feelings of guilt toward their children. Therefore, support for child rearing should be given to mothers. In order to foster mother-infant interaction, it might be helpful to room mothers and their infants together in hospitals, as well as to prescribe psychotropic drugs the safety of which has been confirmed in terms of transfer to breast milk, in promoting the normal development of children and preventing mothers from developing feelings of guilt. In order to prevent the occurrence of, and promote recovery from, the symptoms of psychosis, measures should be taken to remove anxiety and conflict among pregnant women attributable to psychological and social factors.

Key words: Maternity blues; Postpartum depression; Puerperal psychosis; Psychological and social factors

Introduction

There are three major mental health problems associated with pregnancy and delivery that are categorized as major puerperal psychiatric disorders (maternity blues, postpartum depression and puerperal psychosis), but include

many disorders, which may have already developed during the gestation period, such as transient anxiety and confusion, neurosis, personality disorder, and drug or alcohol dependence, etc. Mental health problems which significantly impair the well being of mothers and their children are also deleterious to the children's

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fathers, making fathers more prone to suffer psychological derangement, which, in turn, produces problems within the entire family.

In modern society, pregnancy, delivery and child rearing are deemed to be personal events, and it is difficult for women undergoing these events to obtain assistance from others. In addition, the motives for deciding to become pregnant or to deliver a child as well as the roles to be played by women have recently undergone major changes. Furthermore, the life styles of married couples and the marital state itself have also moved away from those that were generally accepted in the past. As a result, young couples' problems cannot necessarily be resolved through consultation with their parents.

In this complicated social situation, women who deliver and rear children become burdened with various major psychological stresses, which not only produces problems with maternal health but also problems in the children to be reared by such mothers. The psychological influence of, and psychosis associated with, pregnancy and delivery, are described herein, together with the social factors contributing to their occurrence and ways of dealing with them.

Psychological Profile of Pregnant Women

For women, pregnancy is frequently a fight against conflicting feelings. In other words, pregnancy is indeed a joy, but, in many cases, it is accompanied by anxiety and issues requiring resolution, and generates both positive and negative feelings. In addition, in cases of unwanted or unexpected pregnancy, pregnancy is recognized as a nuisance, so women with such pregnancy will have unstable and mixed feelings even when they decide to carry to term.

Pregnant women become more psychologically stable in the second trimester than in the first trimester, but in the third trimester, they again become emotionally unstable due to anxiety about the pregnancy itself or about

related complications. Moreover, relationships between pregnant women and their husbands undergo substantial changes. In other words, simple relationships between women and their husbands undergo a transformation in which the recognition that their husbands are family members rather than partners is implanted. At this stage, pregnant women are convinced that they will be unable to obtain support or assistance from their husbands, if their husbands do not show interest in becoming a parent. In such cases, stress can be removed when pregnant women themselves have the ability to solve problems, but women who lack such ability begin to have subconscious anxiety about child rearing and become emotionally unstable. In addition, in cases where delivered infants require a lot of looking after due to congenital abnormalities or diseases, or cases where women cannot take adequate care of their children because of their own jobs or diseases, they will be subjected to conflicting feelings in rearing the child, and feel unable to love it or that it is obstructing their own lives. Even women who had been emotionally stable without children, may, after delivery, complain of difficulties in child rearing, experience weepiness, loneliness, etc., and may continue to seek assistance with child rearing from their parents or husbands. This may hinder new mothers from becoming mature mothers. Therefore, in such cases, education of, and support to, new mothers is essential.

Labor Pains and Self-control

There are individual differences in uterine contractions and labor pains, and the degree of uterine contraction is not necessarily proportional to the severity of the pain. A pregnant woman who has anxiety or fear about delivery is thought to be psychologically sensitive and will tend to feel relatively strong labor pains. Read¹⁾ (1949) considered that anxiety and fear about delivery caused spastic uterine contraction, leading to severe labor pains, and named

the phenomenon “fear pain tension syndrome.” On the other hand, Morris²⁾ (1983) claimed that fear directly affects the cerebral cortex, leading to the development of severe labor pains. In addition, some researchers insist that labor pain is a conditioned response.

