Heroin Addiction and Related Clinical Problems

the official journal of

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Correlation between hepatitis C serostatus and methadone dose requirement in 1,163 methadone-maintained patients

Sarz Maxwell, Marc S. Shinderman, Alicia Miner, Annette Bennet

Summary

Hepatitis C infection is epidemic in intravenous drug users worldwide. This has great impact on opiate-addicted patients. Prevention of infection must depend on treatment of opiate addiction. This report discusses findings from 1,163 methadone-maintained patients tested for hepatitis C infection. The prevalence of HCV seropositivity in IVDU patients was 68%. Seropositive patients required significantly higher doses of methadone (169 mg/d vs. 100 mg/d, p<.05). This difference in dose was independent of duration of addiction and time in treatment. It is suggested that Hepatitis C infection may be associated with metabolic changes that lead to increased methadone requirement.

Key words: Methadone Maintenance - Methadone Dose - Hepatitis C Infection

Introduction

Hepatitis C infection is increasingly recognized as a world health problem. The most important vector of infection is intravenous drug use (IVDU), and the prevalence of hepatitis C virus (HCV) infection in patients with a history of IVDU averages 75-90%. This infection prevalence is fairly consistent worldwide [2,5,8,11,16].

Though antiviral treatment regimens can be efficacious in the treatment of HCV infection, the most effective intervention is prevention. For prevention of HCV infection, measures must be targeted against intravenous drug use, the most common cause of HCV infection. The most effective method of preventing intravenous drug use is addiction treatment, and the most effective treatment for opioid addiction (the drug most commonly used intravenously) is methadone maintenance treatment (MMT) [6,14,20]. In this study we report epidemiologic trends in 1,163 MMT patients tested for
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HCV, and discuss clinical associations between HCV seropositivity and increased methadone dose requirement.

Method

All patients were enrolled for MMT at Center for Addictive Problems (CAP), a private clinic in a central urban location. The average census at CAP is approximately 1,150 patients, and the mean methadone dose is approximately 130 mg/d. Between 1995 and 1999, most patients tested for HCV-Ab were those identified by counselor or physician as being at high risk for HCV infection, with the most important risk factor being IVDU history. Prior to October 1999, patients could have HCV-Ab testing done through our facility by getting a laboratory requisition from the physician, undergoing phlebotomy during the hours that a phlebotomist was available at the clinic (approximately 6 hours/week), and paying the laboratory fee. The assay used was Abbott HCV antibody enzyme immunoassay. Between October 1999 and January 2001 we were able to offer free and less invasive (fingerstick rather than venipuncture) HCV-Ab testing routinely to all patients, including all new admissions. Counsellors performed HCV education with all patients and actively recommended testing, particularly to patients with significant risk factors for HCV infection. These free tests were offered via Home Access, and the assay used was Ortho HCV Version 3.0 ELISA, with positive results confirmed by repeat ELISA and CHIRON RIBA HCV 3.0 SIA. A database had been maintained by the authors since early 1999, cataloguing clinical and epidemiologic data for all patients tested. Risk factors were determined by patient self-report in a standardized form administered at time of testing. History of cocaine use was determined by patient report and urine toxicology results. Urine toxicology results discussed here are the most recent done for each patient. Correlations between categorical variables were assessed using the chi-square statistic; correlations between quantitative variables were assessed by t-test.

Results

Of the 1,201 patients who underwent HCV-Ab testing, 38 (3%) were excluded from analysis because their test results were indeterminate even after repeated testing. The remaining study group consisted of 1,163 patients, of whom 387 (33%) were female. History of IVDU was reported in 694 (59.7%). Of these IVDU patients, 470 (68%) tested HCV+, and 224 (32%) were HCV-; this correlation was significant at the p<.05 level (r=0.50). HCV status also correlated with mean years of addiction (21.3 years for HCV+ patients versus 9.3 years for HCV- patients, r=0.55, p<.05) and with mean months in treatment (65.0 months versus 25.9 months, r=0.35, p<.05). Both of these findings were consistent with the difference in mean age between groups (44.4 years versus 33.8 years, r=0.50, p<.05). While the differences were modest, HCV+ patients were more likely to be female (r=0.50, p<.05) and Caucasian (r=0.17, p<.05). HCV+
patients were taking significantly higher doses of methadone: 169 mg/day versus 100 mg/day (r=0.27, p<.05). The relationship between HCV status and methadone dose remained statistically significant in partial correlations that controlled for mean years since addiction (r=0.15, p<.05) and for mean months in treatment (r=0.22, p<.05).

