

# CINP 2005 Regional Meeting

Cape Town, 20 - 22 April 2005

## Psychiatry: Selected abstracts

### ANTIPSYCHOTICS ACROSS THE SPECTRUM: AN OVERVIEW OF THEIR MECHANISMS OF ACTION

Anissa Abi-Dargham  
(Professor of Clinical Psychiatry and Radiology at Columbia University)

Imaging studies in schizophrenia have shown an association between dopaminergic hyperactivity in the mesolimbic pathway and positive symptoms, and suggested dopaminergic hypoactivity in the mesocortical pathway underlying cognitive impairment and negative symptoms. In addition, studies of dopamine glutamate interactions have shown that dopaminergic alterations in schizophrenia may be secondary to a glutamatergic dysfunction. These data support a predominant and well established role for D2 antagonism in the treatment of schizophrenia, while providing new strategies for the treatment of cognitive and negative symptoms. Imaging has also contributed to a better understanding of the mechanisms of action of the antipsychotics by relating central occupancy of relevant neuroreceptors to emergence of therapeutic efficacy or even side effects. We will review the evidence implicating the various transmitter systems in the pathophysiology and treatment of schizophrenia.

### RECENT ADVANCES IN THE TREATMENT OF COMMON ANXIETY DISORDERS

Christer Allgulander MD  
(Associate Professor, Karolinska Institutet, Stockholm Sweden)

The neurobiology of anxiety and mood disorders appears to be shared, and patients with primary anxiety disorders are at increased risk of developing secondary depressive episodes. Frequently, these disorders are found within the same family, indicating a shared diathesis. According to twin studies, vulnerable women may develop either generalized anxiety or depression depending on environmental circumstances. The SNRIs and SSRIs are now established as the treatment of choice in major depression and anxiety disorders. In controlled studies the response rate is about 70 per cent, and with maintenance treatment remission is seen in a majority of the cases. There are no known irreversible adverse effects, yet sexual effects and discontinuation symptoms are to be expected. In some children and adolescents, caution must be paid to increased irritability and suicidal ideation with some of these medications. The increased utilization of these medications has been paralleled with reductions in suicide rate in several countries. In Sweden the number of suicides decreased with 31 per cent in the last decade, and 6 per cent of primary care patients are on maintenance treatment with SSRIs or SNRIs. European studies show anxiety and depressive

disorders to be the most common in primary care second only to musculoskeletal conditions. Emerging research shows benefit of antidepressive and anxiolytic treatment in high-risk patients with concurrent stroke, myocardial infarction, and diabetes in whom the risk of subsequent somatic complications is reduced, and the likelihood of successful rehabilitation is increased. Alcohol dependence can sometimes be prevented and treated by identifying subjects with comorbid depression and anxiety who self-medicate with alcohol. Studies show that it is cost-effective to empower nurses to take charge of caring for subjects that doctors have targeted for treatment of anxiety and depression. Treatment adherence can be enhanced by teaching the patient elementary coping skills by means of individual or group counselling. The internet provides access to support groups, to educational websites, and to online cognitive skills training. Yet, a minority of affected persons in the community receive effective treatments for these disorders. Clinical research units in Europe and in South Africa are now working together to further the understanding of the genetics, epidemiology, psychotherapies and pharmacotherapies of mood and anxiety disorders.

### PSYCHIATRY IN AFRICA: THE MYTHS, THE REALITIES, AND THE EXOTIC

Prof O. Gureje (Department of Psychiatry, University of Ibadan, Nigeria)

As in many other areas of human life, Africa has often been presented as an enigma in psychiatry. From claims about the rarity of some mental disorders, to those of paradoxical outcomes of illness and of a traditional life that seems immovable from the past, the true status of Africans in regard to their psychological profile is beclouded in mystery. Claims about the rarity of depressive disorders and of obsessions, the better outcome of schizophrenia, the penchant of the African to somatize, and the supportive nature of the African extended family structure are examples. In this presentation, we examine the various claims about psychiatry and the nature of psychiatric disorders in Africa to determine which claims are empirically supported and to what extent the apparent allure of the exotic has nurtured the growth of myths about the mental health of the African. The presentation will identify the opportunities for research that current knowledge or lack of it offers.

### MENTAL HEALTH POLICY DEVELOPMENT IN KENYA AND TANZANIA- A DFID FUNDED PROJECT

Rachel Jenkins, David Kima, Joseph Mbatia, Frank Njenga  
(WHO Collaborating Centre, Institute of Psychiatry, London, UK)

This talk describes a project between the governments of Tanzania and Kenya, and the WHO Collaborating Centre,

funded by DFID, to conduct detailed situation appraisal, development of mental health policy, implementation plans, epidemiology and integration of mental health into primary care. The project is working closely with a wide range of stakeholders including the professional associations and NGOs, especially KPA, KSF and MEHATA. The project contributes to DFID's overall goal to reduce poverty and contribute to the other Millennium Development Goals. The project was asked to produce a strategic model which can be adapted for use in other countries, and is in the process of producing a practical policy development, implementation and audit toolkit. The project has also undertaken epidemiological studies in Dar es Salaam and rural Kisumu, qualitative work with traditional healers, and adaptation of the WHO primary care guidelines. This talk will describe some of the outcomes of the project so far and additional new projects.

#### VASCULAR FACTORS IN ALZHEIMER'S DISEASE

RN Kalaria

(Wolfson Research Centre, Institute for Health of the Elderly and Department of Psychiatry, University of Newcastle, UK)

Prevailing views dictate that brain vascular changes are solely associated with vascular dementia (VaD) or multi-infarct dementia. Several recent clinical and epidemiological studies suggest that there may be substantially increased risk of developing AD after a stroke episode, transient ischemic attacks or previous history of hypertension, high cholesterol or certain forms of cardiovascular disease. Taking measures to reduce vascular insults including use of statins have been advocated for reducing risk. Our previous observations on a large autopsy series of Alzheimer's disease (AD) cases have shown profound brain microvascular lesions involving degenerative changes in the cerebral endothelium, thickening of the basement lamina and perivascular cellular changes providing support for a vascular role in AD. It is not unlikely that the microvascular changes are compounded by the presence of amyloid angiopathy, a frequent lesion in AD. Vascular amyloid deposits were either focal or more widespread ranging from mild to severe. However, AD pathology was also associated with microinfarcts and to a lesser extent large infarcts. In some 10% we have observed intracerebral haemorrhages accompanied by non-congophilic diffuse amyloid plaques that are largely associated with cerebral amyloid angiopathy. Other features that point to a vascular component in AD relate to the periventricular and deep white-matter changes or leukoariaosis seen upon magnetic resonance imaging and at autopsy in more than 40% of the late-onset AD cases. These findings were confirmed at autopsy by the presence of rarefaction, lacunes and hyalinosis. Such brain vascular pathology in AD may arise from systemic or cardiovascular disease. The causal connection between small vessel lesions and dementia is further illustrated in the hereditary amyloid angiopathies and by the fact that stroke episodes worsen outcome in AD patients. Is it possible that the microvascular lesions or multiple microinfarcts are the underlying primary trigger for subsequent Alzheimer type of pathology in late-onset AD? Indeed treatment strategies that im-

prove the dynamics of the cerebral circulation and alleviate chronic hypoperfusion of the brain would be rational targets for AD.

