INTRODUCTION
The Fourteenth International Symposium of the Foundation for the Promotion of Cancer Research, entitled ‘Pain Control, Palliative Medicine and Psycho-oncology: Present Status and Future Direction’, was held in Tokyo on January 24–26, 2001. The Chairman of the organizing Committee was Dr Tadao Kakizoe, Director, National Cancer Center Hospital, Tokyo, Japan.

The Symposium was opened by a welcoming address given by Dr Takashi Sugimura. Dr Sugimura noted the unique nature of this particular Symposium being entirely devoted to the supportive care of the oncology patient. Previous Symposia have been devoted largely to basic and clinical research pertaining to the types of cancer and the organs involved (1–3). The Symposium is an acknowledgment of the fact that since 1981, cancer has been the primary cause of death in Japan. Currently, one out of every three deaths in Japan is due to cancer.

Dr Kakizoe, in his keynote address, emphasized this point and noted the paradigmatic shift taking place in medical oncology from the pursuit of an ultimate cure of a disease to its palliative treatment when a cure appears to be impossible. This shift in emphasis has been occurring over the last 25 years and acknowledges the fact that ~50% of adult patients with cancer at the National Cancer Center Hospital in Tokyo will ultimately die of their disease or its complications. In view of this paradigmatic shift, the current Symposium ‘Pain Control, Palliative Medicine and Psycho-oncology: Present Status and Future Direction’ was devised.

PAIN CONTROL AND PALLIATIVE MEDICINE

1. PAIN
Dr H. Shibasaki, Department Neurology, Kyoto University, Kyoto reviewed the neurophysiological mechanisms of pain perception in humans. He disclosed the important role of the cerebral cortices in human pain perception which have been demonstrated by manetoencephalogram (MEG), positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) technologies. Pain in humans is perceived in the contralateral S1, bilateral S2, bilateral insula and anterior cingulate cortex. The insula and anterior cingulate cortex are involved in the emotional aspect of pain perception.

Dr T. Yokota, Department Physiology, Shiga University of Medical Science, Seta, Otsu discussed the mechanisms of neuropathic pain in humans. Neuropathic pain is clinically a common cause of pain in patients with cancer and can often be difficult to treat. Dr Yokota discussed mechanisms of neuropathic pain related to tumour invasion of both peripheral nerves and spinal cord, mechanisms related to chemotherapy induced peripheral neuropathy (e.g. vincristine related peripheral neuropathy) and mechanisms of pain in post-herpetic neuralgia (PHN).

The molecular mechanisms of opioid tolerance were discussed by Dr C. Inturrisi, Department Pharmacology, Cornell University, Ithaca, NY. The decrease in sensitivity to opioids such as morphine can be viewed as resulting from within-systems mechanisms affecting opioid receptors (e.g. receptor downregulation or uncoupling) or from between mechanisms which include increases in anti-opioid systems (e.g. cholecystokinin or dynorphin) or neuroplastic changes that increase the gain of the pain transmission system and/or facilitate neuroadaptation to morphine’s effect. A key feature of central sensitization is increased C-fibre activity resulting in increased release of transmitters which produce a cumulative depolarization that can override the voltage dependent magnesium ion block of the NMDA receptor resulting in an influx of calcium ions and a amplification of depolarization. A clinical role for NMDA receptor antagonist in combination with an opioid to improve pain management is suggested.

Dr T. Suzuki, Department Toxicology, Hoshi University, Tokyo discussed clinical research concerning opioid tolerance and dependence in the chronic pain model. The results of studies indicate that the rewarding effects of morphine can be attenuated in the presence of inflammatory hyperalgesia and...
the suppression of the morphine-induced place preference corresponds to the intensity of inflammatory hyperalgesia. It is suggested that endogenous κ-opioid systems may be activated by chronic inflammatory nociception, resulting in the suppression of the development of the rewarding effects of morphine.

‘Recent progress in opioid therapy for cancer pain patients in Japan’ was the title of Dr F. Takeda’s talk. Dr Takeda, Visiting Professor, Saitama Medical School, Saitama illustrated the significant progress that has been made in Japan regarding cancer pain relief. Japan’s cancer pain relief program was initiated in 1982 with a field-test of the WHO Draft Interim Guidelines on Relief of Cancer Pain. The progress that has transpired since that time has included legislative easing of restrictions on opioid availability and increased morphine consumption, a measure of effective pain control, in Japan. Although per capita morphine consumption is rising in Japan, consumption is still less than one-sixth that consumed in the USA, perhaps indicating that some physicians are reluctant to prescribe morphine for severe pain. Postgraduate education has thus been much emphasized in Japan and seminars on cancer pain relief and palliative care have been held at national and district levels. In addition, many medical and nursing schools in Japan now have curricula on cancer pain relief and palliative care.

Dr C. Cleeland, Director, Pain Research Group, University of Texas M. D. Anderson Cancer Center, Texas discussed the assessment of pain and other symptoms of cancer. He emphasized the importance of adequate assessment in treating pain. Assessment should include some systematic way of measuring pain to allow patients an opportunity to give some form of self report. Protocols to treat pain should be in place and measures of pain should be able to elucidate if pain management is effective or not. Dr L. Librach, Temmy Latner Centre for Palliative Care, Toronto, discussed issues related to the choice of opioid prescription. These include the type and severity of pain, the pharmacokinetic and pharmacodynamic properties of the opioid, efficacy to side effect ratio, individual patient differences and care provider and system issues.