**Discussion**

In our population 85.5% of patients who report any history of IVDU are HCV+, a prevalence consistent with the world literature. Our population is also in agreement with the world literature regarding demographic and risk factors. The HCV+ patients tend to be older than HCV-patients (44.4 years vs. 33.8 years) and to have longer addiction histories (21.3 yr vs. 9.3 yr). In our clinic this means that the majority of HCV+ patients have been stable in treatment for years before learning of their HCV infection. This is consistent with the course of HCV infection, which may remain dormant and asymptomatic for 15-20 years [19].

In our sample, women are over-represented in the HCV+ group; other researchers have reported this [17], and a Chicago group has suggested the influence of sexual transmission accounting for this [8]: as with HIV infection, sexual transmission may be more efficient in the infection of female patients. The ethnic demography seems to run contrary to HIV infection, however; in our sample there is a predominance of Caucasian patients.

The yield from screening for HCV infection can be improved significantly by screening first for risk factors, particularly history (even, perhaps especially, remote history) of intravenous drug use. In a Yale analysis of screening algorithms, age, IVDU, and history of hepatitis correlated with HCV infection at the p<.001 level [9]. Measurement of liver function tests is a very insensitive screen; at least of infected patients have normal transaminase levels [1, 22].

MMT is the most effective treatment for opiate addiction, and should be effective prevention for HCV seroconversion, but studies of HCV seroconversion in patients enrolled in MMT [4, 13, 21] have been discouraging. One Australian study reported seroconversion as frequently in MMT patients as those out of treatment [4]. However, in this study the average methadone dose was only 42 mg/d, indicating that the majority of patients in that clinic were being medicated at doses far below those generally recommended. Indeed, 93% of patients in that MMT programme were still using heroin. Many clinics reporting poor efficacy of MMT in preventing new HCV infections did not report the dose of methadone prescribed, and may well have also been using subtherapeutic doses. Dose of methadone is directly related to efficacy of MMT in eradicating illicit opioid use [3, 7, 15, 18].

Unfortunately, the majority of MMT clinics in the United States use inadequate doses of methadone, resulting in high rates of continued illicit opioid use [20]. We have previously reported that the range of doses required to adequately treat opioid addicts may be wider than previously suspected. In our 1999 study we reported patients treated with doses in the range of 120 - 780 mg/d (10); since then we have had experience with
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several patients requiring >1000 mg/d of methadone.

In the mid-1990’s we noticed a clinical trend that interested us enough to being keeping a database about HCV infection. Long-term patients, stable and illicit-drug-free for years or even decades, presented complaining that the methadone dose that had kept them stable for years had stopped “holding” them. Many were impelled to buy illicit methadone in order to prevent opiate abstinence syndrome while continuing to avoid heroin use. As we titrated these patients’ methadone dose against symptoms of opiate abstinence syndrome (OAS), we found that the increases in dose requirement were significant and in some cases startling: up to 10-fold. As HCV-Ab testing became readily available, we noticed that this dose phenomenon was happening in the same long-term, older patients that were testing positive for HCV-Ab.

This large analysis proves a significant correlation between HCV+ and methadone dose. Other clinicians in Europe have noted this correlation [12]. Correlation does not automatically confer causality, and we explored other possible factors involved in this population requiring higher doses, particularly time in treatment. Our analyses showed that the correlation between higher dose and HCV+ status was independent of the patient’s age, length of opioid addiction, and time in treatment. It is tempting to speculate that HCV has specific effects on hepatic function, and these clinical observations suggest a unique effect.

Whereas most other hepatidites impair the activity of the Cytochrome P450 enzyme system, our clinical observations are more consistent with a cytochrome induction phenomenon. This possibility deserves further study, as it could have significant impact on the treatment of HCV and related conditions.

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Is craving for heroin and alcohol related to low methadone dosages in methadone maintained patients?