#### DEPRESSION AS AN IMMUNOLOGICALLY BASED NEURODEGENERATIVE DISORDER

Brian Leonard

(Emeritus Professor of pharmacology, National University of Ireland, Galway)

Clinical, epidemiological and imaging studies confirm that dementia is frequent outcome of long-term depression. There are many clinical and experimental findings that implicate both pro-inflammatory cytokines (such as interleukin-6 and tumour necrosis factor alpha) and glucocorticoids in dementia. In addition, both clinical and experimental studies have shown that depression is linked to an increase in the tissue metabolism of tryptophan via the kynurenine pathway. The key enzyme in this pathway, indoleamine 2,3-dioxygenase (IDO) is induced by both glucocorticoids and pro-inflammatory cytokines. The products of this pathway are the neurotoxins quinolinic acid and kynurenic acid. As these neurotoxins, together with the pro-inflammatory cytokines and glucocorticoids, accumulate in the brain of the depressed patient, such effects might explain the structural signs of neurodegeneration (reduced hippocampal and frontal cortical volumes) and other neurological changes reported in patients with long-term depression. Antidepressants have been shown to ameliorate the inflammatory processes that lead to neurodegeneration. Depression may therefore be considered to be a chronic neurodegenerative disorder.

#### EIGHT YEARS OF PROGRESS IN AFRICAN PSYCHIATRY

F. Njenga

(President, African Association of Psychiatrists and Allied Professions)

For the past eight years, African Psychiatrists have met every year in an African city. Though all the meetings have taken place in East Africa (Kenya, Uganda and Tanzania), the idea of the meetings was conceived in Johannesburg, South Africa. At a meeting of South African Psychiatrists, Prof. Norman Sartorius challenged those from Sub-Sahara Africa to organize a meeting of their own in their region. With little or no thought, I quickly offered to organize the first meeting in Nairobi within six months. Prof. Sartorius promised to come. We both kept our promises and in April 1997, the first of what has now become annual meetings of African Psychiatrists took place in Nairobi. From then on, the movement of African psychiatrists has been one of strength to strength, as the men and women of Africa have worked their way through national, regional and international boundaries of ignorance and prejudice. This meeting in Cape Town is a good example of focused determination to achieve what many thought impossible. A scientific meeting bringing together African Psychiatrists from all parts of Africa. In all respects, it represents a dream come

true, of the day the sleeping giant from the dark continent wakes up to claim his true position in global psychiatry. This presentation traces the path taken to achieve this great goal.

#### TREATMENT OF DEPRESSION: PRESENT AND FUTURE

Dr R.M. Pinder \*

(Treasurer CINP; Private Consultant, 's-Hertogenbosch, The Netherlands)

Effective antidepressant treatments have been available for almost half a century. Antidepressant drugs, mood stabilizers, ECT and the psychotherapies are, however, symptomatic treatments that may have to be administered for sustained periods to prevent relapse and recurrence. Moreover, individual patients vary widely in their response to different antidepressant drugs, and it is still necessary to have at hand a range of medications offering multiple mechanisms of action - tricyclics, MAOIs, SSRIs, SNRIs, NaSSAs and others. Many of the newer agents lack the side effect burden and the lethality in overdose of the older drugs, but they have not in general offered anything in the way of improved efficacy. However, they are not all born equal, and substantial evidence has emerged that dual action antidepressants like venlafaxine and mirtazapine may offer advantages over their modern counterparts the SSRIs in terms of faster onset of action and greater rates of remission. Sadly, many patients do not achieve remission even with our best treatments, whether given alone or in combination. Although monoamine transporters and receptors are still targets for the design of new antidepressants, research efforts have embraced alternative concepts including neurokinin and other neuropeptide receptors, glutamate systems especially NMDA receptors, sigma and nicotine receptors, and various hormones. Drugs capable of combating HPA axis hyperactivity by blocking glucocorticoid or vasopressin receptors may be exquisitely effective in alleviating psychotic and melancholic depression, while CRF antagonists may be more appropriate in anxiety-related disorders. BDNF may play a vital role in maintaining neural plasticity, is lowered in depressive disorders and during stress, and can be manipulated by drug treatment including current antidepressants. New antidepressants are needed and they are on their way.

#### IMAGING THE SEROTONERGIC SYSTEM IN IMPULSIVE AGGRESSIVE PERSONALITY DISORDER PATIENTS

Larry J. Siever<sup>1,2</sup>, Antonia S. New<sup>1,3</sup>, Marianne Goodman<sup>1,3</sup>, Monte Buchsbaum<sup>1</sup>, Erin Hazlett<sup>1</sup>, Karen O'Flynn<sup>1</sup>, Anissa Abi-Dargham<sup>1</sup>, Marc Laruelle<sup>4</sup>

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**Objectives:** Diminished serotonergic activity has been demonstrated in personality disorder patients with impulsive aggressive behaviors, contributing to reduced activity in cortical inhibitory areas such as orbital frontal and anterior cingulate cortex.

**Methods:** FDG PET activity following the 5-HT<sub>2</sub> agonist m-CPP was assessed in 27 impulsive/aggressive Personality Disordered patients and 26 controls. 9 subjects with impulsive aggressive disorder were scanned utilizing PET with [<sup>11</sup>C] McN 5652 and 6 additional subjects with [<sup>11</sup>C] DASB to measure the serotonin transporter and 18 subjects were scanned with [<sup>11</sup>C] MDL 100907 to measure 5-HT<sub>2a</sub> receptor.