Dr S. Tsuneto, Hospice, Yodogawa Christian Hospital, Osaka discussed the treatment of neuropathic pain in patients with cancer. He noted the possible approaches to neuropathic pain, including pharmacological, anaesthetic and neurosurgical approaches. Possible pharmacological approaches include the use of continuous subcutaneous infusions of lidocaine (CSIL) or ketamine (CSIK). Dr Tsuneto outlined the results of a retrospective study comparing these two agents in terms of efficacy and side effects. This study showed that treatment with CSIL or CSIK successfully relieved about half of his
cohort of terminally ill patients with neuropathic cancer pain. CSIL appeared to have less side effects than CSIK.

Dr G. Michael Downing, Victoria Hospice Society, Victoria, British Columbia spoke of the concepts of total pain and suffering in the advanced cancer patient. Cancer continues to be one of the leading causes of death in Canada (65 000 deaths in 2000) and many other countries for the current and foreseeable future. Depending on the type of cancer, the emergence of pain as cancer progresses into the advanced stage occurs in upwards of 60–80% of patients. Qualities of somatic, visceral, nociceptive and neuropathic pain are being pursued with newer understandings of the anatomical, neuromolecular and soon even genetic bases and the expectation for new, more effective opioids, adjuvants and interventional treatments. These are not the only aspects of pain which patients and their families endure. Dr Downing’s presentation focused on the concept of ‘total pain’ and the experience of suffering as a necessary aspect of understanding and thereby appropriately treating cancer pain.

He outlined the seven ‘P’s of pain: physical, emotional, intellectual, interpersonal, financial, spiritual and bureaucratic pain, and, in parallel, the seven ‘C’s of care to provide support and relief: competence, consistency, coordination, climate, cooperation, communication and compassion. One of many unfortunate consequences of unrelenting pain may be for the patient to wish for euthanasia which, although ‘relieving’ the pain by ending life abruptly, carries much deeper implications. Further, it is not only the patient who suffers but also his or her family.

2. DYSPNEA

Dr T. Nishino, Department of Anesthesiology, School of Medicine, Chiba University, Chiba discussed the mechanisms of dyspnoea using the model of breath-holding trials. Dyspnea, defined as an uncomfortable awareness of difficulty in breathing, is not only a subjective sensation but also a serious respiratory symptom. The precise origin of the dyspnic sensation remains largely unknown. Several sensory receptors are considered to be responsible for generation of dyspnic sensation. Among these receptors, the central collateral discharge receptors seem to play the major role in generation of dyspnea. It has been proposed that central collateral discharge receptors consist of interneurons high in the central nervous system that transduce the intensity of motor output to the respiratory muscles and transmit the intensity of motor command to the sensory cortex, yielding a sensation of respiratory effort. This proposal is called ‘the motor command theory’. Among experimental models, breath-holding is the most powerful experimental tool which has contributed significantly to the development of ideas concerning the etiology of dyspnea.

There are two distinctly different periods during the course of breath-holding. Immediately after breath-holding there is a certain period of no particular respiratory sensation lasting for 20–30 s. This period is terminated by onset of dyspnea and followed by the second period during which there is a progressive discomfort until the breaking point. The studies on the genesis of dyspnea during breath-holding showed that (1) there is little training effect on the period of no respiratory sensation whereas the training effect plays an important role in prolongation of the total breath-holding time, (2) hypercapnic ventilatory response is inversely proportional to the period of no respiratory sensation during breath-holding, (3) the period of no respiratory sensation in patients with COPD is apparently shorter than those in normal healthy subjects and (4) measurement of the period of no respiratory sensation can be a useful clinical test for the study of the genesis of dyspnea. The use of the breath-holding test as a clinical test of pulmonary function is not popular now in clinical medicine because the breath-holding time is greatly influenced not only by physiological factors but also by non-physiological factors. Dr Nishino reported that the measurement of breath-holding time still gives a lot of information, particularly when the period of no respiratory sensation and total breath-holding time are measured separately.

Dr E. Bruera, Department of Symptom Control and Palliative Care, University of Texas M. D. Anderson Cancer Center, Texas discussed the current treatment of dyspnea. Dyspnea is a subjective sensation and does not necessarily correlate with clinical findings in a given patient. It occurs in up to 75% of patients with advanced cancer and good symptom control is achieved less frequently in the case of dyspnea as compared with pain, nausea and other frequent symptoms in cancer patients. Dr Bruera noted that in most cancer patients dyspnea is a multidimensional symptom and is frequently caused by multiple mechanisms including direct and indirect tumor effects, treatment side effects and psychological conditions.

The assessment of the dyspneic patient includes searching for the main pathophysiological mechanisms and evaluating the intensity and functional impairment due to dyspnea. Management of dyspnea can only take place after careful assessment and management of possible specific causes. Once optimal management of specific causes has been achieved, a number of symptomatic measures can be applied. Oxygen has been proven to be effective in hypoxemic patients. It can be administered regularly or occasionally on an as needed basis. The effectiveness of oxygen on patients who are not hypoxemic has not been established. There is substantial evidence that systemic opioids have a beneficial effect on cancer related dyspnea. This is possible without inducing respiratory depression. The optimal type, dose and mode of administration have not been determined. If the patient is already receiving opioids, the usual breakthrough dose can be used for the management of dyspnea as well as pain. Nebulized opioids have not demonstrated effectiveness as compared to placebo.

