

a methadone prescription dispensed from a community pharmacy, regular counselling appointments with a community nurse and a treatment objective of detoxification or a place in a methadone maintenance programme where they attended daily to take their methadone on the premises and had stable maintenance as the treatment goal. Subjects who refused to accept their allocated treatment were offered the other condition. They were assessed at intake and again 1, 2, 3, 6, and 12 months after entering treatment.

**Results:** 119 subjects entered the trial, 75 went to CDT treatment, 47 randomised 28 chosen, and 44 to MMC treatment 33 randomised and 11 chosen. The CDT group stayed in treatment for a mean of 5.76 months, the MMC group for 8.69 months. 91% of the whole sample were contacted for follow up at 12 months. Data on the conduct of the study will be presented, alongside preliminary outcome data and analysis.

**Conclusions:** Randomising subjects to different treatment modalities presents special problems in the addictions field. Monitoring the process of treatment may also prove difficult. However the follow up of subjects when they have left treatment in order to obtain good quality data is feasible.

#### COMMONALITIES IN METHADONE SUBSTITUTION THERAPY PROGRAMMES IN EUROPE: A CASE FOR A UNIFIED POLICY?

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A multicentre survey of treatment practices related to Methadone Substitution Therapy was conducted in a cluster of eleven MST programmes in nine European countries (eight EU countries plus Switzerland) during the summer of 1995. The following practice variables were investigated: type of MST; eligibility criteria for admission; treatment contract; pre-treatment orientation of patients; informed consent; dosing policy; length of treatment; and policies on discharge and readmission. The detailed analysis of data revealed the following common practices across programmes: established links with hospital services and family doctors; prescription of methadone only by licensed medical practitioners; programmes are directed primarily by psychiatrists; specialist training in addiction not a prerequisite for employment; multidisciplinary personnel, with nurses in the majority; self referral is the predominate pattern; established interagency collaboration; treatment is predominantly Methadone Maintenance Treatment (MMT); mandatory patient identity common; verification of physical dependence by urinalysis; oral preparation for methadone; and on-site dispensing.

The findings of this survey suggest the possibility of a Europe-wide policy on Methadone Substitution Therapy and the implementation of Article 129 of the Maastricht Treaty as it affects a European health policy on drug dependence, is discussed.

#### THE ROLE PHARMACOKINETICS AND PSYCHOPATHOLOGY IN THE PREDICTION OF CRAVING AMONG OPIATE ADDICTS IN METHADONE MAINTENANCE THERAPY

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**Objective:** The aim of the study is to determine the role of pharmacokinetics and psychopathology in the prediction of craving among opiate addicts in methadone maintenance therapy (MMT).

**Methods:** A consecutive series of 20 long-term opiate addicts currently enrolled in MMT was recruited from a closed ward. During the study period of four days, craving was assessed 10 times per day using the experience sample methodology. On the first day, psychopathology was measured with the 28 item General Health Questionnaire (GHQ-28) and the 90 item Symptom Check List (SCL-90). During the second day 8–9 plasma samples were drawn and plasma methadone concentrations were determined using a newly developed high pressure liquid chromatography (HPLC) procedure.

**Results:** A significant positive relationship was observed between oral methadone dose and craving ( $r = 0.55$ ). No significant relations were found between craving and pharmacokinetic parameters (plasma methadone through level, methadone half-life) or existing psychopathology. Two specific craving patterns were identified: a very high peak around 9 a.m. (methadone dispensing time clinic) and a slightly smaller peak around noon (methadone dispensing time in outpatient MMT).

**Conclusions:** The results suggest that factors other than pharmacokinetics and (axis I) psychopathology are responsible for craving in MMT clients. It is hypothesized that anticipatory conditioned responses or circadian rhythms are responsible for the observed fluctuations in craving. Consequences of these findings and their interpretation for the clinical management of MMT clients are discussed.

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## S80. The history of physical treatments in psychiatry

*Chairmen: P Pichot, D Healy*

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#### A HISTORICAL NOTE ON THE DEVELOPMENT OF ZIMELIDINE, THE FIRST SELECTIVE SEROTONIN REUPTAKE INHIBITOR

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In the early 1960s the development by Hillarp and his colleagues of a histochemical method for the visualisation of monoamines at the cellular level led to the demonstration of monoamines in specific neuronal systems in the brain and opened up possibilities for a precise localisation of different synaptic events in the monoaminergic systems. Together with members of the Hillarp school we were thus able to demonstrate the occurrence of a transmitter reuptake mechanism located to the cell-membrane of serotonergic neurons and to show that imipramine is capable of blocking not only the reuptake of noradrenaline, until then assumed to constitute the major mode of action of the tricyclic antidepressants, but also the reuptake of serotonin [1]. Our subsequent work revealed that the relative power of blocking noradrenaline and serotonin reuptake differed among the tricyclics. For example, the tertiary amines were more potent blockers of serotonin relative to noradrenaline than the secondary amines, and clomipramine was found to be an especially strong blocker of serotonin reuptake. We thereafter discovered a number of antihistamines with relative strong action on serotonin reuptake. Dr. Hans Corrodi and I started a synthetic programme based on one of these antihistamines, i.e. brompheniramine, in order to develop a selective serotonin reuptake inhibitor (SSRI). It turned out that a couple of modifications of the brompheniramine molecule sufficed to arrive at a highly selective serotonin reuptake inhibitor, i.e. zime-