**Results:** Impulsive-aggressive patients did not show activation in response to m-CPP in left orbital frontal cortex and anterior cingulate, while these regions were activated by m-CPP in normal controls. In contrast, the posterior cingulate gyrus was activated in impulsive-aggressive patients and deactivated in controls. Transporter availability was reduced in the patients compared to controls in cingulate cortex. 5-HT<sub>2a</sub> receptor availability was correlated with degree of aggression in several cortical regions.

**Conclusions:** Results of the m-CPP study suggest reduced activation of inhibitory regions in patients with impulsive/aggressive personality disorder presumably because of reduced 5-HT<sub>2</sub> responsiveness. Preliminary results of the neurochemical imaging study raise the possibility that reduced transporter activity and increased 5-HT<sub>2a</sub> receptor availability (perhaps compensatory to reduced 5-HT<sub>2</sub> responsiveness) may characterize patients with impulsive aggression.

#### MODE OF ACTION OF ATYPICAL ANTIPSYCHOTIC DRUGS: FOCUS ON A<sub>2</sub> ADRENOCEPTORS

T.H. Svensson

(Karolinska Institutet, Dept. of Physiology and Pharmacology, Stockholm, Sweden)

Compared with conventional antipsychotic drugs (APDs) clozapine shows superior efficacy in treatment resistant schizophrenia, including positive, negative and cognitive symptoms, in spite of essential absence of extrapyramidal side effects. In view of the classical dopamine hypothesis of schizophrenia the high efficacy of clozapine may seem somewhat surprising, since at clinically effective dosage this drug generates only about 45% D<sub>2</sub> receptor occupancy in brain, whereas typical APDs usually are effective at about 75% D<sub>2</sub> receptor occupancy. Clozapine has also proven superior to both olanzapine and conventional neuroleptics in reducing suicidality in schizophrenia and schizoaffective disorder, and in contrast to most other APDs, clozapine is a potent α<sub>2</sub> adrenoceptor antagonist. Since α<sub>2</sub> receptor blockage represents one of the mechanisms of action of several, clinically effective antidepressant drugs, the α<sub>2</sub> receptor antagonistic action of clozapine may contribute to its suicide-preventive action. Yet, the comparative risk of agranulocytosis requires that its clinical use be somewhat limited. Interestingly, adjunct treatment with idazoxan, a selective α<sub>2</sub> adrenoceptor antagonist, significantly augments the effect of classical APDs in treatment-resistant schizophrenia, including both positive and negative symptoms, BPRS total score, thought disorder and withdrawal retardation. Moreover, our experimental work shows that adding idazoxan to a low dose of a selective D<sub>2</sub> receptor antagonist, raclopride, which causes only about 45% striatal D<sub>2</sub> occupancy, markedly enhances the raclopride-induced suppression of conditioned avoidance response (CAR), a preclinical test of antipsychotic efficacy with high

predictive validity, in spite of the fact that when given alone D<sub>2</sub> antagonists require about 75% D<sub>2</sub> occupancy to generate the same suppression of the CAR. Since previous work shows that atypical, but not typical, APDs enhance glutamatergic transmission in the medial prefrontal cortex, which may substantially contribute to their cognitive enhancing effects, we also studied the effects of idazoxan and raclopride on glutamatergic neurotransmission in prefrontal pyramidal neurons, using intracellular recording techniques. In summary, our results indicate that adjunctive treatment with idazoxan may provide augmentation of both typical and atypical APDs lacking appreciable  $\alpha_2$  antagonistic action, and suggest that the unique efficacy of clozapine may to a significant extent reside in its potent  $\alpha_2$  receptor antagonistic activity. Tentatively, adjunctive use of idazoxan with APDs other than clozapine may also, by inference, contribute to reduce suicidality in schizophrenia. Finally, our data challenge concurrent hypotheses regarding noradrenergic targets for memory enhancement in schizophrenia, demonstrating that the effect of idazoxan is executed at presynaptic, and not postsynaptic,  $\alpha_2$  adrenoceptors in the prefrontal cortex, and propose a procognitive effect of adjunctive idazoxan treatment.

## Neuroscience: Selected abstracts

### CHEMICAL MODULATION OF FRONTO-EXECUTIVE FUNCTIONS: NEUROPSYCHIATRIC IMPLICATIONS

Trevor W Robbins

(Dept. of Expt. Psychology and MRC Centre for Behavioural and Clinical Neuroscience, University of Cambridge)

The neuromodulation of frontal-executive and cognitive function is reviewed in the context of experiments on rats, monkeys and humans. I define 'executive function' to mean the optimisation of performance on complex cognitive tasks with several components. 'Neuromodulation' is defined as the enhancement or curtailment of processing of fast-signalling neural networks by the chemically identified systems of the reticular core of the brain including the monoaminergic (especially dopamine and 5-HT) and cholinergic ascending pathways from the basal forebrain. The functions of these systems are analysed from the perspective of their possible different interactions with the prefrontal cortex and its associated structures such as the striatum, using tests sensitive to working memory, attention and inhibition. The experiments involve cognitive neuropsychological testing in three species, intra-cerebral psychopharmacology, *in vivo* neurochemistry and functional brain imaging. Effects of drugs or dietary manipulations in human patients or normal volunteers are used to draw parallels with conclusions based on experiments with monkeys or rats employing paradigms recruiting 'building blocks' of cognitive function hypothetically present in more complex tests of human cognition (e.g. using the CANTAB battery). The factors influencing the use of drugs to optimise cognitive function are illustrated by several examples, including functional genomics and in the treatment of Parkinson's disease, in which L-dopa treatment can lead to cognitive deficits as well as improvements, depending on the cognitive functions studied and their differential mediation by cortico-

striatal circuitry. Hypotheses are advanced that afford the ascending systems a greater deal of specificity in modulating cortico-striatal function than has hitherto been entertained, and the clinical and theoretical implications of this hypothesis are discussed, including the possibility of enhancing intellectual function with so-called 'cognitive-enhancing' drugs.

