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Industry Satellite Symposia

IL1 – Meiji Seika Kaisha, LTD. Satellite Symposium – Management of late life depression and suicide prevention

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IL1-1

Community-based intervention to depressive elderly in Japanese rural towns with special reference to suicide prevention

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Compared to other countries, Japan has a relatively high suicide rate. The suicide rate in 2006 was 23.7 per 100,000, with a particularly high number of suicides among the middle-aged and the elderly. Among Japan's 47 urban and rural prefectures, Akita prefecture in the Tohoku region has had the highest suicide rate since 1997. In view of this, measures to prevent suicide have been promoted with a clear focus on community-based health promotion for depression. In order to reduce the suicide rate in Akita prefecture, community-based public health intervention through the positive implementation of suicide prevention measures in six towns has been conducted with the cooperation of Akita University.

Public awareness raising activities focusing on depression and suicide were conducted. The welfare measures of promoting a sense of purpose among senior citizens and creating a community network were also taken. As a result, the suicide rate in the intervention towns decreased from 70.8 before intervention (1999) to 34.1 after intervention (2004). The suicide rate in the control towns was 47.8 before intervention and 49.1 after intervention. Public health measures emphasizing the population approach of empowerment through specialists and public awareness raising activities regarding depression and suicide prevention aimed at local residents had the effect of increasing mental health literacy concerning depression and suicide, and therefore have the potential to reduce the suicide rate.

In conclusion, community-based intervention for depressive elderly with special reference to suicide prevention has the effect of reducing suicide rates in Japanese rural towns.

IL1-2

Management of late life depression and suicide prevention in Korea

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Depression is frequent in older adults and is the second most disabling psychiatry syndrome (following memory loss) in this population group. We performed the epidemiological study of geriatric depression in a Korea urban area 9 years ago. The prevalence of mild, moderate and severe depressive symptoms was 18.8%, 7.4%, and 17.8%, respectively. Prevalence of major depressive disorder was 7.8%. In this study, we also showed that depressed persons had more psychological distress, stressful life events and cognitive dysfunction than non-depressed persons.

Geriatric depression is distinct from depression in other age ranges in that it causes frequent somatic symptoms, psychomotor retardation, high suicidal rates or cognitive decline. Elderly depression aggravates the global health state, deteriorates quality of life and causes substantial social waste, by obliging others to be responsible for nursing those afflicted with this disorder.

Psychopharmacologic development has provided elderly patients with a number of safe antidepressants. This often enables the successful treatment of the depression accompanied with physical diseases, which frequently occurs among elderly patients. Despite this improvement, geriatric depression is still not properly recognized or diagnosed and lacks appropriate treatment.

The clinical management of geriatric depression involves pharmacotherapy, electric convulsive therapy (ECT), psychotherapy, and collaboration with

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the family members. The treatment plan should start with an assessment of whether there are any medications or illnesses that predispose the patient to depressive symptoms. Any effective therapy for depression in older persons must include collaboration with the family. Families are often the most important allies of clinicians treating depressed older patients.

Although South Korea does not have a long tradition of self-inflicted death, the number of suicide has increased during recent two decades. Two decades ago, Korea had a fairly low suicide rate (under ten per 100,000 in the 1980s), but now it has one of the world's highest (24.7 in 2005). Especially, most people who kill themselves are elderly or middle-aged men in Korea. For these reason, systematic and governmental suicide prevention program for elderly depression is urgently needed. In Korea, the associations for suicide prevention and government action have started in recent years; however they need more manpower and financial support. We think that more comprehensive evaluation and case management for geriatric depression would help preventing suicide.

IL1-3

Vascular factors and depression: An opportunity for potential new therapeutic approaches?

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There is increasing evidence that depression in later life is associated with a number of vascular changes. Depression is common in those with cardiovascular and cerebrovascular disease, and predicts poor vascular outcome accounting for all other prognostic factors. Depression is also an independent risk factor for subsequent development of vascular disease, while vascular changes in older depressed subjects include an increased burden of vascular risk factors and an increased load of white matter hyperintensities on MRI, which may be associated with frontal and temporal lobe atrophy and persisting cognitive impairments. Autopsy studies suggest vascular and associated inflammatory changes in frontal cortex, suggesting a possible aetiological role in development of depression. Only a few prospective studies have been undertaken to determine whether vascular brain changes predict future depression, but positive findings have been described in some studies. It has been proposed that a distinct disease entity of "vascular depression" should be recognised, though as yet there is no agreement over appropriate diagnostic criteria and the validity of this concept remains controversial.