In addition, when a woman in labor loses self-control, she may abruptly become agitated using violent language or shouting to reject delivery, or may struggle and become restless. However, once she has delivered her baby, she will settle down and become so quiet that no one is aware of her existence after delivery. Morris indicated that women who have experienced such delivery themselves feel disappointed in their behavior. In cases where a woman has experienced negative psychological factors such as anxiety and fear during gestation and, unfortunately, has gone into labor without having confided in someone or dealt with such mental health problems, she may lose psychological self-control during delivery.

Women are forced into the realization that delivery is an unexpectedly harsh experience from which one cannot turn back and will realize that there is no escape other than to go through with the delivery. In addition, during delivery, women feel that no one can remove the burden on their shoulders or help them, resulting in the development of negative feelings toward their husbands and the unborn child. Therefore, delivery in the presence of persons who can have sympathy with women in labor, including their husbands, their mothers, and doulas³⁾ (attendants who take care of women during delivery), may effectively reduce the above-mentioned psychological impact of delivery on women.

Types of Psychological Disorders

There is almost no difference between the types of psychological disorders which may occur before delivery and those occurring postpartum. Psychological disorders observed during the postpartum period include postpartum

depression and puerperal psychosis (schizophrenia). In addition to these disorders, various diseases or symptoms have been observed after delivery, including anxiety, manic-depressive psychosis, schizophrenia, personality disorder, agoraphobia, drug dependence, alcohol dependence, anorexia, and obsessive-compulsive neurosis. In the current Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV; 1994) published by the American Psychiatric Association (ICD-10; 1992), these disorders are not regarded as obstetrically specific diseases and are classified into the categories of common mental disorders.

Maternity Blues

Maternity blues, which is also dubbed 3-day blues, are the symptoms of depression which appear 3–4 days after delivery, including depressed mood, anxiety, weepiness, irritability, insomnia and fatigue.

Brockington and Kumar⁴⁾ (1988) also included the following in the category of maternity blues symptoms: headache, derangement, forgetfulness, feeling of restlessness, depersonalization (feelings of unreality), negative feelings toward infants, thirst, anorexia, and breast engorgement. These symptoms usually disappear in a short time, and do not adversely affect mothers or their children in the long term.

Kumar and Robson⁵⁾ (1984) failed to establish conclusive evidence that maternity blues are associated with postpartum depression. However, Dennerstein *et al.*⁶⁾ (1989) claimed that a relationship existed between maternity blues and late postpartum depression. The incidence of maternity blues is estimated to be 50–80% (Yalom *et al.*,⁷⁾ 1968; Pitt,⁸⁾ 1973), which varies among country, ethnic group or investigator. In Japan, the incidence of maternity blues in pregnant women is said to be more than 50%, which is somewhat lower than that in North America and Europe. Such difference in the estimated incidence of maternity blues is thought to be caused by the fact that the oppor-

tunity for diagnosing maternity blues tends to be missed because, for example, the symptoms are apt to be mild and to disappear in a short period of time, as well as by differences in cultural factors. Multiple etiologic factors, as opposed to a single factor, are thought to be truly involved in the development of maternity blues.

Unlike in depression, the symptoms of maternity blues disappear in a short period of time. Therefore, even in cases where women experience negative feelings toward newborns because of difficult delivery or painful obstetric procedures during delivery, such feelings would be driven away, inducing few effects on the development of the newborn child (Robson and Kumar,⁹ 1980).

Maternity blues are treated symptomatically, and, if necessary, with antianxiety or hypnotic drugs. During the symptomatic treatment of maternity blues, breast feeding is not contraindicated, although if mothers of newborns and family members are nervous, it may be better, in terms of recuperation and mental health, to feed the baby artificially on the day (night) of delivery and to allow the mother to get sufficient sleep. Although antianxiety drugs are transferred to newborns by way of breast milk, the doses used to achieve night sedation can be administered with almost no safety concern (Matheson *et al.*,¹⁰ 1990). Erkkola and Kanto¹¹ (1972) reported, however, that diazepam transferred into breast milk and that breastfeeding during administration of this drug was a risk factor for inactivity of children. Therefore, in cases where the mother requires continuous administration of diazepam, attention should be paid to the ability of the baby to suckle its mothers' breast and to the development of children who are breast-fed by such mothers.