### NEURAL MECHANISMS OF RECOGNITION MEMORY AND OF SOCIAL ATTACHMENT

Prof. G Horn

(University of Cambridge, UK CB3 8AA)

Memory allows past experiences to modify current behaviour and, by providing a link between the past and present, gives individuals their personal identity. If memory consists of a 'trace' made in the brain, where is the trace and what is its nature? When we see an object we have previously seen, we recognize it. This kind of 'perceptual learning' also occurs in animals. It takes a dramatic form in the case of visual imprinting, where the young of some animals, including the domestic chick, are able to learn the characteristics of the first object they see. By analysing the neural basis of visual imprinting it has been possible to localize a brain region in which information is stored. I shall give an account of the changes that occur in the region during and after the formation of a memory of the imprinted object. There is another benefit of studying visual imprinting. Visually naïve chicks have an untrained tendency (predisposition) to attend to features of the face/head. The predisposition may 'guide' the chick to its mother whose characteristics it learns. There is now abundant evidence that a similar predisposition exists in newborn babies and, as in the chick, that this predisposition influences the course of subsequent learning. Chicks form a stronger attachment to a member of their own species (a conspecific) than to an artificial object. If the predisposition is experimentally suppressed chicks behave as if their attachment to a conspecific is no stronger than to an artificial object. These findings may parallel some aspects of autism in humans in which there is an impairment of face recognition that is manifest early in life. Thus the chick may also serve as a useful experimental animal to help understand such aspects of the autistic disorders.

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### ESTROGEN SIGNALLING AFTER ESTROGEN RECEPTOR $\beta$ (ER $\beta$ )

Jan-Åke Gustafsson

(Departments of Medical Nutrition and Biosciences, Novum, Karolinska Institute, Huddinge, Sweden)

The discovery of ER $\beta$  has radically changed our views on estrogen signaling. This lecture will focus on the role of ER $\beta$  in control of cellular proliferation and in the CNS. In many contexts ER $\beta$  opposes the actions of ER $\alpha$  ("yin/yang relationship"); e.g., whereas ER $\alpha$  often stimulates proliferative events in estrogen sensitive tissues, ER $\beta$  seems to promote apoptosis in these tissues. Of special interest is the prostate gland, which has a high concentration of ER $\beta$  in its epithelial

cells; ER $\beta$   $-/-$  mice have hyperplastic ventral prostates as a consequence of the lack of the antiproliferative action of ER $\beta$ . The ER $\beta$   $-/-$  prostatic epithelial cells show less apoptosis and are less well differentiated than in WT prostate. Therefore, ER $\beta$  agonists might be valuable in treatment of prostate cancer. Interestingly, Eli Lilly recently reported on the development of a non-steroidal ER $\beta$  agonist which, when administered to rodents, results in enhanced apoptosis and shrinkage of the prostate. In addition, tumors formed from LnCAP human prostate carcinoma cells implanted under the skin of nude mice, are eliminated following treatment of the recipient mice with the ER $\beta$  agonist. These are indeed exciting data which give strong support to the antiproliferative action of ER $\beta$ .

Also in the mammary gland ER $\beta$  exerts an antiproliferative action. High concentrations of ER $\beta$  are found in both normal and malignant breast tissue; ER $\beta$  is a favorable prognostic indicator in breast cancer. Controlled expression of recombinant ER $\beta$  in predominantly ER $\alpha$  containing MCF-7 human breast cancer cells lead to cell cycle arrest, further supporting ER $\beta$  as an antiproliferative principle. The antiproliferative actions of ER $\beta$  seem to occur also in other tissues. Indeed, ER $\beta$   $-/-$  mice develop a syndrome reminiscent of chronic myeloid leukemia in man, apparently resulting from eliminated ER $\beta$  suppression of stem cell replication in the bone marrow. Nuclear receptor ligands are used in clinical practice to treat various forms of leukemia and it may be argued that an ER $\beta$  agonist might be a valuable addition to this pharmaceutical cocktail. Yet another malignancy where ER $\beta$  agonists might prove useful as antitumor agents is colon cancer. Estrogen replacement therapy in postmenopausal women appears to decrease the incidence of colon cancer by 30%, an interesting fact in view of the predominance of ER $\beta$  over ER $\alpha$  in this tissue. Again, ER $\beta$  agonists might offer some hope in prevention/treatment of this type of cancer. Interestingly, ER $\beta$  seems to have several important roles in the CNS. It is the predominant ER in the raphe nucleus and the use of ER $\beta$  agonists has been proposed in treatment of depression since they increase the serotonin content in the raphe nucleus. Lack of ER $\beta$  leads to increased anxiety in mice and, furthermore, ER $\beta$   $-/-$  mice are significantly more aggressive than controls. It appears that ER $\alpha$  promotes aggressive behaviour whereas ER $\beta$  has the opposite effect, again illustrating the yin/yang relationship between ER $\alpha$  and ER $\beta$ , respectively. Furthermore, ER $\beta$  appears to be essential for the appropriate development of the CNS, since deletion of ER $\beta$  results in diminished migration of neurons from the ventricular zone to the cerebral cortex, leading to a smaller size of the cerebral cortex. The adult ER $\beta$   $-/-$  brain is also more vulnerable to neurotoxic agents than control brain.

#### **GETTING LOST: HIPPOCAMPAL CONTRIBUTIONS TO AGE-RELATED MEMORY DYSFUNCTION**

Carol Barnes

Aging is associated with specific impairments of learning and memory, some of which are similar to those caused by hippocampal damage. Studies of the effects of aging on hippocampal anatomy, physiology, plasticity and network dynamics have contributed to a better understanding of age-related cognitive deficits. For example, anatomical and

electrophysiological studies indicate that the hippocampus of the aged rat sustains a loss of synapses in the dentate gyrus, and a loss of functional synapses in area CA1. Such changes may contribute to the observed age-related impairments of synaptic plasticity, which include deficits in the induction and maintenance of long-term potentiation (LTP) and lower thresholds for depotentiation and long-term depression (LTD). This shift in the balance of LTP and LTD could, in turn, impair the encoding of memories and enhance the erasure of memories. Such altered plasticity also changes the dynamic interactions among cells in hippocampal networks, causing deficits in the storage and retrieval of information. Studies will be reviewed that link changes in cognition to deficits in these plasticity mechanisms and altered hippocampal network dynamics. Specifically, experience-dependent place-field expansion, which requires NMDA receptor activation is impaired in hippocampal 'place cells', which may decrease both the spatial information content of the hippocampal map and the ability of the hippocampal network to store sequences of locations. Furthermore, plasticity deficits may also affect network dynamics by impairing the binding of cues to the hippocampal map, leading to the retrieval of inappropriate maps, or impaired use of external cues to guide navigation. All of these neural changes could lead to a behavioral outcome that would predispose older to becoming lost.