More studies are required in order to characterize better this route of administration. Benzodiazepines have not been found to be effective in the general management of dyspnea but may be helpful for the treatment of episodes associated with anxiety attacks. Regular use should be avoided when possible to limit side effects such as confusion or falls. A number of conditions which cause cancer dyspnea respond to corticosteroid medication including superior vena caval obstruction, carcinomatous
lymphangitis and COPD or obstruction of the airway by head and neck tumors. The main drawback of these drugs is the presence of serious toxicity with long-term, high-dose administration. Since dyspnea is a variable symptom that can be exacerbated by physical and psychological stressors, patients and families should be educated so they can identify factors likely to worsen dyspnea. Medication or oxygen can be used for symptomatic relief prior to dyspnea causing manoeuvres. The family should be educated that dyspnea is subjective and that tachypnea and the use of accessory muscles do not necessarily indicate that the patient is suffering. Dr Bruera said that the aim of treatment is to relieve the patient’s subjective dyspnea and not abatement of physical signs of respiratory distress.

3. FATIGUE AND CACHEXIA

Dr O. Spruyt, Peter MacCallum Cancer Institute, Melbourne discussed the mechanisms of fatigue in advanced cancer. Fatigue was defined as a general feeling of debilitating tiredness or loss of energy. Fatigue is the most commonly reported symptom in patients with advanced cancer. This symptom can impact on all the dimensions of the person, the physical, social, emotional, psychological and spiritual dimensions, and result in severe distress and alienation. Patients with cancer rate fatigue as having a greater impact on their daily lives than pain. This impact of fatigue on the lives of cancer patients and their quality of life, is only now being recognized and addressed in palliative care research.

Dr Spruyt discussed the results of the Fatigue Coalition indicating that 78% of patients experienced fatigue during the course of their disease and treatment, 86% of caregivers reported fatigue in the index patients and oncologists perceived fatigue in 76% of their patients. However, 74% of patients considered fatigue a symptom to be endured and 80% of oncologists believed it to be both overlooked and undertreated. Fatigue is a complex and multifactorial symptom. Most often, however, it has been measured and assessed by single items in general symptom checklists. It may co-exist with and be influenced by depression, other physical symptoms and cancer-related therapies. Cited physical associations include anaemia, pain, infection/fever, hormonal or nutritional deficiencies, depression/anxiety, sleep disturbances, excess inactivity or rest. Fatigue severity has been shown to be significantly associated with pain and dyspnea scores in cancer patients and with anxiety and depression. Severity of fatigue was unrelated to age, gender, diagnosis, presence of site of metastases, anemia, dose of opioid or steroid, any hematological or biochemical indices (except urea), nutritional status, voluntary muscle function or mood.

Dr Tatsuo Akechi, Psycho-Oncology Division, National Cancer Center Research Institute East, Kashiwa discussed the assessment and treatment of fatigue in cancer patients. He noted that fatigue now probably represents the most common unrelieved symptom of cancer. For patients with cancer, fatigue can be a chronic problem that is caused by a combination of physical, psychological and situational factors. Dr Akechi noted that instruments for comprehensively assessing the fatigue experienced by cancer patients must have several qualities. First, the format must be based on self-rating, because fatigue is a subjective symptom and the questionnaire must be brief and simple enough to be completed by cancer patients suffering from fatigue. Second, a multidimensional approach is needed, because fatigue is thought to be a multi-dimensional symptom containing aspects of at least physical and affective sensations. Third, the scale must be specifically designed for cancer-related fatigue and the reliability and validity of the scale for use by cancer patients must be established. Although there is currently no gold standard, several instruments (the Multidimensional Fatigue Inventory, the Cancer Fatigue Scale) are available. The therapeutic interventions for fatigue include non-pharmacological and pharmacological approaches. Non-pharmacological management includes exercise, patient education, psychosocial intervention, etc. Pharmacological management includes corticosteroids, psycho-stimulants, etc. There are very few interventions with proven efficacy in clinical trials, Dr Akechi noted.

4. PAIN AND PALLIATIVE MEDICINE FOR CHILDREN

Dr J. Collins, Head, Pain and Palliative Care Service, The Children’s Hospital at Westmead, Sydney discussed the management of cancer pain in children. The basis of his talk was Cancer Pain Relief and Palliative Care in Children (Geneva: WHO 1998), which advocates the global application of the principles of pain management and palliative care for children with cancer. Irrespective of geographical location and acknowledging that treatment options for some children may be limited, the WHO has mandated pain management and palliative care as a standard of care for all children with cancer.

The principles of pain management espoused by the WHO include pain assessment and measurement, guidelines for non-drug pain relief therapy and guidelines for analgesic drug therapy. The principle of the WHO analgesic ladder, the principle of opioid dose escalation and management of opioid side effects, adjuvant analgesic prescription and approaches to procedural pain were outlined. New developments in the management of cancer pain in children were outlined. These developments included the epidemiology of pain and other symptoms, novel analgesic study design and therapies, insights into the integration of psychological and pharmacological interventions in the management of procedural pain and an evolving model of care that incorporates the care of the child dying of cancer as part of the constituency of a pediatric pain service.

Dr Tsunematsu, National Children’s Hospital, Tokyo outlined research on the perceptions of family members who have a history of multiply affected relatives with cancer, including pediatric cancer. The identification of some cancer-predisposing genes has been developed by recent advances in molecular biology. By using this new predictive testing, many ethical and psychosocial issues arise. These issues may arise in the context of Li–Fraumeni syndrome. It is regarded that p53 gene altera-
... which can cause multiple cancer is related to these syndromes, although not all patients have the mutation.