Despite the strong bidirectional association between depression and vascular disease, little is understood about potential mechanisms, while ultimately understanding of these is essential for adequate treatment and ultimately the prevention of depression. Studies of nimodipine in vascular depression have been undertaken, with promising results. Other possible mechanisms include shared environmental factors, autonomic dysfunction, platelet activation and hyper aggregation, endothelial dysfunction, HP axis activation, inflammatory and cytokine activation, changes in polyunsaturated fatty acids, genetic factors, adverse effects of current antidepressant treatments and raised levels of homocysteine. The evidence base for these mechanisms will be reviewed and relevant treatment studies summarised. Novel therapeutic strategies, based on these mechanisms, should be developed and tested as older depressed subjects with vascular changes tend to respond poorly to traditional antidepressant treatments.

IL2 – Otsuka Pharmaceutical Co., Ltd. Satellite Symposium – How to manage psychotic elderly

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Psychosis is a major mental health concern in the elderly. Either in the context of dementia, Schizophrenia, Bipolar Disorder or medication induced, the symptoms of psychosis can have a profound negative impact in the life of the elderly patient.

The goal of the symposium is to present all available existing tools to clinically manage psychosis in the elderly and provide general criteria on how to use them.

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IL3 – Myriad Pharmaceuticals Satellite Symposium – New directions in Alzheimer's disease (AD) – Targeting Aß42 as a potential disease modifying strategy

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Globally it is estimated that the number of people with dementia will double every 20 years to reach over 80 million by the year 2040. This may indeed be underestimated in areas such as the Asia Pacific region, where prevalence rates in some countries are forecast to increase by more than 300%. Alzheimer's disease (AD) accounts for most of the dementia cases diagnosed after age 65. In light of the aging population worldwide, AD is expected to remain a looming epidemic with major clinical, economic, and societal consequences.

Over the last two decades, major advances in genetics and basic research have led to a more in-depth understanding of the basic biology of AD. The predominant theory as to the etiology of the disease is known as the "amyloid hypothesis." This theory links alterations in the production, aggregation, and metabolism of the toxic 42-amino-acid form of the amyloid beta (Aß) peptide, Aß42, to a cascade of pathological events leading to neuritic plaque formation, neuronal loss, and ultimately to AD. These advances in elucidating the pathophysiology of the disease have led to several advanced-stage clinical development programs for anti-amyloid therapeutics – each targeted to intervene at various points along the amyloid cascade. These agents are not only being assessed for their safety and efficacy in the management of AD but also for their ability to impact the course of the disease process – thus holding out the potential to act as disease modifiers. If disease-modifying agents were to become a clinical reality, there would be an attendant change in the epidemiology, clinical treatment paradigm, and overall costs of AD to society in the future.

This symposium will address the overall prevalence and impact of AD on a global basis with specific attention to Japan and the Asia Pacific Region. It will also highlight current research surrounding the pathophysiology of AD and the rationale for anti-amyloid treatments. Emerging anti-amyloid therapies will be reviewed, with a focus on Selective Aß42 Lowering as a novel intervention strategy for AD.

IL4 – Pfizer Inc and Pfizer Japan Satellite Symposium – Use of sertraline in elderly patients

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IL4-1

Treatment of depression in the elderly

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Treatment of depression in the elderly is complicated by decreasing hepatic and renal drug clearance, and the presence of comorbid medical illness. According to the World Health Organization, nearly 20% of people older than 60 have some depressive symptoms, and nearly 30% of the medically ill elderly have associated depression. However, only 5% of the elderly actually receive a diagnosis of depression. The use of many drugs at the same time is common among the elderly. One European study found that elderly outpatients used an average of 7 drugs per person. This practice increases the risk of drug-drug interactions (DDIs). The importance of antidepressant drug effects on the hepatic cytochrome P450 (CYP) enzyme system has become increasingly recognized. Drugs that inhibit these enzymes can critically alter the metabolism of other pharmacologic agents, affecting both efficacy and safety. Drug-drug interactions can have serious and sometimes fatal consequences. All of the currently available SSRIs have inhibitory effects on certain enzymes; the particular enzymes affected and the degree of the effect differ among agents.