### **Metals and the brain: Selected abstracts**

#### **MODELING THE CONTRIBUTION OF IRON MISMANAGEMENT TO NEUROLOGICAL DISORDERS**

Prof JRC Connor \*  
(Penn State University)

A loss of iron homeostasis in the brain has been demonstrated in Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Amyotrophic Lateral Sclerosis and Hallorvorden-Spatz disease. In these diseases the iron imbalance has been traced to too much iron or limitations in iron storage capacity. However, too little iron in the brain also has neurological consequences. Iron deficiency during development can have a lasting impact on cognitive and motor impairment that may be associated with a myelin deficit. Recently, the adult disorder, Restless Legs Syndrome, has been associated with brain iron insufficiency. This lecture will review the findings of loss of iron homeostasis in the brain in the neurodegenerative disorders and examine animal models and cell culture models designed to test hypotheses about the contribution of iron to neurodegeneration. Data from a mouse line that recreates the imbalance between iron and ferritin that is seen in Parkinson's and Alzheimer's Disease will be presented. Data from cell culture models that specifically examine the contribution of iron to cellular oxidative stress and the inflammatory reaction of microglia also will be presented. A particular focus of this lecture will be the new observations that a mutation in the Hfe gene, commonly associated with iron overload disorders, is more prevalent in individuals with Alzheimer's Disease and Amyotrophic lateral Sclerosis than in the general population. Data from newly created cell culture models that examine the consequence of carrying the Hfe mutation will be presented.

Finally, the consequences of insufficient iron status will be addressed from studies of individuals with Restless Legs Syndrome and animal models of iron deficiency. The goal of this lecture is to establish the contribution of iron to neurological function and the need for a greater understanding of the mechanisms and the regulation of the mechanisms that maintain brain iron homeostasis.

#### ALUMINUM-TRIGGERED FIBRILLOGENESIS OF B-AMYLOIDS

Prof PZ Zatta (CNR-Italy), Dr D Drago\* (CNR-Italy), Mr G Tognon (CNR-Italy), Dr F Ricchelli (CNR-Italy)

CNR-Institute for Biomedical Technologies, "Metalloproteins" Unit, Department of Biology of the University of Padova, Padova, Italy

Amyloid b-peptides (Ab), as insoluble fibril deposits, are the major component of the brain senile plaques that characterize Alzheimer's disease. The conformational changes induced by Cu<sup>2+</sup>, Zn<sup>2+</sup> and Al<sup>3+</sup> on Ab 1-40 and 1-42, and the subsequent aggregation and fibrillogenesis processes have been studied at physiological pH. Ab structural changes induced by Cu<sup>2+</sup> binding did not favour peptide aggregation. On the contrary, Ab conformation adopted in the presence of Zn<sup>2+</sup> and Al<sup>3+</sup> led to formation of surface hydrophobic clusters (as followed by the fluorescence of 8-anilino-1-naphthalene sulfonic acid-ANS) and increase of the aggregational potential (as followed by Thioflavin-T (ThT) fluorescence), as compared to the metal-free peptide. These effects were more pronounced for the complex Al<sup>3+</sup>-Ab 1-42. Moreover, aggregates of Al<sup>3+</sup>-Ab 1-42 evolved to fibrillar structures even at very low peptide concentration. The conformational and aggregational effects of Al<sup>3+</sup> were specifically abolished in the presence of desferoxamine mesylate, a trivalent metal ion chelator used in therapy to treat toxic Fe<sup>3+</sup> and Al<sup>3+</sup> overload conditions.

## Psychiatry in Africa

#### PSYCHOSOCIAL ASPECTS OF KHAT USE AMONG THE YOUTH OF NAIROBI

Ms TM Khamis

Prof DMN Ndetei

Prof JM Mburu

(University of Nairobi/Africa Mental Health Foundation)

The aim of the present study was to determine the socio-demographic correlates of khat users, patterns of khat use, attitudes and evaluate the associated social and psychological problems in residents of a Nairobi neighbourhood. 201 youth (15-30), (138 males and 63 females) were interviewed using socio-demographic data questionnaire, (NOK) Scale for Depression and anxiety, Beck's Depression Inventory and W.H.O Quality of life instrument. Data was analyzed using the EPI INFO Version 10 to generate descriptive statistics. Muslims 108 (54%) were more than Christians 93 (46%), Somalis (23.8%) more than other ethnic groups, unmarried 76 (37.8%) more than married 34 (17%) who were khat users. 104 (52%) denied of awareness of any harmful effects of khat. 77 (35%) stated that khat use was not a problem in Eastleigh area, 83 (41%)

claimed that it was a problem but only to a minor extent. The following were significantly associated with khat use:

- There was a strong association between khat use and use of other drugs ( $p < 0.001$ ).
- A strong association was observed between working status and the quantity of khat consumed ( $p < 0.001$ ).
- There was a significant relationship between level of income and quantity of khat consumed ( $p < 0.001$ ).
- There was a strong association between marital status and the amount of khat used, those who were not married chew more than the married ( $p < 0.001$ ).
- There was a significant relationship between the duration of khat chewing and changes observed in the relationships ( $p < 0.001$ ).

(NOK) scale for depression and anxiety revealed mild cases of depression and anxiety of 60 (29.8%) and 29 (14.4%) severe cases. Beck's depression inventory revealed 120 (59.7%) cases of mild – moderate cases of depression and 25 (12.4%) severe cases

#### PTSD AMONG MOTOR VEHICLE ACCIDENT SURVIVORS, KENYA

Dr FA Ongecha

Prof DMN Ndetei

(University of Nairobi/Africa Mental Health Foundation)

The 264 patients were interviewed using a questionnaire to collect the socio-demographic data, the Self Rating Questionnaire (SRQ) and the Impact of Event Scale (IES-R). Diagnosis was made using the Diagnostic and Statistical Manual (DSM-IV). **Results:** The mean age was  $34.63 \pm 12.71$  years (range 18-65). Overall the prevalence rate of PTSD was 13.3%. None of the cases had been previously diagnosed as having PTSD. Females had a higher rate of 17.9% ( $n = 67$ ), compared to the males 11.7% ( $n = 197$ ). The majority of those with PTSD (42.9%) were young, 20 – 29 years. Other risk factors were having post-primary education (62.9%), experiencing the first motor vehicle accident (14.1%), previous psychiatric illness, and other medical illnesses. The type of accident, role status and immediate reactions to the accident were not significant. **Conclusion:** PTSD following motor vehicle accidents is common. Although the MVA survivors do develop significant rates of PTSD, it is not easy to identify those at risk but some of the parameters documented in this study may help. A multidisciplinary approach is therefore essential in the management of the RTA survivors at the orthopaedic and trauma clinics if their physical and psychological needs are to be adequately addressed.