Sonia Lubrano¹, Matteo Pacini¹², Giuseppe Giuntoli¹², Icro Maremmani¹²³

Summary

The craving for heroin, alcohol and cocaine of 84 heroin-addicted patients under Methadone Maintenance Treatment have been evaluated to highlight possible craving clusters, and to underline contingent correlations with clinical characteristics such as addiction history, positive symptom distress and methadone dosages. The results show a correlation between methadone dosage and a craving for heroin and alcohol. Patients treated with low dosages of methadone show more psychopathological symptoms and a stronger craving for heroin and alcohol. On this basis, the search for an appropriate methadone dosage should be viewed as crucial to the success of the treatment, because it minimizes alcohol and heroin craving, and reduces the risk of psychopathological symptoms during treatment.

Key words: Methadone Maintenance - Methadone dose - Craving

The term craving initially was used to refer to the overpowering urge for opiates experienced by opiate-dependent patients during acute withdrawal [18]. It has subsequently been utilized for describing the desire to use any abused substance at any time. Nevertheless several similarities and differences can be found between the craving for opiate, for cocaine and for alcohol. The association between craving and physical withdrawal symptoms appears to be stronger among opiate-dependent than among alcohol-dependent patients. Among cocaine-dependent patients this relationship is even more tenuous than it is among alcoholics [14]. The subjective experience of “craving” alcohol, cocaine, or opiates has played as significant a role in theories of relapse as it played in theories of drug dependence. Yet a number of retrospective surveys of relapsed alcohol or drug dependent patients call its role into question.
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Psychological distress, family problems, social pressure, interpersonal conflict and the pleasurable effects of the drugs were the most frequently cited explanations by drug addicts for their relapse [3].

The aim of the present study has been to investigate heroin, alcohol and cocaine craving during Methadone Maintenance Treatment Programmes and to focus on contingent correlations with clinical characteristics such as addiction history, positive symptom distress, and the methadone dosages being taken by patients at interview time.

Method

Subjects
Patients diagnosed as affected by heroin addiction, on the basis of the DSM-IV criteria, and under Methadone Maintenance Treatment have been evaluated. Patients enrolled were at different phases of the Methadone Treatment (induction, stabilization, maintenance and detoxification), so as to guarantee the greatest possible variety of different forms of craving.

The sample consisted of 84 patients, 60 men (72.3%) and 24 women (27.7%) with a mean age of 32±6 (ranging from 19 to 50 years).

The stereotypical demographic features of the sample were as follows: male (72.3%), not married (63.5%), with less than 8 years of education (71.1%), and unemployed (51.8%). Their financial situation was, subjectively, considered to be adequate by 53%. Most of the subjects were living with their families (91.6%). Most had been born and were living in Central Italy (95.2). Physical and psychological features included liver diseases (79.5%), odontopathy (42.7%), mood disturbances (65.5%) and anxiety (53.6%). Their social adjustment was generally not troublesome, apart from problems with the law. 48.8% had been arrested at least once. Many were polyabusers (75.6%), with quite frequent abuse of stimulants and cannabinoids (59.5% and 92.9%, respectively). Opiate intake took place more than once a day (61.3%), and almost all the patients (96.3%) had succeeded in interrupting the use of drugs for varying periods of time. Almost all (97.6%) had already been treated, without any significant results. They had come into contact with drugs for the first time when they were about 16 and had started to use them regularly at about 21. The mean duration of their dependence was 145 months; they had first request treatment at the age of 25. They had been under treatment for an average time of 4 years.

Study setting
Patients were recruited in an Italian Public Drug Addiction Outpatient Clinic (SerT) that has been available to heroin addicts since the Seventies in Central Italy. Relapse into heroin use was not a reason for excluding patients from the programme. Reasons for treatment exclusion were the sale of drugs and continued addictive behaviours, with the violation of therapeutic goals, or physical violence at the clinic.
Study design and data collection

This has been a cross-sectional observational study of all patients on the Methadone Maintenance Treatment Programme, lasting almost one year. After informed consent has been given, members of the PISA-SIA (Study and Intervention on Addiction) Group administered rating scales to explore patients’ socio-demographic characteristics, addiction history and the psychopathological symptoms, and their craving for heroin, alcohol and cocaine. No members of the PISA-SIA Group belonged to the staff of the Addiction Unit where the study was held or knew the identity of probands. Probands had no reason to expect therapeutic changes or restrictions as a result of what was reported on the rating scales.