Postpartum Depression; Puerperal Depression

The incidence of depression occurring during the first year postpartum center around the

period from the 6th-puerperal week to the 8th-puerperal month. The incidence of postpartum depression is 10–15% (Kumar and Robson,⁵ 1984). Based on the DSMIII diagnostic criteria, Okano¹² indicated that the incidence of postpartum depression in Japan in 1988 was 3.2%, much lower than the 15% in Britain and the 10% in the U.S. Moreover, the incidence of postpartum depression in 1990 according to the Research Diagnostic Criteria was 8.2% in Japan, which was again much lower than the 14.9% in Britain or the 19–26% in the U.S. One factor contributing to this low incidence in Japan is delivery at the home of the maternal grandparents, which has recently become the focus of attention. Taking these data into account, psychological, social and cultural factors are thought to be of major relevance to the prevention and treatment of psychological disorders associated with pregnancy and delivery. Therefore, support and assistance from husbands, parents and friends or, as a substitute, those from the community or society are essential.

The problem with postpartum depression is that its detection and diagnosis tend to be delayed, because it often manifests after postpartum women have discontinued regular visits to obstetricians, i.e., after hospital discharge or after the completion of 1st-month postnatal examination. Consequently, the maternal depressive state can be sustained for long periods, with the result that maternal love for children and mother-infant interaction may be weakened, leading to the disturbed development of the child (Coghill *et al.*,¹³ 1986; Caplan *et al.*,¹⁴ 1989). In addition, husbands of postpartum women are also affected and sometimes develop depression and/or the women commit suicide with their children.

The symptoms of postpartum depression include weepiness, depressed mood and anxiety. The symptom of depressed mood is likely to be aggravated in the evening. Women with postpartum depression have strong feelings of anxiety about their children, and experience

feelings of guilt due to their inability to undertake child care. Furthermore, in cases where newborns have siblings, mothers are afraid that they might feel jealous of the babies. In addition, women with postpartum depression may have feelings of guilt because of their inability to care for family members or undertake household chores. Other symptoms of postpartum depression include insomnia, which mainly manifests as difficulty in falling asleep, as well as feelings of restlessness, diminished interest, decreased appetite, decreased libido, etc.

Development of postpartum depression is associated with many factors, and cannot be explained only in terms of fluctuations in biological factors. However, the following psychological and social factors are generally thought to be associated with the development of postpartum depression: brittle, vulnerable and neurotic personality; history of depression or depression associated with menstrual cycle. The recurrence rate in women with a history of such depression after a previous delivery is estimated to be 50% or higher.

Risk factors for postpartum depression include a history of depression or infertility and primiparity at older ages. Another possible associated factor is the experience, before the development of postpartum depression, of serious events such as the death of a parent or change in marital state. Furthermore, in some studies by Fisher *et al.*¹⁵⁾ (1997), combinations of the following factors are judged to be risk factors for postpartum depression: High academic achievement; private medical insurance; delivery by caesarian section at older ages; and breast feeding.

Taking into account access to primary care, it is desirable that diagnosis of postpartum depression be given, through active approaches to postpartum women, by general physicians, psychotherapists, or obstetricians and gynecologists, and, in some cases, pediatricians who routinely examine children, as well as maternity nurses or public health nurses, etc. The Edinburgh postnatal depression scale (EPDS)

published by Cox *et al.*, and the Hamilton Depression Rating Scale (HAMD), etc. are available as methods of screening for postpartum depression. The severity of depression can be evaluated based on the duration of depression, its intensity (patients' feelings and stage of depression), as well as the presence or absence of suicide ideation or a suicide attempt, etc. When a postpartum woman has a concrete plan to commit suicide, she may be at risk of putting the plan into action.

The idea of committing infanticide may arise in cases, for example, where postpartum women are subjected to fear and agony because they believe that it is better for "a bad mother" to dissociate herself from her baby or they fear injuring the child.

Postpartum depression is treated by medication, as well as with cognitive therapy, psychotherapy, therapeutic methods established by supporters' groups, etc. Women with moderate to severe depression or with suicide ideation should be hospitalized in the department of psychiatry. In order both to treat the depression, and to remove feelings of guilt as well as the notion of being an inadequate mother, through learning the methods of child care to establish mother-infant interaction, it is better for mothers not to be separated from their children. However, it is difficult to conduct child care in psychiatric hospitals, so it is ideal for a mother and her baby to be roomed together in a facility with units for mothers and children. Risk factors for postpartum depression which deserve special mention include a history of depression, family history of depression, marital problems, severe neurosis, and sexual abuse in childhood. Conversely, postpartum depression can be prevented by dealing appropriately with these risk factors.