#### PSYCHIATRIC REALITIES WITHIN AFRICAN CONTEXT - THE KENYAN CASE STUDY

Prof DMN Ndetei\*

(University of Nairobi/Africa Mental Health Foundation)

Africa faces several real challenges in her attempt to make available and affordable mental health services to all its citizens. Available data suggest that the need for mental health services at all levels are the same across most countries in the world, despite gross disparity in resources. The two most needed resources are manpower and research

based data for appropriate evidence based policies. The constraints are social-economic and cultural contexts, which vary from country to country. Yet significant advances can still be made in the areas of manpower and research within the peculiar prevailing constraints and contexts. It is unlikely many Africa countries, including Kenya, which has one of the best psychiatrist/population ratio of 1:500,000 in Africa will achieve an acceptable ratio in the foreseeable future that compares with what currently obtains in Western countries, with even internal distribution. While still training psychiatrists, there has to be a policy that focuses more on medical and paramedical students. The move towards making these policy changes in manpower and appropriate, prioritized service and cost-effective structures will have to depend on locally obtained data, on such areas as epidemiological patterns, cultural, social, stigma and economic determinants of mental health seeking behaviour and also the most appropriate prevention and management, including psychopharmacotherapy. Western studies on pharmacokinetics and pharmacogenetics cannot be applied to the Africa context wholesome. Hence the need for ethnopsychopharmacology studies. All of these will be a joint effort of researchers, policy makers and consumers. This paper will use Kenya experience and locally derived data to illustrate these challenges and the way forward. It concludes that it is possible to approximate available and affordable services in the next decade or so.

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#### **ADOLESCENT-PARENTAL INTERACTIONS FROM INFANCY, NAIROBI KENYA**

Dr LK Khasakhala  
 Prof DMN Ndeti \*  
 (University of Nairobi/Africa Mental Health Foundation)

This study aims to identify the parenting styles and classify the types/forms of child abuse that occurred during childhood development among adolescents in secondary schools of Nairobi Province, Kenya, using the EMBU questionnaires. This questionnaire measures four parenting styles authoritative, authoritarian, permissive and uninvolved and four forms of child abuse (physical abuse, physical neglect, emotional abuse and emotional neglect). 145 male and 110 female students aged between 13-19 years in secondary schools of Nairobi Province were recruited in the study. Factor analysis, descriptive and inferential statistics were done using the SPSS 11.0 version. There was association between authoritative parenting and two forms of child abuse among the father; emotional child abuse  $p < 0.001$  and physical child abuse  $p = 0.004$ . Among the mothers the significant finding,  $p = 0.004$  was scored with physical child abuse. Authoritarian parenting had high significant scores between the parenting style and three forms of child abuse: fathers, physical child abuse  $p = 0.006$ , emotional child abuse  $p = 0.001$ , and for mothers; physical child abuse  $p < 0.001$ , emotional child abuse  $p < 0.000$  and emotional child neglect  $p < 0.001$ . The fathers showed no association between this parenting style and two forms of child neglect (emotional or physical), but for mothers there was no association with physical child neglect. Uninvolved parenting, the child's emotions are neglected by both parents, fathers  $p = 0.02$  and mothers  $p < 0.001$ , but there is

no association between this parenting style and the other three forms of abuse.

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#### **ALCOHOL USE AMONG YOUNG PERSONS: A FOCUS GROUP STUDY IN SOUTHWEST NIGERIA**

OA Obeijide  
 (Professor of Psychiatry, University of Ibadan, Nigeria)

Research reports show that a major increase in alcohol availability and consumption has occurred in Nigeria since 1977 when the number of alcohol industries increased from 7 to 34 in 1985. Alcohol policies in Nigeria remain silent on the legal age for alcohol purchase/drinking, hours of purchase and blood alcohol level when driving vehicles. Children and young persons have been reported to start consuming alcohol at tender ages of 10-12 years contrary to the cultural norms. Also, research in Western countries (NIAA) show that young people who begin to drink before age 15 are four times more likely to develop alcoholism and twice as likely to develop a maladaptive drinking pattern that repeatedly causes life problems. Our findings from focus group discussions held among male and female young persons of between ages 15 to 25 are that peer pressure, parental attitude and emotional problems commonly influence drinking behaviour. Drinking takes place more often at social gatherings where drinks are free, and the common drinks are beer, spirits, and fruity alcohol beverages. Adolescents and young persons were found to be occasional drinkers who sometimes deliberately drink to intoxication (binge drinking). Drunkenness predisposes them to maladaptive behaviours such as risky sexual behaviours, road traffic accidents, alcohol poisoning, violent acts and poor academic performance. A longitudinal study is desirable to identify possible outcome of young persons with early drinking history. Also, our findings reinforce the urgent need for evidence-based alcohol policies at the Federal and State levels to design prevention strategies for alcohol use and abuse among adolescents and young persons.

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#### **PERSONALITY DISORDERS AND PERSONALITY TRAITS AMONG TYPE2 DIABETIC PATIENTS**

Prof O El Rufai \* (Prof.), Dr M Sabosy (PHC-GP), Dr M S Abuzeid (PHC-GP)

The objectives of this study were to determine the prevalence and nature of personality disorder (PD) and personality traits, among a primary health care (PHC) sample of type 2 diabetic patients, and to investigate their association with the blood glucose control. A random sample of type 2 diabetic patients, attending a PHC clinic were recruited. The International Personality Disorder Examination, the ICD-10 module (IPDE ICD-10) was used for personality measurement. Glucose control was assessed by glycated haemoglobin (HbA1c). Patients interviewed were 69 males and 74 females. Definite PD was identified in 8.4%. Prevalence rates among males and females were 13% and 4.1% respectively. The commonest PD identified was the anankastic (7%). Patients with definite PD demonstrated predominance within the range of borderline glucose control,

while subjects with probable personality disorder were divided between the ranges of borderline and poor levels of glucose control. Negative PD subjects showed closer association with borderline control. The dimensional mean score of personality traits showed a consistent rise with poor glucose control. On comparison with a similar PHC sample, irrespective of illness, the personality profile was different from the diabetic group. It is concluded that in management of type 2 diabetic patients, caregivers should give particular consideration to the unique personality characteristics of each patient, and their potential impact on management.