CYP3A4 is the most abundant enzyme, important to the metabolism of such drugs as alprazolam and carbamazepine. Fluvoxamine has a substantial effect on this enzyme, whereas available evidence suggests that a clinically meaningful effect of sertraline or paroxetine is unlikely.

CYP2D6 is integral to the metabolism of a wide variety of drugs, including TCAs, venlafaxine, fluoxetine, paroxetine, antipsychotics, ß-blockers, type IC antiarrhythmics, and morphine derivatives. Among the SSRIs at usual starting dosages,

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fluoxetine and paroxetine are significant inhibitors of CYP2D6, whereas sertraline exhibits only a modest effect. An inhibitory effect is unlikely with citalopram and fluvoxamine. In a study comparing paroxetine and sertraline, paroxetine increased desipramine plasma levels more than 300%, compared with a 30% increase with sertraline. Given the potential fatality of such interactions with TCAs, both the degree and duration of SSRI effects on drug metabolism must be taken into account when switching between these drug classes or when combination treatment is considered.

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IL4-2

Medical Comorbidities and the Treatment of Depression

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Note: The term "coronary artery disease" has been standardized to "cardiovascular disease" for consistency.

Depression is highly prevalent in patients who have chronic medical disease such as Parkinson's disease, Alzheimer's disease, diabetes, stroke, and cardiovascular disease. Comorbid medical illness is also common in elderly depressed persons. Depression is a risk factor for the development of cardiovascular illness. The association with cardiovascular disease has been shown in multiple large-scale studies that have followed depressed patients who did not have cardiovascular disease. For these depressed patients, the risk of developing cardiovascular disease is 1.5 to 2 times that of nondepressed patients. The nature and direction of this relationship is not well understood. Proposed mechanisms include effects on platelet activation, inflammation, alterations in autonomic nervous system and hypothalamic-pituitary-adrenal axis functioning, lifestyle, and poor treatment adherence.

Depression increases the risk of having a stroke. In addition, patients who have had a stroke are at an increased risk of developing subsequent depression. There are only a few clinical trials that have evaluated the efficacy, safety and tolerability of antidepressants in this patient population. For the treatment of depression in patients with cardiovascular disease, the antidepressant sertraline has been studied. In the SADHART (Sertraline Anti-Depressant Heart Attack Randomization Trial) study, patients receiving sertraline not only showed a decrease in symptoms of depression, but also were also less likely to have a serious cardiovascular event (MI, mortality, angina, CHF) in the first six months after the initial MI. A subsequent study in Denmark found sertraline to be more effective than placebo for preventing depression in the first year after a stroke, as well as improving clinical outcomes after stroke. The ENRICHD (Enhancing Recovery in Coronary Heart Disease) study found that treating depression with SSRIs and cognitive behavioral therapy improved depressive symptoms. A follow up to the ENRICHD study concluded that depressed patients from that study who had been treated with SSRIs had a significantly lower risk of recurrent MI or death by any cause than depressed patients not treated with SSRIs, suggesting that treating depression with these medications can have an effect on

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morbidity and mortality in patients who have cardiovascular disease.

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IL5 – Eisai Europe Ltd. and Pfizer Inc Satellite Symposium – Why treat severe Alzheimer's disease – An evidence-based approach

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For some medical professionals, the severe Alzheimer's disease (AD) patient is viewed as bedridden, mute and in a vegetative state; in short, only suitable for palliative care and not likely to benefit from pharmacological interventions with antidementia drugs. In contrast, other physicians recognize that although severe AD patients have a wide range of disabilities, most still retain capabilities that are worth enhancing or preserving for the benefit of the patient and their family. The speakers will reflect upon their own experiences and explore the different approaches towards the care of people with severe AD. The disability/ability profile of a typical person in the severe stage of AD will be examined, with the aim of exploring whether such patients should be treated with pharmacological agents.