Since antidepressants need to be used for several weeks in the medical treatment of postpartum depression, informed consent should be obtained from patients prior to the initiation of such treatment. While tricyclic antidepressants are most commonly prescribed, those

with longer half-lives are not suitable for the treatment of postpartum depression, because they are transferred into breast milk. Buist *et al.*¹⁶⁾ (1995) examined the association between the concentration of dosulepin (dothiepin), an antidepressant, in breast milk with child development, and stated that, in the follow-up conducted for several years subsequent to the lactation period, no abnormality in the development of children was observed even in cases where transfer of the drug into breast milk had been detected during lactation. This is due to the fact that infants have a high metabolic function, leading to rapid excretion of the drug from the body (Wilson,¹⁷⁾ 1980). Recently, SSRIs (selective serotonin reuptake inhibitors) and other new drugs are also used in the treatment for depression.

Psychotherapy for patients with postpartum depression covers family counseling, management of psychological factors such as anger and conflict, relationships between mothers and their children, promotion of the recognition of becoming parents, and methods of relaxation, and deals with problems between mothers and their children. Measures to be taken to manage patient anxiety with postpartum depression include periodical visits by family members or friends, avoidance of leaving patients in a solitary state for long periods, regular relaxation, cognitive therapy, and so on. In addition, according to Ballard¹⁸⁾ (1994), the incidence of psychosis among the husbands of women with postpartum depression is also high, and there may be cases where both the woman and her husband suffer from depression after childbirth.

In order to prevent postpartum depression, women should undergo periodical medical examinations before and after delivery, and their husbands should give support for the resolution of problems with motherhood by attending such periodical medical examinations with their wives. Therefore, education for both parties on becoming parents and on the prevention of psychic traumata caused by delivery should be given. When women are

in the early puerperal period, their husbands should take time off work and take care of their wives, or, in cases where women have already delivered children (siblings of newborns), should seek their parents' help to leave those children in their charge. Furthermore, cooperation with, for example, public health nurses in the community, especially maternity nurses giving consultation on breast feeding, is effective in preventing postpartum depression. In the treatment of intractable cases, cooperation among two or more doctors or multidisciplinary cooperation is also required.

Postpartum Psychosis

Among the psychoses occurring after delivery, puerperal psychosis is associated with the most severe symptoms. Unlike maternity blues or depression, the incidence of puerperal psychosis in Japan is as low as 1–2 cases/1,000 deliveries (incidence: 0.1–0.2%), which is similar to the figures in the world. Most symptoms of puerperal psychosis manifest in the first puerperal week, and diagnosis is made easily based on the symptoms. Patients with puerperal psychosis often complain of delusion and anxiety about newborns, and suffer from auditory hallucination, hallucination, emotional upset, incoherence of thought, agitation, derangement, perturbation, etc.

Puerperal psychosis is treated medically with chlorpromazine, haloperidol, lithium, etc., and in cases presenting with depression, tricyclic antidepressants are prescribed. During treatment, it is necessary to hospitalize patients with puerperal psychosis. With regard to this hospitalization, hospital stays with the child are ideal for the promotion of mother-infant interaction. Unlike in cases of depression, children of mothers with puerperal psychosis are to be given artificial nutrition. Women whose babies are being given artificial nutrition should be made to take an active role in caring for their child by the assistance of staff in due consideration of easing any feelings of guilt that such mothers

may harbor toward their children.

In patients with puerperal psychosis, the prognosis is better as compared to those who developed non-puerperal psychosis, and symptoms undergo comparatively rapid improvement. Although patients with puerperal psychosis rarely commit suicide, they might commit infanticide if they believe that their lives are being obstructed by their children. According to Kendell¹⁹⁾ (1970), risk factors for puerperal psychosis include primiparity, unstable marital state, premature delivery, experience of stillbirth, delivery by caesarean section, etc. In addition to these factors, family history of puerperal psychosis, history of puerperal psychosis, psychic traumata caused by delivery, experience of massive bleeding during delivery, etc. are also thought to be risk factors.

