S59-6
OPTIMISING COMPLIANCE WITH TREATMENT

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It is well established that antidepressants, antipsychotics and mood stabilisers prevent relapse if taken long-term. Patients however, will only comply with medication if they accept that something is wrong with themselves, that it needs correcting, that drugs correct it and that the risk:benefit ratio to them is acceptable. Common reasons for discontinuing psychotropics include side effects (even though these can often be managed), fear of addiction, lack of knowledge that drugs prevent relapse and (usually uninformed) pressure from friends and relatives.

A positive attitude towards drugs is generally essential for compliance or concordance, particularly in the long-term. Current compliance techniques tend to revolve around provision of information using the traditional sender-message-receiver communication model. A number of studies have shown the advantages of structured education of patients and the subsequent positive effect on attitude and hence compliance and relapse. Individual or group sessions covering dependence, chronic and acute illness, how drugs work etc. improve attitude to drugs, particularly if follow-up or reinforcing support material and resources are available. Pharmaceutical care of patients e.g. by structured education, will minimise negative attitudes towards drugs and reduce relapse.

S60. Biological and clinical aspects of treatment-resistant depression

Chairs: J Mendlewicz (B), P Bech (DK)

S60-1
DEFINITION CRITERIA FOR TREATMENT RESISTANT DEPRESSION

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Outcome studies have demonstrated that approximately one third of patients treated for major depression do not respond satisfactorily to antidepressant pharmacotherapy. Long term observations reveal that a considerable number of patients have a poor prognosis, with as many as 20 percent remaining unwell two years after the onset of the illness. These outcome data are usually used to estimate the frequency of Treatment Resistant Depression (TRD). The key parameters that characterize and define TRD include the basic criteria used to specify the diagnosis, the response to treatment, previous treatment trials, the adequacy of treatment and compliance to treatment. Diagnostic aspects include the need to reach an accurate diagnosis; the various forms of treatment relating to other subtypes of depressive disorders; comorbidity with other psychiatric or personality disorders and chronicity. The assessment of treatment response raises the problems of how to evaluate remission and the minimum length of remission required. Previous failed treatment trials remain a subject of controversy and refer to the number and type of adequate antidepressant treatment trials required by the patient before the question of resistance can be considered. Finally, treatment adequacy has to be considered in terms of dosage, duration and compliance. A lack of consensus on these points restricts comparison between clinical trials and limits interpretation of the efficacy of treatment in the management of treatment resistant patients. We have re-examined the available data in TRD to indicate the limitations of the existing definitions and we propose conceptual and operational criteria for collaborative research projects. It appears that a number of variables commonly associated with treatment resistance, relate mainly to misdiagnosis and inadequate treatment and are independent of the characteristics of patients. The proposed criteria are intended for use in therapeutic trials in TRD, both to evaluate the efficacy of treatment and to examine the conceptual aspects of the subject. In major depression, the operational definition we propose for TRD is a failure to respond to two adequate consecutive trials of treatment with different classes of antidepressants. The rationale for this definition is discussed in the context of alternative definitions.

S60-2
CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF RESISTANT DEPRESSION

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During the last decades, it has been a constant that about 1/3 of depressed do not respond to antidepressants: this is true across diagnostic subgroups and pharmacological mechanisms of action. 20% of patients treated are still ill 2 years after onset (Paykel 1994) and 10% resist to multiple interventions (Nieremberg & Amsterdam 1990). In the NCA, a small proportion of patients represents most of the morbidity and cost.

Therefore, even if resistant depression in no way can be considered a diagnosis per see, it is a practical and theoretical problem of great importance. No agreement on the definition exists since this is a multifactorial problem. Prevalence is obviously influenced by the definition of treatment response (full, partial), on the definition of what an "adequate" treatment or an "aggressive" treatment is (dose + duration), and on the number of failed trials to acknowledge resistance.

The factors usually involved in resistance will be discussed. These are:
- Misdiagnosis and/or diagnostic subtypes. A special attention should be given to comorbidity with other axis I disorders, with axis II disorders, with alcohol and drug addiction and with physical problems such as thyroid dysfunction, neurological disorders or drug treatment of physical condition. However, most studies exclude comorbidity.
- Inadequate treatment is a major cause and probably explains up to 2/3 of resistant patients. The switch from one class (e.g.: SSRIs) to another (e.g.: TCAs) may improve response although some data suggest that moving from an SSRI to another may also be effective.
- Evolution is also a major factor: a) the duration between onset of symptoms and onset of treatment is related to response, b) the persistence after treatment of residual symptomatology may predict long term and poor outcome and therefore resistance.

Discussions about resistance within specialists are only the top of the iceberg when evaluating the situation in primary care. It is proposed that pharmacological resistance should be separated from patient resistant and management resistance.

S60-3
NEUROBIOLOGY OF RESISTANT DEPRESSION

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Patients for whom the diagnosis of depression was established and who did not respond to adequate treatment are defined as suffering