Evidence from randomized, placebo-controlled trials in patients with severe AD suggests beneficial effects can be achieved in the symptom domains of cognition, global function, activities of daily living and sometimes behavior for the N-methyl-D-aspartate receptor antagonist memantine and the cholinesterase inhibitor donepezil. Data from studies with these agents that have taken place over the past 7 years will be presented and their implications for patient care examined.

Assessing the benefits of treatment, and how they might relate to issues of health-related quality of life, can be difficult in severe AD patients. Although cognitive, functional and behavioral improvements remain the ultimate goal of AD therapy, stabilization or less-than-expected decline may be realistic and desirable outcomes even in severe disease. Issues surrounding the appropriate measures of treatment success, and the clinical meaningfulness of trial results and responder analyses, will be discussed.

IL6 – Janssen Pharmaceutical KK Satellite Symposium – Treatment strategy for neuropsyhiatric disorders in the elderly

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IL6-1

Strategies for treating and preventing Alzheimer's disease: Usefulness in nicotinic acetylcholine receptor-mediated neurocognitive enhancement and neuroprotection

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Although multiple neuronal systems are affected in Alzheimer's disease (AD), a key component of the neurodegenerative process is a loss of cholinergic neurons. Thus, the aim of many treatment regimens is to support this cholinergic system by inhibitors of acetylcholinesterase (AChE), being able to increase the concentration of acetylcholine. AChE inhibitors and memantine are licensed for AD and have moderate symptomatic benefits, but additional disease-modifying therapies are urgently needed.

The amyloid hypothesis – the leading mechanistic theory of AD – states that an imbalance in production or clearance of amyloid beta (Aβ) results in accumulation of Aβ and triggers a cascade of events leading to neurodegeneration and dementia. Different classes of potentially disease-modifying treatments that interrupt early pathological events including decreasing production or aggregation of Aβ or increasing its clearance and potentially prevent downstream events are in phase II or III clinical studies. These include Aβ vaccine therapies; β- and γ-secretase inhibitors; selective Aβ42-lowering agents; α-secretase activity enhancing agents; anti-Aβ aggregation agents; and others.

Loss of cortical nicotinic acetylcholine receptors (nAChRs) in AD patients is a common finding and the PET studies reveal deficits in nAChRs as an early phenomena in AD. Presynaptic nAChRs enhance the release of multiple neurotransmitters and postsynaptic nAChRs mediate a fast excitatory transmission. In addition, nAChRs have roles in synaptic plasticity and development. Stimulation of nAChRs in AD patients can improve the acquisition and retention of verbal and visual information and decrease errors in cognitive tasks. In addition, nicotine protected cultured cortical and hippocampal neurons from Aβ- and glutamate-induced neuronal death, and that protective effect of nicotine is essentially mediated via both $\alpha4\beta2$ and $\alpha7$ nAChRs. Furthermore, stimulation of nAChRs enhances α-secretase cleavage and reduces the pathogenic Aβ level. These data suggest that nicotinic stimulation may facilitate neuron survival and delay neurodegeneration in AD. If so, nicotinic stimulation may have more than just neurocognitive enhancement effect and could alter the clinical course of AD. Galantamne, one of the AChE inhibitors, positively modulates nAChRs through an allosteric interaction by binding to a site on the nAChR distinct from that occupied by acetylcholine, increases receptor sensitization to acetylcholine, enhancing nicotinic neurotransmission, and influencing the release of multiple neurotransmitters. Galantamine also protects neurons from excitotoxic insults via $\alpha7$ nAChR. Therefore, nAChR allosteric potentiating ligands or specific nAChR subtype agonists are particularly interesting compounds that provide neurocognitive enhancement and neuroprotection, thereby slowing or halting the progress of AD.