Other Psychoses during Puerperal Period

In addition to the major postpartum psychiatric diseases mentioned above, neurosis, hypochondria, drug dependence, drinking alcohol, etc. also affect the mental health of women after delivery. Since all of these diseases may develop before pregnancy, it can be said that they are also attitudinal or behavioral problems. When a woman with neurosis who has experienced strong anxiety and been making regular use of anti-anxiety drugs becomes pregnant, concern may arise that the effects of the drugs might be exercised on the fetus. However, maternal use of anti-anxiety drugs does not necessarily cause developmental abnormalities, so administration of such drugs is often continued after adequate informed consent is obtained from the mother.

Postpartum women who are exposed to domestic violence by husband or who have experienced psychological or physical violence (sexual violence in childhood, in particular) by their parents, have keen anxiety about becoming parents, and tend to complain of insomnia, headache and pains in other parts of the body,

unidentified symptoms, etc. In addition, such women sometimes become addicted to drugs or alcohol to escape from emotional and physical distress. In the presence of severe premenstrual tension syndrome, such women have stronger anxiety that they may ill-treat their children.

In order to cope with the above-mentioned problems, medical treatment, as well as psychotherapy, assistance from husbands or parents, etc. are required. In addition, it is desirable that women with postpartum psychological disorders should deal with such problems through cooperation with obstetricians and gynecologists, psychiatrists, physicians, pediatricians, psychotherapists, etc.

Conclusion

The mental health of women during pregnancy, as well as during and after delivery is thought to be affected by a combination of psychological, social and cultural factors. Therefore, when a couple planning to have a child face problems with mental health, assistance and help should be given to the couple. In order to assist such couples, it is necessary to recognize anxiety or conscious/subconscious conflict among pregnant women, and to take measures to enable them to get assistance from their husbands and parents as well as social assistance, and to further promote early diagnosis and treatment. Moreover, obstetricians and gynecologists should play leading roles in preventing the occurrence of mental health problems associated with pregnancy and delivery, through association with specialists at other departments.

REFERENCES

- 1) Read, G.D.: The discomforts of childbirth. *BMJ* 1949; 1: 651–654.
- 2) Morris, N.: *Handbook of Psychosomatic Obstetrics and Gynecology*. ed. Dennerstein, L. and Burrows, G.D., Elsevier Biomedical

- Press, Amsterdam, 1983; 281–308.
- 3) Sosa, R., Kennell, J., Robertson, S. and Urrutia, J.: The effect of a supportive companion on perinatal problems. Length of labor, and mother-infant interaction. *N E J Med* 1980; 303: 597–600.
 - 4) Brockington, I.F. and Kumar, R. (translation supervised by Hideo Hosaki): *Motherhood and Mental Illness*. Gakugei-sha, Tokyo, 1988; pp.146–156. (in Japanese)
 - 5) Kumar, R. and Robson, K.: A prospective study of emotional disorder in childbearing women. *Br J Psychiatry* 1984; 144: 35–47.
 - 6) Dennerstein, L., Lehert, P. and Rphagen, F.: Postpartum depression-risk factors. *J Psychosom Obstet Gynaecol* 1989; 10(supp): 53–65.
 - 7) Yalom, L., Lunde, D., Moos, R. *et al.*: Postpartum blues syndrome. *Arch Gen Psychiatry* 1968; 18: 16–27.
 - 8) Pitt, B.: Maternity blues. *Br J Psychiatry* 1973; 122: 431–435.
 - 9) Robson, K.M. and Kumar, R.: Delayed onset of maternal affection after childbirth. *Br J Psychiatry* 1980; 36: 347–353.
 - 10) Matheson, L., Panell, P.K.M. and Bredsen, J.E.: Midazolam and nitrozapam in the maternal ward: mild concentrations and clinical effects. *Br J Clin Pharmacol* 1990; 30: 787–793.
 - 11) Erkkola, R. and Kanto, J.: Diazepam and breastfeeding. *Lancet* 1972; 1: 1235–1236.
 - 12) Okano, T.: Current state and treatment of postpartum depression – Review from the standpoint of the association between biological factors and sociopsychological factors –. *J Jap Soc Psychosom Obstet Gynecol* 2000. (in Japanese)
 - 13) Coghill, S.A., Caplan, H.L., Alexandra, H. *et al.*: Impact of maternal postnatal depression on the cognitive development of the young child. *Br Med J Clin Res Ed* 1986; 292: 1165–1167.
 - 14) Caplan, H.L., Cofgill, S.R., Alexandra, H. *et al.*: Maternal depression and the emotional development of the child. *Br J Psychiatry* 1989; 154: 818–822.
 - 15) Fisher, J., Asthbury, J. and Smith, A.: Adverse psychological impact of operative obstetric interventions: A prospective longitudinal study. *Australian and New Zealand Journal of Psychiatry* 1997; 31: 728–738.
 - 16) Buist, A. and Janson, H.: Effect of exposure to dethiepin and Northiaden in breast milk on child development. *Br J Psychiatry* 1995; 167: 370–373.
 - 17) Wilson, J.T.: Drug excretion in human breast milk: Principals, pharmacokinetics and projected consequences. *Clin Pharmacokinet* 1980; 5: 1–66.
 - 18) Ballard, C.G.: Prevalence of postnatal psychiatric morbidity in mothers and fathers. *Br J Psychiatry* 1994; 164: 782–788.
 - 19) Kendell, R.E. and Gourlay, J.: The clinical distinction between the affective psychosis and schizophrenia. *Br J Psychiatry* 1970; 117: 261–266.