Dr Tsunematsu presented data on a study conducted regarding parental attitude towards genetic testing. When parents who did not have an increased risk of familial cancer were asked about their attitude towards genetic testing, they showed a considerable level of interest in pre-symptomatic testing for cancer for themselves and their children under the hypothetical situation. Most of the parents were willing to have their children undergo genetic testing for research purpose and wanted to know the whole result. Based on the results of this study, genetic counselling with families who had a history of multiply affected relatives was provided. Parental reaction to counselling in this situation was variable; however, it was the general belief of the care-providers that provision of genetic counselling was of vital importance.

5. NURSING ROLE IN PALLIATIVE CARE

Jie S. Willey, Research Nurse Supervisor, Department of Symptom Control and Palliative Care, The University of Texas M. D. Anderson Cancer Center, Texas discussed nursing perspectives in palliative care. She noted that palliative care nursing still remains an area that requires more attention in oncology nursing education, clinical practice and research. She stated that it is evident that the training for palliative care nursing has not been adequate in the USA and therefore, basic knowledge of pain and symptom management is lacking among oncology nurses. Nursing roles in palliative care, in general, can be defined as intensive caring, collaborative sharing, continuous knowing and continuous giving. Other palliative care nursing roles include maintaining patients' identities, providing spiritual care and recognizing and helping in bereavement.

The Cage Questionnaire has been adopted and used by the nurses in the Department of Symptom Control and Palliative Care at the M. D. Anderson Cancer Center. This assessment tool is used to evaluate patients’ overall expression of suffering, cognitive function and tendency to use maladaptive coping mechanisms. It has proven to be an effective tool in assessing palliative care patients. Once the assessment has been completed, the palliative care nurse plays a critical role in the development of a plan of care, explanation, education and continued reinforcement of the plan of care to the patient and family. It is also essential to the palliative care nurses to follow up with symptom assessment to measure the success of the plan. Providing the best quality of life for patients throughout their cancer experience is a challenging, complex endeavor. The skill and knowledge of palliative care nurses are viable solutions in meeting the physical, psychological, social and spiritual needs of cancer patients, Ms Willey noted.

Mikako Okada, Palliative Care Unit, St. Luke’s International Hospital, Tokyo presented data on the nursing role in Japan concerning symptom management. She noted that it is well recognized that nursing has responsibilities in symptom management since nurses communicate with patients and caregivers very closely. Although nurses in Japan are not allowed to prescribe medications, nurses play important roles in assessing symptoms, in evaluating management of symptoms and in providing multidimensional interventions.

In the Palliative Care Unit at St. Luke’s, the nursing role in symptom management are as follows: (1) assessing patterns and characters of symptoms, (2) choosing and using the rescue medication appropriately, (3) evaluating the effects of symptom management closely and systematically, (4) discussing with physicians and pharmacists changes in medications if needed, (5) assessing and relieving the factors influencing symptoms, (6) providing physical interventions, (7) educating patients and caregivers and (8) advocating for patients concerning symptom management. Effective symptom management is indispensable for the quality of life (QOL) of cancer patients and caregivers. Nurses' efforts to acquire sufficient knowledge and skills in symptom management significantly contribute to their QOL.

6. PALLIATIVE CARE SYSTEM

Dr N. Shimoyama, Head, Pain and Palliative Care Division, National Cancer Center Hospital (NCCH), Tokyo discussed the activities of the palliative care team at NCCH. Improvements in palliative care at the NCCH started 6 years ago. The first step was making a truth-telling manual, which was a very new concept at that time, because most doctors in Japan still hesitated to tell the truth to cancer patients. The second step was making close connections with hospitals near the patients’ homes to fulfil the patient’s need to spend their remaining days at home (Division of Liaison and Home Care). The third step was making palliative care guidelines, which focused on improvement of quality of life of cancer patients. These guidelines give information on how to treat cancer pain, dyspnea and other symptoms.

On the basis of these developments, the palliative and supportive care team of NCCH came together in July 1999. The team consists of the following members: (1) one pain medicine and palliative care specialist; (2) two psychiatrists and psychoncologists; (3) three medical oncologists; (4) six pharmacists; and (5) one medical social worker. Although there are no beds exclusively for palliative care patients at NCCH, the plan was to build a palliative care system in which the team had one or two palliative care beds in most of the wards of the hospital. Nurses, in charge of the palliative care patients in the wards, work closely with the team. They provide information on the patient to the team members and participate in discussions at case conferences, which take place once per week.

The role of the palliative team members at NCCH is as follows:

(1) The pain and palliative care specialist assesses the pain and suffering of the patient and treats the pain and other physical symptoms such as dyspnea, nausea, vomiting, hiccups and itching etc.
(2) The psychiatric specialists assess the psychiatric status of the patient and treat conditions such as anxiety, depression, confusion and adjustment disorders.

(3) The medical oncologists attend case conferences and give advice in setting the patient’s goal of management.

(4) The pharmacists frequently visit the wards to talk to patients about medications they are taking. Special emphasis is placed on providing information on opioids, so that the patients may be dispelled from incorrect beliefs concerning opioid therapy.

(5) The medical social worker acts to support cancer patients who have social problems such as hospital payment and also locates a hospice or a hospital near the patient’s home, which can manage the patient for the remaining days of his or her life.