Assessment

Addiction History

The characteristics of opioid dependence were investigated through the RSDA (Rating Scale for Drug Addiction) by Maremmani et al. [9]. The RSDA is an observer evaluation questionnaire. It is divided into several areas. The first investigates physical condition at evaluation time (hepatic, vascular and lymph node pathology, gastroenteric disorders, sexual disorders, dental pathologies and HIV infection). The second studies the mental state in terms of psychopathological symptoms in different areas (insight, memory disorders, anxiety disorders, mood disorders, aggression versus others and self-aggression, thought disorders and sensory perception disorders). The third reports socio-environmental conditions at evaluation time (employment, family, sex, socialization and leisure time, and legal problems). The fourth examines lifetime substance abuse (alcohol, opiates, CNS depressants, CNS stimulants, hallucinogens, phencyclidine, cannabis, inhalants, and polysubstance abuse). The fifth examines the clinical picture of substance abuse (age at first use, age during continued use, frequency of drug use, modality, pattern of use, phase, nosology and age at first therapeutic contact), previous therapies, the current therapy and methadone dosage.

The index card automatically provides a total score and ten factor scores. The first five factors record physical problems (number of pathologies), mental problems (number of psychopathological areas with presence of symptoms), polyabuse (number of lifetime substances abused), previous treatments (number of), combined present treatments (number of). The last five factors register categorical (0=absence of problems; 1= presence of problems) social adjustment factors: occupational and family situation, sexual problems, socialization and/or leisure time, and drug-related legal problems. The total score is the sum of all the categorical factors (0=absence of problems; 1= presence of problems).

Inventory Check List (SCL-90)

The SCL-90 [5; 6] is a self-administered inventory consisting of 90 items, each grading from 1 to 5 according to severity. Items are grouped in nine subclasses: Somatic Symptoms; Interpersonal Sensitivity, Obsession-Compulsion, Depression, Anxiety,
Anger-Hostility, Phobic Anxiety, Paranoid Ideation, Psychoticism.

**Craving Analogue Visual Scale (CAVS)**

The CAVS is an analogue visual scale consisting of three 10-cm long bars, which are displayed in a vertical sequence. The right margin indicates the highest degree of craving for the specified substance, according to the subject’s addictive experience. The left margin corresponds to the absence of craving. The intermediate grades of length are proportionally expressed in numerical values along a 1-to-100 scale.

The CAVS has been used for the simultaneous assessment of the subjective intensity of craving for heroin, cocaine and alcohol as experienced by subjects during the administration of their daily methadone dose.

**Statistical Analyses**

The canonical correlation analysis was performed to compare the craving profile with clinical features (positive symptom distress, RSDA total score and patient’s methadone dosage at interview time). SPSS statistical routines were used. The canonical correlation analysis is the best statistical analysis for a comparison between different profiles of behavioural characteristics.

**Results and comment**

Only 25/84 patients (29.8%) had no craving for heroin. The severity of craving in the other 59 was about 45% of the maximum craving experienced in the past. At the interview, only 7.1% of the patients reported a severity of craving as high as the maximum experienced in the past. 88.1% of the subjects reported no craving for cocaine. Among those who did report craving, values ranged from 5% to 70% of the maximum experienced in the past. A craving for alcohol was not present in 77.4% of subjects; among those who did report craving, values ranged between 1% and 70% of the maximum.

The average methadone dose utilized was 48.60±26.6 (min 5 max 160) mg daily. 25% of the sample were assuming dosages less than, or equivalent to, 30mg/daily. 50% had an intake less than 45 mg/daily, and 75% less than 60 mg/daily.

The positive symptom distress score of the SCL-90 ranges between 16 and 83, compared with a maximum of 90; the intensity of these symptoms is mostly between 1 (mild) and 2 (moderate), anyway ranging from mild to severe. Table 1 shows the SCL-90 factorial scores. The most frequently represented symptoms belong to the depressive and obsessive-compulsive factors. Patients show also somatic symptoms that look like withdrawal symptoms.