Health Risk Assessment as Educational Tools for Health Promotion

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Abstract: Health risk Assessment (HRA) was developed to have patients modify their lifestyle from a viewpoint of primary prevention of lifestyle-related diseases. HRA has the following functions; 1) to estimate the risk of occurrence of lifestyle-related diseases, 2) to specify lifestyles which deteriorate these diseases, and 3) to evaluate health age and life expectancy after these lifestyles are modified. This paper discusses the criteria for selecting risk factors in developing HRA. The selected risk factors are predictable enough to alter the natural course of the diseases. HRA provides appropriate information to detect unsound lifestyles and offers life skills to recognize suitable approach to change the lifestyle. This paper also reviews effectiveness of HRA as the health educational tools. There have not been enough researches which show capabilities of HRA in primary prevention. Combination of health check-ups and HRA in Japan is expected to be a useful tool for individual health. Efficacy of HRA in modifying unsound lifestyles should be elucidated.

Key words: Health risk assessment; Health education;
Lifestyle-related disease; Health promotion

Introduction

The Japan Medical Association organized the Health Investment Project Committee in 1997 and proposed the basic concepts for health, medicine and welfare in response to the structural reform of medical care. The Committee pointed out the importance of prevention and promotion of national health asset beyond the current framework of early detection and early treatment for health of

the Japanese people in the future.

In order to promote health asset, it is indicated that health activities preceding primary prevention are important just as securing the life-long system for health and medicine. For preventive medical activities preceding the onset of disease, prevention of lifestyle-related diseases centering on health education has been advocated.

However, these activities, though objective and highly reproducible, have not yet been

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adequately studied. Health risk assessment (HRA) is an educational tool for health promotion proposed by Robbins and Hall in the 1970s in the United States.¹⁾

For adopting HRA techniques in daily clinical medicine, the author reviewed current references related to the method and utility of health risk assessment.

Historical Background of HRA

HRA is an educational tool to motivate its subjects to improve their lifestyle by predicting their health in the future based on their current lifestyles and laboratory test results and by proposing the expected levels of improvement for their health through modifiable lifestyles. It is characterized by the following features.

- To analyze the future health risks using a disease model based on the current lifestyle
- To express health risks by using three indexes of the risk for disease occurrence, the life prolonging effect, and the health age
- To re-evaluate the health risks of the subjects in view of their lifestyle modification targets and express the level of improvement using three indexes
- To offer materials for understanding usefulness of improvements that should be made for lifestyles.

Kondo *et al.*²⁾ and Nakamura *et al.*³⁾ developed the Japanese version based on HRA originally developed in the United States.

When carrying out HRA, the following questions are asked regarding seven lifestyle factors proposed by Breslow.⁴⁾

- (1) Optimum alcohol intake
- (2) Bodyweight control
- (3) Physical exercise
- (4) Eating breakfast
- (5) Not eating between-meal snacks
- (6) Sleeping hours
- (7) Non-smoking

Questions are so designed as to obtain con-

crete answers regarding these factors.

Self-reported information on family history and past history that may participate in development of the disease and laboratory test results (total cholesterol and HDL cholesterol) are also used.