The special palliative care issues pertaining to Japan were discussed by Dr Shimoyama and included the following: (1) informed consent and truth telling to cancer patients are not common in Japan; (2) many patients in Japan are denied of their rights as a patient; (3) patients and their families are not provided with information and education on palliative care by the hospital; (4) the number of hospices and palliative care units in Japan is far from adequate; (5) there are very few pain and palliative care specialists for children; and (6) the choice of opioids is very limited.

Dr. B. Gagnon, Montreal General Hospital, Quebec discussed the challenges and rewards of working as a palliative care team. Dr Gagnon noted that it is imperative that the physician involved in caring for palliative care patients assesses pain in all its dimensions. He said that there was a need for cooperation for a complete team of paramedical members such as nurses with expertise in pain management, social workers, physiotherapists, occupational therapists, psychologists, pastoral care experts, etc. in the assessment of pain. The fulfillment of the responsibilities of each team member in the assessment and treatment of the ‘total pain’ needs close coordination and a complementary/working together. Special emphasis is placed on the challenges of good communication between team members especially when cases become very complex. In reality, most patients are aware of their terminal condition and lack of open communication may result in exacerbation of their distress. Simple acknowledgment by the treating team may have tremendous power in relieving this distress, Dr Gagnon stated.

**PSYCHO-ONCOLOGY**

**1. DEPRESSION AND ANXIETY**

Dr D. Kissane, Centre for Palliative Care, Peter MacCallum Cancer Institute and Department of Medicine, St Vincent’s Hospital, University of Melbourne, Victoria discussed the history of psycho-oncology and palliative medicine. He noted that it was only during the second half of the twentieth century that systematic study of the universal human responses to cancer and care of the dying began. Two distinct but related movements emerged: psycho-oncology and hospice care.

Psycho-oncology grew out of the psychosomatic concepts of the 1940s, with Arthur Sutherland commencing a psychiatric research unit at the Memorial Sloan-Kettering Cancer Center in New York in 1950. He was followed by Drs Mastrovito and Holland. Psycho-oncology concerns itself with the biopsychosocial influences on cancer development and morbidity, including the emotional responses of patients, families and carers to the illness and its treatment. Special units developed throughout Europe and America during the 1970s, followed by societies such as the British Psychosocial Oncology Group (1983), the International Psycho-oncology Society (1984) and the Japanese Psycho-oncology Society (1985). Dr Kawano initiated the latter for Japan. Conferences, journals (*Journal of Psychosocial Oncology*, 1982; *Psycho-Oncology*, 1992), textbooks and training programs followed thereafter.

Although the notion of hospice dated back to the tenth century and religious nuns formed hospices during the nineteenth century, the start of the modern hospice movement is credited to Cecily Saunders with the development of St. Christopher’s Hospice in London in 1967. Others such as Balfour Mount in Montreal and Robert Twycross in Oxford made substantial contributions. The first hospice in Japan was Seirei Mitakagahara in Hamamatsu City, established in 1981. By 1995, the Japanese Ministry of Health and Welfare recognized 20 palliative care units.

As both psycho-oncology and palliative care have developed their clinical and educational programs, research has been vital to build these respective disciplines. The communication of a diagnosis of cancer and its associated treatments bring psychospiritual and existential challenges to the adjustment process for each individual. The past decades have concentrated on descriptive and observational studies and gradually moved more into refining interventional programs. Sustaining quality of life is an expected emphasis within oncology today. At the beginning of this new millennium, both psycho-oncology and palliative medicine have emerged as new disciplines in their own right, being seamlessly integrated into the patient’s total care. They bring standards of care and practice guidelines, based on empirical data, which will enrich the practice of oncology. As the population ages and the number of new cases of cancer in the world rises to 15 million by 2015, we need to strive to ensure that psycho-oncology and palliative care are available to all.

Dr Y. Uchitomi, Psycho-Oncology Division, National Cancer Center Research Institute East, Chiba discussed the issue of depression in cancer patients following the disclosure of diagnosis. Depression in cancer patients is common and occurs throughout the course of the illness. Anxiety in cancer patients is also common but not usually clinically significant. In 1983, Derogatis et al. reported on the prevalence of psychiatric disorders among 215 patients, both ambulatory and hospitalized, after the initial diagnosis of various cancer types and disease stages in three Cancer Center Hospitals using the Structured Clinical Interview for DSM-III classification of psychiatric disorders. About 6% were diagnosed as having major depression and 27% as having adjustment disorders with depressive.
mood and/or other features. Recently, these findings were confirmed in consecutive Japanese cancer patients from two National Cancer Center Hospitals in Japan. The most common psychiatric disorders were adjustment disorders with depressed mood and major depression.

In recent studies, depression and depressive ways of coping with lung cancer were significantly associated with shorter survival, independent of the influence of biomedical prognostic factors. However, previous studies have revealed that physicians are poor at detecting emotional distress in patients and at helping them to resolve these problems. Some possible strategies were suggested as being helpful: (1) prevention of depression, (2) detection of depression and (3) standard treatment for depression.

2. PSYCHOSOCIAL FACTORS AND SURVIVAL

Dr M. Watson, Consultant Clinical Psychologist, the Royal Marsden Hospital, London discussed the issue of coping and cancer survival. Psychological response to breast cancer has been suggested as a prognostic factor with an influence on survival. A few studies have examined the influence of psychiatric symptoms on disease outcome. A psychological response of fighting spirit or an attitude of helplessness has been suggested as being of prognostic significance. Most studies in this area are limited by their small sample size or short period of follow up.