Table 2 shows two different profiles of clinical characteristics and craving clusters that maximize the correlation. In the clinical set, patients who assume lower methadone dosages declare a higher number of psychopathological symptoms. Drug addiction history is related neither to psychopathology nor to methadone dosage taken at the
Table 1. Psychopathological symptoms in 84 heroin-addicted patients under methadone maintenance treatment

<table>
<thead>
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<th>s</th>
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<td>.79</td>
<td>.08</td>
<td>3.54</td>
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<tr>
<td>Obsessive-compulsive</td>
<td>1.05</td>
<td>.71</td>
<td>.00</td>
<td>2.90</td>
</tr>
<tr>
<td>Somatic Symptoms</td>
<td>.96</td>
<td>.66</td>
<td>.08</td>
<td>3.25</td>
</tr>
<tr>
<td>Paranoid Ideation</td>
<td>.87</td>
<td>.58</td>
<td>.00</td>
<td>2.35</td>
</tr>
<tr>
<td>Anger-Hostility</td>
<td>.77</td>
<td>.68</td>
<td>.00</td>
<td>3.33</td>
</tr>
<tr>
<td>Interpersonal Sensitivity</td>
<td>.75</td>
<td>.64</td>
<td>.00</td>
<td>3.00</td>
</tr>
<tr>
<td>Anxiety</td>
<td>.74</td>
<td>.59</td>
<td>.00</td>
<td>2.70</td>
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<tr>
<td>Psychoticism</td>
<td>.47</td>
<td>.46</td>
<td>.00</td>
<td>2.20</td>
</tr>
<tr>
<td>Phobic Anxiety</td>
<td>.31</td>
<td>.40</td>
<td>.00</td>
<td>2.57</td>
</tr>
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Interview time. In the craving set, patients who simultaneously experience a craving for heroin and for alcohol do not report a craving for cocaine. The overall outcome is that when patients are treated with low dosages of methadone, they experience heroin and alcohol cravings and undergo psychopathological symptoms.

Cravings for heroin, cocaine and alcohol are experienced during Methadone Maintenance Treatment. The craving for heroin is strongly related to the craving for alcohol, to low dosages of methadone and to the presence of psychopathological symptoms.

Table 2. Relationship between clinical aspects and craving for heroin, cocaine and alcohol in 84 heroin-addicted patients under methadone maintenance treatment. Canonical correlation analysis

<table>
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<td>Clinical aspects</td>
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<td>Positive symptom distress</td>
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</tr>
<tr>
<td>RSDA total score</td>
<td>.20</td>
</tr>
<tr>
<td>Methadone dosage</td>
<td>-.56</td>
</tr>
<tr>
<td>Craving for</td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>.93</td>
</tr>
<tr>
<td>Cocaine</td>
<td>-.15</td>
</tr>
<tr>
<td>Alcohol</td>
<td>.49</td>
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</table>

Statistics: Wilk's lambda = .79 p=.03
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Psychopathological symptoms have often been observed during the treatment of heroin addiction, and have been interpreted in different ways [8]. Earlier, we demonstrated that patients with a high number of psychopathological symptoms at the start of treatment need more methadone as a stabilization dosage during a methadone maintenance treatment [4]. In this study, when psychopathology is at low, or very low, level, cravings for heroin and alcohol tend to be absent. On the other hand, craving for cocaine appears, regardless of psychopathology. So, in patients under methadone treatment, cocaine craving may be unrelated both to methadone and to psychopathology.

One hypothesis for the observed cravings for heroin and alcohol should be methadone undermedication. In fact (1), the craving for these two substances is inversely related to the amount of methadone taken; (2) less than 20% of the patients receive a dose of methadone greater than 60 mg/daily, which is considered the minimum effective dose [1; 2; 7; 15-17].

Moreover, the main trend followed by the Italian Public Services for Drug Addiction (SERTs) is to treat subjects with 40-60 mg of methadone as a standard dose. These dosages are often not sufficient to negativize the urine sample of the patients [1; 2; 7; 15-17]; we can hypothesize that at these dosages craving is not under control.

Besides, such patients are likely to try to satisfy their craving for opiates by taking any substance capable of influencing the dopaminergic system in some way. They will thus manage to calm their hunger for heroin by alcohol or other substances when insufficient doses of methadone are used [11].

Doses of methadone in excess of 100 mg/die have been indicated as necessary to prevent illicit opiate use, and to stabilize psychiatric symptoms and diminish the abuse of alcohol and benzodiazepines [13]. The presence of craving for heroin, cocaine and alcohol during a methadone maintenance therapy could simply indicate that the treatment is not powerful enough. These conclusions are based on the following results:
1. A craving for heroin develops alongside a craving for alcohol, whereas a craving for cocaine follows a separate path.
2. Craving does not depend on addiction history.
3. A craving for heroin and alcohol correlates with low doses of administered methadone.