#### ASSOCIATION OF TRAUMATIC EXPERIENCES WITH DEPRESSION AMONG NIGERIAN ADOLESCENTS

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Ms O B Yusuf

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Dr O Esan

(University College Hospital, Ibadan, Nigeria)

**Objective:** To determine the prevalence and pattern of traumatic stress experiences and their association with depression in adolescents in rural Nigeria.

**Method:** Adolescents in two rural school districts in Southwestern Nigeria were randomly selected for this study. Using the Yoruba version of the World Health Organization, Street Children project questions and the Youth DISC Predictive Scale (DPS), information on traumatic events and depression were obtained from 484 adolescents. Questions on life events were analysed using both qualitative and quantitative methods.

**Results:** One hundred and fifty seven adolescents (32.4%) reported that they had been in situations in which they were afraid they would lose their lives or be severely harmed. Of this number 135 went on to describe these situations. Nine were attacked by armed robbers, 68 were in car accidents or near car accidents, 3 were confronted by persons with dangerous weapons, 3 by animals, 8 had health problems and 44 had other conditions. Adolescents who had been in such situations were more likely to meet the criteria for major depression than those who had not experienced such events ( $p < 0.05$ ). The greater the number of depressive symptoms the adolescent had, the more likely it was that they had experienced a traumatic event ( $p < 0.05$ ). Reporting ever being in a situation of severe trauma was also significantly related to the occurrence of four out of the seven symptoms of depression which include suicidal ideation, suicide attempt, low energy and poor concentration ( $p < 0.05$ ).

**Conclusion:** Nearly one-third of adolescents in rural Southwest Nigeria reported that they had experienced very traumatic events and these experiences are associated with depression and suicidal symptoms. There is a need to reach these adolescents with mental health care services.

#### PREVALENCE OF DEPRESSION AMONG WOMEN ATTENDING OUTPATIENTS CLINICS IN MALAWI

Dr J M Tugumisirize \*

(Department of Psychiatry, Makerere University, Uganda),

Prof Agren

(Division of Psychiatry, Karolinska Institutet, Sweden),

Dr Musisi

(Department of psychiatry, Makerere University)

**Objective:** To determine the prevalence of depression among women attending outpatient clinics in Malawi

**Methods:** Systematically selected samples of adult women from two outpatient clinics, at Mzuzu Health Centre in Northern Malawi and at Mulanje Hospital Southern Malawi were screened for depression using the Edinburgh Depression Scale (EDS). Women who screened positive (10 and above) and a sample of those who screened negative were interviewed using the depression module of the Mini International Neuropsychiatric Interview (MINI). A diagnosis of depression was made according to modified DSM IV criteria

**Results:** Two hundred and eleven and 200 women were interviewed at Mzuzu Health Centre and Mulanje Hospital out-patient clinic respectively. The mean age of women at Mzuzu was 30.9 (range 16-63, SD 9.48) years, compared to the mean age at Mulanje of 34.1 (range 18-65, SD 12.28) years. Of 211 women at Mzuzu, 118 scored 10 and above on EDS and 117 of these were interviewed with the MINI. Of 93 women who scored below 10 on EDS only 39 were interviewed with the MINI. Twenty eight women at Mzuzu had major depressive disorder (weighted prevalence, 16.6%) and 26 had minor depressive disorder (weighted prevalence, 13.1%). At Mulanje of 200 women 93 scored 10 and above on EDS and 92 of these were interviewed with the MINI whereas 107 scored below 10 and only 59 were interviewed with the MINI. Eighteen women at Mulanje had major depressive disorder (weighted prevalence 9.9%) and 37 had minor depressive disorder (weighted prevalence, 21.6%).

**Conclusion:** There is a high un-recognized burden of depression among women at out-patient clinics in Malawi

#### NON-FATAL SUICIDAL BEHAVIOUR AT THE JOHANNESBURG GENERAL HOSPITAL

Dr MYH Moosa \*

Prof FY Jeenah

Dr A Pillay

Prof M Vorster

Dr R Liebenberg

(University of Witwatersand)

**Aim:** To outline the demographics of a group of patients with NFSB; and to determine, if any, factors associated with this behaviour.

**Method:** The study included all patients treated for NFSB in the Johannesburg Hospital. A control group (age and gender matched) was obtained from individuals in the pharmacy queues at the hospital. The information was gathered by means of a questionnaire.



**Results:** The study sample comprised 43 patients with NFSB (mean age = 29.7 years) of which 26 (60%) were females. The control group consisted of 45 non-suicide attempters (mean age = 30.9 year) of which 33 (73%) were females. There was no significant difference between the two groups with respect to age and gender ( $p > 0.05$ ). Patients with a past history of a psychiatric illness or a history of physical or sexual abuse were significantly more likely to attempt suicide as compared to the control group ( $p < 0.05$ ). Characteristics of the patients with NFSB included: being female (60%); 18-30 years of age (70%); and previous NFSB (24%). The common methods employed with this behaviour were overdosing with medication (63%) and the ingestion of household poison (33%). Significant factors associated with a repeated NFSB included: being female (90%), age group of 18-30 years (76%), having children (90%) and a past psychiatric history (50%).

**Conclusions:** Patients who threaten deliberate self-harm and who have a history of previous NFSB, psychiatric illness and physical or sexual abuse, are at a higher risk of carrying out this behaviour as compared to the general population. Significant factors associated with a repeated NFSB include: being female; in the age group of 18-30 years, having children and a past psychiatric history. It is important for health care workers in this population group to identify these factors and institute appropriate intervention.

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#### **INTEGRATING MENTAL HEALTH INTO GENERAL PRIMARY HEALTH CARE – UGANDA'S EXPERIENCE**

Dr N Kigozi \* (Uganda Psychiatric Association)

Most developing countries and indeed many African countries have been undertaking reforms of their Mental Health policies and strategies to improve access and equity for the community to mental health and psychiatric services. This has been in conformity with the philosophy for health policies which emphasize integrated delivery of health services. The guidelines from the Alma Ata (1978) and WHO recommendations have naturally provided a softer ground during the implementation of this strategy. However, despite embracing the philosophy and having developed sound policy and implementation programs, practical realities are being experienced on the ground. Research and an evidence-based approach is needed to evaluate the success of the programs, which appear to be lacking in most developing countries and indeed worse in Africa. The paper will review some of the evidence available with a case for Uganda, discuss the challenges and propose a way forward.