IL6-2

Pharmacotherapy of Alzheimer's disease and depression in elderly

Guk-Hee Suh

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Dementia and depression in the elderly contribute to personal suffering and family disruption and increase disability, medical comorbidity, and healthcare utilization. Dementia and depression in the elderly are recognizable, diagnosable, and treatable, but unfortunately under recognised, under diagnosed, and under treated. Alzheimer's disease (AD) is so common that its pandemic has been predicted in this century. Clinical trials of anti-dementia drugs have demonstrated meaningful therapeutic benefit that can ameliorate the progressive cognitive and functional decline to which patients have historically been resigned. This presentation briefly reviews data from these trials, along with new information that expands our appreciation of what effects available anti-dementia therapies can be expected to yield. Most information exists regarding cholinesterase inhibitors (galantamine, donepezil, rivastigmine) and NMDA antagonist (memantine), which were developed primarily for relief of cognitive dysfunction in AD. Long-term observational data suggest that they may show some promise in altering progression of symptoms as well. The new and on-going researches are paving the way to future treatments for this devastating illness.

Although the existing empirical treatment literature is limited, the available published treatment studies and expert consensus recommendations find that antidepressants are effective in the treatment of geriatric depression. In general the

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SSRIs and SNRIs pose a low risk for the most serious side effects. Treatment of psychotic depression has not been adequately investigated in the elderly. However, common practice includes treatment with an selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) in conjunction with an atypical antipsychotics. Continuation and maintenance treatment at an adequate dose and for an adequate length of time is critical in minimizing relapse. More empirical clinical trials are needed to evaluate the selection and effectiveness of pharmacologic combination therapy and other treatment strategies for treatment-resistant and partially responsive clinical depression in the elderly.

IL6-3

Pharmacotherapy of BPSD

Michael Davidson

Tel Aviv University, Tel Aviv, Israel

Although progressive cognitive decline is the clinical hallmark of degenerative dementia, behavioral and psychological symptoms (BPSD) are often the most prominent and burdensome manifestation of the illness. Delusions, hallucinations, agitation, severe anxiety, and apathy affect the quality of life of both patients and their respective families. Although neuronal degeneration can well account for BPSD manifestation the specific biological mechanism of BPSD has not been elucidated. Since onset, fluctuations and, remission of BPSD are too often spontaneous and unrelated to specific triggers, attempts to manipulate the environment to create a serene and quite atmosphere are not very helpful. Most but not all clinical trials have demonstrated that treatment with antipsychotics particularly of the second generation benefit BPSD however, elderly individuals are also very vulnerable to EPS. Treatments with Risperidal 0.75 mg – 1.5 mg per day have been show to be both effective and well tolerated.

IL7 – Eisai Co., Ltd. – Dementia and the Driver's License – Controversy and Social Impact

Peter Whitehouse[1]; Yasuyoshi Ouchi[2]; Peter Nestor[3]; Manabu Ikeda[4]; Germaine L. Odenheimer[5]

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This talk will provide an overview of current safety, assessment, management and legal issues related to older drivers with dementia and the types of situations that put them at excessive risk.

Dr. Odenheimer will highlight the physician's role in addressing driving safety issues with their patients, especially as they relate to medical conditions and medications. In response to a growing need and physicians' reluctance to address the issue, the American Medical Association has produced materials to help physicians approach this issue. Key topics from these materials will also be presented.

Most driving proficiency studies have focused on Alzheimer's disease (AD), while little has been reported on frontotemporal lobar degeneration (FTLD), which is characterized by changes in personality and social conduct. The impact of FTLD on driving behavior may differ from that seen in AD, although there has been no report regarding driving skills for those with FTLD. Dr. Nestor will focus on driving behavior and its risks in FTLD compared with those in AD.

"The Japanese Road Traffic Law" will be modified to state that anyone over 75 years of age who wishes to have his or her license renewed is legally obliged to be examined in terms of cognitive tasks. If the renewal applicant shows deficits in these tasks and has experienced any traffic accidents within a six-month period, officers will request a medical certificate indicating his or her fitness to drive. Dr. Ikeda will review this revised road traffic act of Japan and introduce the proposal made by the Japanese Psychogeriatric Society for a renewal act and related regulations.