Often-used HRA predictive indexes are described below.

- Risk for developing disease
- Life prolongation effect
- Health age

The risk for developing disease is calculated by using the disease development model based on the lifestyle and disease-related factors obtained from the questionnaire sheet. For calculating risks of a group, the ratio of the group possessing each factor is used. For calculating life prolongation effect, risk of death in addition to occurrence of the disease should be calculated.

Life prolongation effect is the difference between life expectancy calculated with mortality of the time when the problematic lifestyle was improved and life expectancy at the current time point. This index was devised for use in understanding effectiveness of improving lifestyle.

Health age represents the current level of health risk of an individual as compared to the health risk of the general population. Since the health risk of the general population increases uniformly with advance in age, indicating the health risks of an individual corresponding to those of a group would inform the individual of the problems of his/her lifestyle in view of the difference between his/her actual chronological age and the age of the group to which his/her health age corresponds.

Selecting Diseases for HRA

HRA aims to improve lifestyles and the following standards are needed to select its object diseases.

- (1) Lifestyle is related to the disease.
- (2) Degree of improvement made for life-

Table 1 Studies on Effectiveness of HRA

Authors	Subject population	Period of observation	Result index	Achievements
Connel <i>et al.</i> (1995) ⁵⁾	2,196	12 months	Total cholesterol BP Frequency of physical exercise Obesity	• Decreases in BP and BMI
Dunton <i>et al.</i> (1990) ⁶⁾	1,735	6 months	Safety belt use	• Increased belt use • Use of auxiliary materials irrelevant
Gemson and Sloan (1995) ⁷⁾	161	3 years	Frequency of physical exercise Seat belt use Cholesterol Bodyweight BP	• Improved health age and physical activity • Greater improvement in cholesterol, frequency of physical exercise, BP, and bodyweight in group with larger health risks
Merrill and Sleet (1984) ⁸⁾	3,947	1 year	Seat belt use	• Improved seat belt use ratio
Nice and Woodruff (1990) ⁹⁾	625	1 year	Health related factors	• Those taking HRA are younger than those not taking and have shorter education record. Improved in smoking and excessive drinking, but not significantly
Spilman <i>et al.</i> (1986) ¹⁰⁾	4,721	1 year	Health related factors	• Improved physical activity and cessation of smoking • Improvement in health risks

style can be confirmed.

- (3) The disease places significant burden on the subject population.

Standards for Selecting Risk Factors

Possible risk factors are shown as the lifestyles that are relevant for occurrence of the disease once the disease is selected. To implement effective HRA for such lifestyle-related risk factors, the following standards must be used.

1. Quantity

- 1.1 Risk ratio
- 1.2 Attributable risks

2. Reliability and consistency

- 2.1 Removing biases
- 2.2 Consistency
(supported by plural studies)
- 2.3 Biological validity

3. Effect of improvement

- 3.1 Degree of improvement of risk ratio, etc.

4. Effect of intervention

- 4.1 Adaptability to the subject population
- 4.2 Quality of information

Lifestyle and Life Skill

In order to implement HRA, lifestyles for evaluating health risks must be analyzed. While HRA uses such lifestyles as smoking and drinking, it is necessary to analyze the factors that habituate such habits.

Recently, the focus is on health education using life skills. Life skills mean techniques to establish the lifestyle, which is desirable for self, not to offer traditional health education such as stopping smoking or moderating drinking.

Life skills include the following:

- Cognition of the situation
- Cognition of the role
- Alternative activity
- Selecting lifestyle

- Re-organizing targets of life
- Utilization of environmental resources
- Positively processing and modifying environment
- Breaking away
- Compromise
- Dealing with difficulties

To recommend smokers to stop smoking requires explaining not only the health hazards of smoking, but also the ways to avoid the behavior by life skills.

References Regarding Efficacy of HRA

Table 1 shows the studies⁵⁻¹⁰⁾ which investigated effectiveness of health education using HRA.

Some report recognize improvements to health risks by health education techniques using HRA, but others do not observe significant differences.

Improvements of HRA

1. Extending HRA from Primary Preventive Activity

HRA has so far been developed and used mainly for disease prevention by improving lifestyle. In addition to conventional uses as preventive activities, it is necessary to develop HRA related to daily clinical medicine.