In 1987, Dr Watson began a large population-based cohort study with the aim of examining the role of such psychological factors in disease prognosis for breast cancer patients. Some 578 women with early-stage breast cancer were enrolled in a prospective survival study. Psychological response was measured within 3 months of diagnosis by a number of reliable pre-validated measures: the Mental Adjustment to Cancer (MAC) scale, the Courtauld Emotional Control (CEC) scale and the Hospital Anxiety and Depression (HAD) scale. Women were followed up for ~5 years (median 4.93, IQR 4.58–5.18). Cox’s proportional-hazards regression was used to obtain the hazard ratio for psychological response, with adjustment for known clinical prognostic factors.

At 5 years follow up a high helpless/hopeless score on the MAC scale [HR 1.55 (95% CI 1.07–2.25)] and a high score on the HAD scale for depression [HR 3.49 (95% CI 1.39–9.24)] have a moderate detrimental effect. Dr Watson presented further data that examined the link between psychological response, psychological therapy and survival in this cohort. Possible mechanisms for these effects were examined and included theories of psycho-neuro-immunology (PNI) and health behavior activities that may modify the risks or promote the maintenance of health.

Dr Yasuo Ohashi, Department of Biostatistics, School of Health Sciences and Nursing, University of Tokyo presented data on the psychosocial variables and cancer survivors. To reveal the clinical significance of health-related QOL measurements data of 390 untreated patients with advanced NSCLC, who participated in two randomized phase III trials, were analysed. The measurements were done using the QOL–ACD developed for Japanese patients receiving cancer chemotherapy. It was shown that the psychosocial domain was significantly associated with both survival and tumor response, by Cox regression and logistic regression, respectively. A multilevel (time × domain) linear model showed that the clinical parameters influenced the mental and psychosocial as well as physical and functional domains. Random coefficient models revealed that the larger PA weight of the physical domain was found under treatment and the PA weight and a diversity of the SS weights in the psychosocial domain were large in the later courses and after treatment. These findings suggest the importance of psychosocial (individualized) intervention for cancer patients, at least those with advanced disease.

3. PATIENT–DOCTOR COMMUNICATION

Dr A. Akabayashi, Department of Biomedical Ethics, School of Public Health, Kyoto discussed the issue of truth telling in cancer care. The Western tradition holds as fundamental a four-principle model that includes patient autonomy, beneficence, non-maleficence and justice and embraces an approach of universal disclosure. The primary arguments against disclosure include concerns about a patient’s loss of hope and resultant depression that may harm the patient. Dr Akabayashi presented three conclusions: first, Japan is in a transitional period regarding medical information disclosure; second, ‘autonomy’ or ‘something close to autonomy’ as a concept should be further developed by taking into account human values in the Japanese context; and finally, improved understanding of cultural differences such as communication styles and roles of the family in decision-making may enhance the development of more pluralistic biomedical ethics, especially regarding palliative care.

Dr W. F. Baile, Professor and Chief, Psychiatry, The University of Texas M. D. Anderson Cancer Center, Texas discussed the issue of breaking bad news with a patient-centered approach. He noted that cancer is often a chronic disease and patients may receive bad news many times over the course of their illness. These include the cancer diagnosis, disease recurrence and failure to obtain a response to treatment, irreversible side effects and the lack of further treatment options.

In Western society, most patients wish to have as much information as possible about their diagnosis and prognosis, the success of treatments offered and the possible side effects. Furthermore, when patients have information about their illness, they can make informed choices and participate in decision-making. Giving patients information and encouraging them to participate in decision-making also reflects a shift in medical care away from a ‘paternalistic’ or doctor-centered model to one that is more ‘patient-centered’ where the patient participates in the important decisions about medical care.

Dr Baile described a six-step protocol called SPIKES which meets the stated goal of providing sensitive information in a way that is supportive to the patient and is guided by the
patient’s wishes for information and participation, need for emotional support and preferences for decision-making. **Breaking bad news: ‘SPIKES’ protocol**

**STEP ONE:** Create a **SETTING** which facilitates the transmission and reception of the news. **RATIONALE:** Bad news is best transmitted when there is a plan for giving the bad news and the environment is conducive to discussion. Physicians should have a plan to create a setting conducive to information exchange (e.g. sit down, greet patient warmly) and how to support the patient who becomes upset.

**STEP TWO:** Find out how much the patient knows about the illness—the patient’s **PERCEPTION**. **RATIONALE:** Breaking bad news to a patient who is not expecting it may cause unnecessary trauma. Finding out what the patient knows can allow the clinician to fill in an educational gap or detect the presence of denial. There are many ways of asking this question, such as ‘tell me what you understand about your medical situation up to now’.

**STEP THREE:** Finding out how much information the patient would like to have—the **INVITATION** to give information. **RATIONALE:** Information needs should be tailored to individual coping styles. While many patients desire complete information, a minority may want to know, for example, if the situation is bad and what action can be taken. One way of asking this question is ‘how much information would you like to have about your illness?’

**STEP FOUR:** Providing **KNOWLEDGE** and information to the patient and family. **RATIONALE:** Patients should be given information in ways they can comprehend. This is a prerequisite to informed consent and patients’ ability to participate in decision-making. This means giving information in small chunks, avoiding vagueness and jargon or excessive bluntness.