The idea that subjects who report persistent craving are undertreated with methadone and need alcohol as a substitute for opiates is supported by the presence of psychopathology correlated with low amounts of methadone. We have noted that psychopathological symptoms and psychiatric comorbidity are sensitive to methadone [4; 10; 12].

References

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Methadone maintenance is intended to be part of a long-term therapeutic plan of variable length, which allows opioid-dependent persons to lead a normal and productive life. Methadone is a synthetic opioid with peculiar kinetics, which accounts for its merits as a means of therapeutic intervention on opiate addiction. After oral administration, it is wholly absorbed through the enteric (intestinal) wall, and is not subject to a first pass metabolism in the liver; as a result, it can be up to 98% bioavailable. The peak level in the plasma is reached as late as 2–4 hours after intake - that is, quite slowly. Its subjective effect is perceived as a feeling of well-being beginning 20–30 minutes after administration and lasting for as much as eight hours. The intensity of the perceived effects depends on the subject’s baseline condition: if opiate withdrawal has begun by the time of administration, the subjective effect will be described as intense relief; otherwise, in a condition of chronic administration, the effects may only be perceived by subjects who are explicitly asked to check for their onset. After the first administration, methadone’s plasma half-life is biphasic, showing a quite rapid early phase (lasting about 14 hrs.) during which methadone spreads into the body tissues, followed by a second, prolonged phase, possibly lasting over 50 hrs., during which the level of methadone in the blood gradually decreases. After a two-week period of administration, the raceme mixture’s half-life is about 24 hrs.. In reality, methadone has two stereo-isomeric variants, D and L; L only possesses an intrinsic activity on µ-opioid receptors. The L isomer, has a steady state half-life as long as 36 hrs.. The raceme lasts for a shorter time, probably due to isomerism-dependent changes in metabolic rapidity. Methadone’s absorption and bioavailability follow a linear pattern, which means they do not respond to any dose-related variation. This is why methadone’s effect is always predictable and only depends on the subject’s tolerance threshold. Methadone is metabolised by the liver enzymatic system known as cytochrome P450, subtype 3A4 (CYP3A4). Resulting metabolites do not possess any pharmacological activity. After the first few weeks of administration, methadone mildly enhances its own metabolism, which explains why kinetic balance is
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only achieved after at least 15 days, if dosages are left unchanged. Due to its long plasma half-life, a single administration of methadone is effective in preventing the onset of withdrawal for 24 hrs. in most subjects. A sharp difference separates heroin and methadone in terms of pharmacokinetics, whereas the pharmacodynamics of the two compounds are essentially similar. Unlike methadone, and like morphine, heroin is completely absorbed after oral administration, but undergoes a major first-pass effect through the liver. Heroin is rapidly de-acetylated to monoacetyl-morphine and then morphine, by a variety of esterases, so that its plasmatic half-life after intravenous administration lasts no longer than 10 minutes. It cannot be excluded that its initial effect is partly due to its interaction with other specific opioid receptors. The effect produced by a single dose of either morphine or heroin lasts as long as 3 to 6 hrs. (1.5 to 3 hrs. is the plasma half-life of morphine). After intravenous administration, heroin elicits a ‘rush’, coinciding with a higher, fast-dwindling plasma peak. A phase of acute intoxication follows, which may vary in length according to the ratio between the subject’s tolerance threshold and the dose administered. Afterwards, a period of subjective well-being or a neutral condition is experienced, lasting 2-3 hrs. It may be that, when people administer heroin to themselves frequently and at a stable dose, the eventual phase starts immediately after the rush, with no intoxication interlude. For habitual users, withdrawal can be expected later; its intensity, as with somatic symptoms, depends on the tolerance level reached by subjects. On the other hand, withdrawal-related mood alterations are still excruciating for any addict. The continuous intravenous administration of heroin, when able to keep plasma levels in a range corresponding to normality/well-being, is effective in preventing withdrawal from setting in. The same result can be achieved by a µ-opioid agonist characterized by a long-lasting, stable effect, which is what methadone appears to be. Moreover, the differences in the kinetics of methadone and heroin have further implications. The intravenous administration of heroin and the subsequent peaking blood levels, make it unlikely that maximum tolerance levels are ever reached, so that