In daily clinical medicine, we need to consider encountering patients who are disease carriers or who are about to manifest symptoms. Although current HRA calculates the degree of risk for development of diseases, HRA should be developed to show how the prognosis might be affected for asymptomatic patients.

Concretely speaking, guidance on lifestyle is important for DM or glucose intolerance patients, and evaluation of future health risks (prognosis and complications) attributable to lifestyle is necessary.

2. Extending Subject Population

Current HRA mainly addresses lifestyle-

related diseases and is applied to those in their 30s to 60s. The concept of HRA is not to be limited to lifestyle-related diseases, but should be adapted to decrease the burden on health of the subject populations.

More concretely, HRA should be developed and adapted for the elderly or the younger populations and for those in the perinatal period. Departments of Gynecology & Obstetrics and Preventive Medicine of St. Marianna University School of Medicine have prepared an Obstetric Data Base to study disease models on abnormal deliveries.

Disease-specific HRA should also be studied. HRA for osteoporosis that can increase burdens on health of the aging society is necessary, and it can be used to evaluate younger women.

3. Coordination with Health Screening Programs

Development and adaptation of HRA coordinated with conventional health screening programs are also necessary. Yoshida *et al.*¹¹⁾ developed a system of health education by incorporating general health screening and HRA to predict changes in health screening results of the following year by improving lifestyles.

HRA model for predicting changes in hypercholesterolemia is being built in order to relate HRA with the health-screening program under the Law of Health and Medical Services for the Aged.¹²⁾

Conclusion

In addition to secondary preventive activities, family physicians are expected to incorporate primary preventive activities in their daily clinical services.

Optimum tools for primary preventive activities are required, and HRA is a useful technique for expressing the effects of intervention for health promotion by disease simulation.

This paper reviewed references on current

HRA and studied the components of HRA in daily clinical medicine in the future.

REFERENCES

- 1) Robbins, L.C. and Hall, J.H.: *How to Practice Prospective Medicine*. Indianapolis, Methodist Hospital of Indiana, 1970.
- 2) Kondo, T., Yoshida, K. and Sakurai, H.: Development of health prediction system in health management. *J of JMA* 1984; 91: 2187–2192. (in Japanese)
- 3) Nakamura, M., Oshima, A. and Miura, M.: Science of health prediction. Ed. Morimoto, K. *et al.*; In *Lifestyle and Health*, Igakushoin, Tokyo, 1991: pp. 262–279. (in Japanese)
- 4) Belloc, N.B. and Breslow, L.: Relationship of physical health status and health practices. *Prev Med* 1972; 1: 409–421.
- 5) Connel, C.M., Sharpe, P.A. and Gallant, M.P.: Effect of health risk appraisal on health outcomes in a university worksite health promotion trial. *Health Education Research: Theory and Practice* 1995; 10: 199–209.
- 6) Dunton, S., Perkins, D. and Zoph, K.: The impact of work-site-based health risk appraisal programs on observed safety belt use. *Health Education Research: Theory and Practice* 1990; 5: 207–216.
- 7) Gemson, D. and Sloan, R.: Efficacy of computerized health risk appraisal as part of a periodic health exam at the worksite. *Am J Health Promot* 1995; 9: 462–466.
- 8) Merrill, B. and Sleet, D.: Safety belt use and related health variables in a worksite health promotion program. *Health Educ Q* 1984; 11: 171–179.
- 9) Nice, D. and Woodruff, S.: Self-selection in responding to a health risk appraisal: Are we preaching to the choice? *Am J Health Promot* 1990; 4: 367–372.
- 10) Spilman, M., Goetz, A., Shultz, J., Bellingham, R. and Johnson, D.: Effect of a corporate health promotion program. *J Occup Med* 1986; 28: 285–289.
- 11) Yoshida, K., Okazaki, N., Honohara, S., Sugiyama, J., Nakamura, A., Iwashimizu, Y. and Kitagawa, T.: Health risk appraisal applied to ordinary AMHTS. *Meth Inform Med* 1993; 32: 260–263.
- 12) Takahashi, E., Kishimoto, T., Iida, Y., Yoshida, K., Miyakawa, M., Sugimori, H., Izuno, T., Okazaki, N., Tamura, M. and Hinohara, S.: HRA model for hypercholesterolemia based on a longitudinal health database. *Meth Inform Med* 1998; 37: 130–133.