**STEP FIVE:** Addressing patients’ **EMOTIONS** using empathic, exploratory and validating statements. **RATIONALE:** Providing psychological support when patients become upset is an important strategy for assisting patients to cope with bad news and to decrease their sense of isolation. Empathizing with and exploring and validating feelings and emotions are important verbal techniques for providing support.

**STEP SIX:** Develop a **STRATEGY** of continued care and **SUMMARIZE** the treatment plan. **RATIONALE:** A treatment plan reduces patient uncertainty. Some treatment is always possible even if it is not geared towards cure. Providing realistic hope, offering treatment options and answering patients’ questions are important tools in this step.

### 4. Genetic Counselling

Dr C. Hughes, Georgetown University Medical Center, Department of Oncology, Washington, DC discussed emerging issues in genetic testing and counselling for inherited cancer risk. Genetic testing for BRCA1 and BRCA2 (BRCA1/2) mutations is increasingly being integrated into the clinical management of individuals who have a family history of cancer that is suggestive of inherited cancer risk. There has been a significant amount of research to understand the ethical, psychosocial and clinical implications of genetic testing in order to ensure informed decision-making about whether to undergo genetic testing, evaluate psychosocial responses to BRCA1/2 test results and to characterize behavioral outcomes of genetic testing.

Thus far, studies have demonstrated that rates of test acceptance range from 57 to 82%; however, utilization rates are substantially higher among newly ascertained clinic-based samples. Further, although early research has shown that individuals who had higher levels of knowledge about breast cancer genetics and those with greater perceptions of the benefits of testing were significantly more likely to undergo testing, recent studies have demonstrated that sociocultural factors such as spiritual faith and family relationships are significantly associated with decisions to receive BRCA1/2 test results. For example, women who had high levels of spiritual faith were about four times less likely to have genetic testing than women who had low levels of spiritual faith. Although there is limited evidence to support long-term levels of adverse psychosocial functioning following genetic testing, receiving BRCA1/2 test results may adversely affect specific domains such as medical decision-making and familial relationships. For example, a recent study has shown that only 13% of female BRCA1/2 mutation carriers elected to have prophylactic oophorectomy despite the fact that preventive surgery may significantly reduce one’s risk of developing cancer. As a result of the empirical evidence available thus far regarding the psychosocial and behavioral impact of genetic testing, an emerging issue in genetic testing and counselling for inherited cancer risk is the development of interventions designed to improve medical decision-making and to facilitate effective coping.

Dr Hughes et al. are conducting a prospective randomized trial to evaluate the impact of a psychosocial telephone counselling intervention on psychosocial functioning, decision-making about cancer surveillance and screening options and family communication about genetic testing among female BRCA1/2 mutation carriers. Women who are identified as carrying a deleterious BRCA1/2 mutation are randomly assigned to receive Standard Genetic Counselling (SGC) or Standard Genetic Counselling plus Psychosocial Telephone Counselling (SGC + PTC) following disclosure of test results. The SGC + PTC intervention is based on the Transactional Model of Stress and Coping and consists of five telephone counselling sessions which are conducted by a professional counsellor over a 5-week period. Study accrual is ongoing; however, analysis of our baseline data has identified mechanisms which are likely to influence psychological reactions to receiving positive test results. These mechanisms include greater perceptions of stress regarding medical decision-making and management of family concerns as well as decreased perceptions about one’s ability to cope with these stressors.

Dr H. Okamura, Professor, Hiroshima University discussed the psychosocial aspects of genetic counselling. He noted that
the impact of genetics in cancer medicine has been marked in
the three areas that define clinical cancer genetics: cancer
genetic counselling, diagnostic cancer genetics and prognostic
cancer genetics. Cancer genetic counselling has become popu-
lar owing to the recent development of genetic tests that pin-
point familial cancer risk. It is composed of presymptomatic
risk assessment and management (cancer risk counselling) and
reproductive risk counselling and the former has two compo-
nents: risk assessment and counselling regarding behavioral,
medical and surgical options to decrease risk.

A basic goal of cancer risk counselling is to derive and
explain an individual's cancer risk in clear terms and the coun-
seller’s role is to educate and enumerate options for patients
and clinicians, answer questions regarding what is known and
suggest appropriate referrals to help reach difficult decisions.
Throughout these discussions, a sensitivity to psychological
and ethical aspects of counselling is essential. Therefore, con-
tinued follow up by the counsellor after the session is the best
way to limit the potential for adverse effects as a result of the
knowledge of inherited cancer risk and ready access to liaison
mental health professionals with experience in cancer genetics
is thought to be a valued asset in cancer risk counselling.

Psycho-oncology research on aspects of cancer genetic
counselling has focused on three broad areas: factors predict-
ing interest in cancer genetic testing, the psychological impact
and effect of genetic counselling and testing for inherited
cancer risk and the relationship between psychological distress
and preventive behaviors. It is difficult for these data to be
applicable to every case, because there are cultural differences
in populations studied and the complexity of the instruments
used in research studies.

At the National Cancer Center in Japan, three protocol
studies regarding cancer genetic testing are approved by the
Institutional Review Board and the Ethics Committee of the
National Cancer Center: APC mutations for familial adenoma-
tous polyposis (FAP), hMSH2 or hMLH1 mutations for heredi-
tary non-polyposis colon cancer (HNPPC) and RB mutations
for retinoblastoma, and genetic counselling started in 1999.
Utilizing these studies, Dr Okamura has developed a research
protocol for examining the psychological, social and behavio-
rnal impact of genetic testing for gene mutations that are associ-
ated with HNPPC or FAP. The impact is evaluated using both
a structured clinical interview and a questionnaire before
(baseline) and 1 month and 12 months after (follow up) coun-
selling for disclosure of genetic test results. To date, 35 sub-
jects have participated in this study and 18 have undergone the
1-month follow-up examination. None of the 18 subjects ful-
filled the diagnostic criteria for psychiatric disorders.