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#### **DEPRESSION AMONG NIGERIAN SURVIVORS OF STROKE: PREVALENCE AND ASSOCIATED FACTORS**

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Dr M A Komolafe

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Dr A. O Adewuya

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Prof M.A Lawal

(Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife)

In spite of the abundant body of information on the adverse

consequences of depressive symptoms among stroke patients, few cases are recognized, fewer treated and there is dearth of information on the effectiveness of treatment methods. In Nigeria, and in many developing countries in Africa, available information on poststroke depression is scanty and the influence of socio-cultural and psychosocial factors largely unexplored. Consecutive survivors of stroke (105 subjects) were evaluated and compared with 105 matched controls who were attending hypertensive clinics in a Nigerian teaching hospital. All the patients were evaluated with the Beck Depressive Inventory, the Modified Mini Mental State Examination and socio-demographic schedule. The results show that the stroke survivors were more depressed and performed poorer on some aspects of the modified MMSE. Comparison of depressed and non depressed stroke survivors revealed the contribution of some clinical and culturally determined factors which could influence outcome. It is important to pay attention to post-stroke depression in developing countries so that sufferers can benefit maximally from hard-pressed treatment facilities.

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#### **NGO INVOLVEMENT IN MENTAL HEALTH CARE - THE WAY FORWARD**

Dr K Basangwa \*

(Uganda Psychiatric Association)

The contribution of Mental illness on the Global Burden of Disease is now known to be significant the world over. In Africa, the situation is even worse because the continent suffers gross scarcity of both human and financial resources. The scarce resources are currently overstretched by the increasing burden of disease caused by poverty, civil strife and the HIV/AIDS pandemic. It is now known that the majority of the global AIDS sufferers are on the African continent. Amidst all the above problems are challenges that are posed by upcoming industrialization, urbanization and all the stress that goes with a rapidly changing society. In many areas the result of this has been an increase in psychiatric morbidity. While governments are doing all that is possible to improve mental health care, their capacity is many times overwhelmed by the day to day increasing demand for service. In such situations, NGOs (Non Government Organisations) have become key partners in the prevention of mental illness and promotion of mental health. The paper discusses Mental Health intervention by NGOs as seen in the region with particular reference to the Ugandan situation.

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#### **PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG AFRICAN SCHOOL CHILDREN**

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Prof T Tylleskar

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Dr I Elgen

Dr K Sommerfelt

(Haukeland University Hospital/Bergen-Norway)

**Objectives:** To estimate the prevalence of and determinants for attention deficit and hyperactivity disorder (ADHD) symptoms among school children in an African urban setting.

**Methods:** The 18-items of the Disruptive Behaviour Disorder

rating scale (DBD), which are based on the Diagnostic and Statistical Manual for mental disorders 4th edition (DSM-IV), were used to investigate the presence of ADHD symptoms. Parents interview, using a questionnaire specially designed for the study, was performed to identify socio-demographic characteristics. In addition, all children were subject to a clinical examination.

**Results:** The estimated prevalence of DSM-IV ADHD symptoms was 6%. Those with family health problems, younger age at start of primary school, good nutritional status and poor school performance more often had DSM-IV ADHD symptoms.

**Conclusions:** ADHD symptoms are as common among school children in Kinshasa as elsewhere. The sociodemographic factors described as risk factors for ADHD in high-income countries were not identified in this study.

**Keywords:** ADHD, DSM-IV, school children, risk factors.

### BARRIERS TO EFFECTIVE MENTAL HEALTH CARE IN NIGERIA

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There is a wide gap between need and treatment of psychiatric disorders in many regions of the world, and particularly so in resource-poor countries in Africa. For example, there is evidence that only about 10% of persons with mental disorders in a 12-month period receive any form of treatment in Nigeria. The reasons for this large unmet need are many and varied. Systemic neglect of the health sector in general and mental health issues in particular by various tiers of government is one major reason. However, other factors contribute to the impermeability of the filters to health care service. In this presentation, such factors will be reviewed and supported with recent epidemiological and health service data from the country. Evidence will be provided to demonstrate the link to inadequate mental health care of factors such as poor knowledge about the causation of mental illness, stigmatization of the mentally ill, inadequacy of mental health service, and health financing system that is largely dependent on out-of-pocket payment by patients. The presentation will emphasize the problems with mental health service provision in a large African country that is probably typical of the continental scene. An attempt will be made to provide the template for health service reform that can improve health care provision within the constraints of limited resources.

### QUALITY OF LIFE EVALUATION IN PATIENTS WITH HIV-1 INFECTION WITH RESPECT TO THE IMPACT OF PHYTOTHERAPY (TRADITIONAL HERBS) IN ZIMBABWE

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**Background:** Absence of conventional antiretroviral drugs has increased the use and popularity of traditional herbs in Zimbabwe and elsewhere. However, the effects of traditional herbs in quality of life of HIV infected persons are not known.

**Objective:** To evaluate the impact of phytotherapy (traditional medicine) in persons with HIV infection and assess the quality of life of those persons with respect to HIV disease progression. Main Outcome Measures: (a) Improvement of quality of life of HIV infected persons on phytotherapy using the WHOQoL instrument, and (b) Reduction in quality of life associated with a disease progression using CD4 and viral load as a measure of disease progression.

**Methods:** We interviewed one hundred and five patients at various stages of HIV-1 infection in a community-based cohort study from June 1996 to May 1998, in Harare. The ninety-six (91.4%) asymptomatic and six (8.6%) symptomatic patients who underwent regular physical examinations and had their blood drawn for laboratory tests at the baseline afterwards at 3-month intervals over a period of two years.

**Results:** The mean (s.d.) age was 34.9 (7.3) years; 64.4% were women and 60.3% were married. In multivariate analyses, age was significantly correlated with the level of independence domains ( $P=0.032$ ), whereas, gender was significantly correlated with social relationships, domains ( $P=0.034$ ). The type of treatment received was significantly correlated with spiritual domains ( $P=0.045$ ). Proportions of scores on five domains measuring different aspects of quality of life for patients on phytotherapy were much lower than those on conventional therapy ( $P<0.0001$ , for all variables).



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