IL8 – Eli Lilly and Company Satellite Symposium – From the epidemiology to treatment strategy of geriatric setting with mental illness

IL8-1

Yoshibumi Nakane, M.D., Ph.D.

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The World Health Organization (WHO) organized a detailed regional survey on common mental disorders, or the World Mental Health (WMH) Survey Initiative, in cooperation with a number of countries. In Japan, Professor Norito Kawakami at the Faculty of Medicine, the University of Tokyo and other researchers conducted the survey in six different locations in Japan – namely, Okayama,

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	Mood disorder of some kind			Neurotic/stress-related disorder of some kind			Mental disorder of some kind		
	Lifetime Prevalence	Annual prevalence	Monthly prevalence	Lifetime prevalence	Annual prevalence	Monthly prevalence	Lifetime prevalence	Annual prevalence	Monthly prevalence
Aged 65 and over	3.8	0.8	0.2	5.7	3.6	2.6	10.6	4.4	2.8
Total	7.5	2.5	0.5	9.2	5.4	3.7	17.0	7.5	4.1
Male	4.6	1.4	0.3	7.6	4.5	3.3	16.3	6.1	3.7
Female	9.9	3.4	0.7	10.6	6.1	4.0	17.6	8.6	4.5

Nagasaki, Kagoshima, Tochigi, Yamagata, and Kanagawa – between 2002 and 2006. Since some of the results have already been released, the following survey results are those for subjects aged 65 and over in particular.

This survey was made by collecting data based on the computer version of the Composite International Diagnostic Interview (CIDI) developed by WHO, and it is the first strict epidemiological study targeting multiple regions throughout Japan. The characteristics of this survey are that it does not aim at any particular disorder and excludes psychotic disorders; that it encompasses a wide range of mental disorders which general physicians are likely to encounter; and that it can obtain prevalence at various levels. The survey was conducted on 8,316 persons aged 20 and over, including 4,134 interviewees consisting of 1,871 males and 2,263 females. There were 1,205 interviewees aged 65 and over. This report presents several epidemiological indices regarding this latter group of more elderly subjects based on the results classified according to the chapter of ICD-10.

When the odds ratio in the group aged 65 and over is 1.00, the odds ratios from lifetime diagnosis in other age groups are found to be between 1.93 and 2.70 for mood disorders, between 1.90 and 2.80 for neurotic or stress-related disorders, and between 2.00 and 2.28 for mental disorders of some kind.

Source: Health and Labour Sciences Research Grants, Mental Health Science Research Project, "Studies on Epidemiological Surveys concerning Mental Health" (senior researcher: Norito Kawakami), 2006 reports of the summary and assigned researches, March 2007.

IL8-2

Jun Ishigooka, M.D., Ph.D.

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In Japan, in particular, it is expected one in four people will be aged 65 years or older in the near future. Psychiatrists are required to better understand the characteristics of new antipsychotic drugs and use them properly in clinical settings in order to maximize the quality of life (QOL) of the aged.

In this session, we will discuss how to maximize the effects of drugs, while minimizing pain in patients, what are the characteristics of aged people that require special attention, and so on, taking account of the pharmacological characteristics of each drug.

IL8-3

Treatment of geriatric psychosis in the community in Ireland

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Psychiatry of Old Age is a relatively new specialty in Ireland and is most commonly delivered using a service model based on community-based assessment and treatment. This approach utilises a multidisciplinary team model and integration with various community supports including voluntary and health service facilities. A community-based service for psychosis presents challenges in terms of risk management and responsibility for informal/family caregivers but also has advantages for quality/patient-centered care.

Community-based multidisciplinary teams provide care for psychosis both in the context of functional psychiatric disorders and organic disorders. While there are similarities in the management of psychosis whatever the underlying diagnosis, the approach taken requires adaptations where there is co-existant cognitive impairment. The aim of this presentation is to provide an overview of the community-based interventions available, the development of multidisciplinary team approaches including assertive outreach, the challenges and advantages of the community-based approach, and the differing challenges of treating psychosis in the context of functional illness versus dementia.

The presentation will provide a context in terms of a brief explanation of demographic trends and health policies in Ireland. The above topics will then be explored using case examples to illustrate and discuss the issues involved.

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