In Japan, clinical cancer genetics including cancer genetic
counselling and testing has started recently. However, as this
area progresses, the importance of methods to estimate and
deal with psychosocial problems will increase in both heredi-
tary cancer patients and individuals at risk of hereditary cancer.
Extensive psycho-oncology research in this area was recom-
mended by Dr Okamura.

5. PSYCHOSOCIAL INTERVENTIONS FOR CANCER PATIENTS

Dr T. Hosaka, Department of Psychiatry and Behavioral Sci-
ence, Tokai University School of Medicine discussed data
from a study of a group intervention for Japanese breast cancer
patients. The purpose of his study was to investigate the effec-
tiveness of a group intervention program for Japanese patients
with breast cancer. Two studies were conducted. In the first
study, breast cancer patients were asked to participate in a
structured group intervention program which was developed
generally based on Fawzy’s model. This program consisted of
five 90-min weekly sessions including psycho-education,
problem-solving, psychological support, relaxation training
and guided imagery. In this study, short-term effectiveness
and its persistence were investigated. In the second study, the other
patients participated in three additional bi-monthly interven-
tions following the five-session intervention program.

In the first study, 57 patients participated and completed the
POMS at the periods of pre- and post-intervention and 6
months after the completion. The POMS scores significantly
decreased at the period of post-intervention and its effect per-
sisted 6 months later. However, the scores of the patients with
nodal metastasis and/or adjustment disorders became higher up
the pre-intervention level. Therefore, in the second study,
another 40 breast cancer patients were recruited for a new pro-
gram which consisted of the five weekly structured group interventions followed by three additional bi-monthly inter-
ventions. As a result, the scores at 6 months after the comple-
tion of the additional interventions remained decreased even
for the patients with nodal metastasis and/or adjustment dis-
orders.

This study demonstrated that this program was effective in
improving psychological distress for breast cancer patients.
Patients with nodal metastasis and/or adjustment disorders are
more likely to have emotional distress, and therefore they need
to be supported by this program including additional interven-
tions. This study also demonstrated that an educational pro-
gram would be needed for family members who did not under-
stand or support the patients. The follow-up survey revealed that two-thirds of the participants kept in contact with
each other, which meant that a group intervention might also
be significant for providing a social network.

Dr D. Spiegel, Department of Psychiatry and Behavioral Sci-
ences, Stanford University School of Medicine discussed the
integration of psychotherapy into health care. As advances in
medical treatment extend life with cancer, converting it in
many cases from a terminal to a chronic illness, problems in
coping with the disease and its treatment become more impor-
tant. Finding means of helping people live with a chronic life
threat, cope with the side effects of arduous treatments and
management of the personal, social and vocational conse-
quences of disease-related disability is of growing importance.
Psychosocial problems include fears of recurrence or death,
family stresses, social isolation, energy reduction, alterations
in body image, unanticipated demands on time and financial
burden. While any of these problems can be stressful, their co-
occurrence and chronicity can produce serious adjustment problems, including depression, anxiety and family and vocational disruption. Recent studies indicate that psychiatric comorbidity complicates medical treatment because of increased demand for care, decreased satisfaction with it and poor adherence to treatment.

Cancer patients suffer not only the physical effects of the disease, but frequently a withdrawal of social support at a time when they need more help than ever, Dr Spiegel said. The utility of structured supportive/expressive group psychotherapy for cancer patients and others with life-threatening illness was described. Evidence was presented that psychotherapy for medically ill patients results in reduced anxiety and depression and often pain reduction also. In addition, psychotherapy has been shown to have a surprising effect on disease progression. In three randomized studies, it has resulted in longer survival times for patients with breast cancer (18 months), lymphoma and malignant melanoma.

These interventions are safe and inexpensive, Dr Spiegel said. Additionally, there is some evidence that such interventions may also have effects on disease course. Studies of these outcome effects were reviewed. Possible mechanisms linking psychosocial intervention with effects on disease course were described. The physiological mechanisms for these findings have not yet been determined, but there are at least four fundamental possibilities for psychotherapeutic effects on physiological change: (1) health maintenance behavior, i.e. diet, sleep and exercise; (2) health care utilization through better treatment adherence, interaction with physicians or through more aggressive treatment regimens; (3) endocrine environment, for example by reductions in stress-induced elevations in cortisol or prolactin, which have been shown to influence rates of tumor proliferation; and (4) immune function, possibly through social support-mediated reduction in stress-induced suppression of natural killer cell activity.

Such therapeutic techniques have shown themselves to be humane, effective and cost-efficient.

**SUMMARY**

Dr C. Cleeland gave a summary of the Symposium, highlighting the many insights into pain control, palliative medicine and psycho-oncology that had been presented. The need for ongoing assessment of these issues, education and research was emphasized.

**Acknowledgments**

The organizing Committee greatly appreciates the contributions of all the speakers and participants of this international Symposium and their contributions to its ultimate success. This Symposium was supported by the Foundation for Promotion of Cancer Research to promote the program of the Second Term Comprehensive 10-year Strategy for Cancer Control by the Ministry of Health and Welfare, Japan.

**References**