heroin addicts, even if they inject themselves heavily and frequently, always run a risk of overdosing events. Apart from that, the administration of gradually increasing dosages of methadone makes it possible to achieve a maximum tolerance condition, where methadone blood receptors saturate still available receptors. Such a dose is referred to as “blocking dose”; it shields the addict from the toxic effect of the heaviest heroin (or other opiate) dose as far as possible. The shielding effect is equally strong in situations of opiate-induced euphoria and breath inhibition. In other words, the administration of methadone at blocking dosages separates heroin from its expected and sought-after pleasurable effect in the experience of the addict; this may lead to the gradual dwindling of self-administering behaviour, along with the disappearance of desired gratification. Maintaining patients on methadone doses at blocking values is often a crucial step towards stopping a severe drug-taking behaviour. Administering heroin does not change the individual’s sensitivity to narcotic drugs, which can be shielded, as explained above, by the use of methadone within a range of 60-100 mg/day. With heroin, the craving (urgent desire) for narcotics is
continuous and it recurrently soars; by using methadone, it is usually suppressed. Withdrawal from heroin usually sets in within 3-6 hrs. after administration; it is intense and can be controlled by methadone. Withdrawal from methadone begins 24 hrs. after the latest administration, reaches a lower level of severity and lasts longer. When appropriate - that is, when methadone maintenance has been accomplished - slow, steady methadone tapering can be performed, under medical supervision and in a safe context, in such a way as to avoid the emergence of withdrawal symptoms. The risk of HIV or hepatitis infection is higher when heroin is self-administered by injection, using unsafe methods and without hygienic prophylaxis. Conversely, it appears to be lower for methadone-maintained patients. The immune system and endocrine functions of HIV-negative heroin addicts are usually abnormal, but tend to normalize as methadone treatment proceeds. HIV-positive patients run the risk of starting a rapid evolution towards AIDS, as long as they keep on using heroin, whereas the disease-free interval appears to be longer for methadone-maintained patients. As regards the hypothalamic-hypophysis-surrenal axis, heroin addicts continue to swing between a state of overstimulation, during withdrawal, and one of suppression, during peak heroin stimulation. Sexual functioning and gratification are also discontinuous in heroin addicts of both sexes, and menstrual periods are often disturbed. All such abnormalities tend to become slighter as methadone maintenance develops. Ongoing heroin use during pregnancy implies severe risks both for the mother and the foetus. Peak-related hypoxia and withdrawal-related uterine spasms may cause damage to the placenta, especially at its roots within the endometrial layer, and may thus hamper, directly or indirectly, the development of the embryo and, later, of the foetus. On the other hand, methadone-maintained pregnant patients can benefit from medical, social and nursing interventions, and so be able to face any accident or critical decision. Moreover, the foetus does not undergo any stress; nor does it show growth abnormalities or retardation. The phenomenon of neonatal withdrawal, though expected, is predictable in its intensity, depending on how much methadone the mother is taking, and it is, anyway, easy to buffer pharmacologically. During heroin use, mood instability is the rule, affective and intellectual functioning are both severely disturbed, emotions and pain perception are enhanced, reactions are reckless, and interpersonal relationships and social adaptation are disrupted too. During methadone treatment, all affective and relational abnormalities tend to improve. This is especially true when counselling or psychotherapy facilities, and possibly Therapeutic Community in-treatments, are available, together with pharmacological interventions, in a way that does not interfere with the principles of methadone maintenance. Under the impact of heroin-induced dysphoria, educational activities and the achievement of working skills are quite likely to fail, and it may be difficult, in any case, for patients to keep a currently held job. On the other hand, when methadone maintenance is in place, educational and working areas are strongly favoured, so that any job may be done efficiently, including those involving the driving or supervision of machines. Heroin addicts with additional psychiatric diseases are awkward to treat, very often engage in polyabuse, and commit crimes. High
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rates of criminal behaviour, drug-related deaths and disease-spreading must therefore be expected. Within a well-managed methadone programme, psychiatric comorbidity can be treated as well, polyabuse may be eliminated, and illegal acts can be expected to dwindle, often, to the point of extinction. Social safety is thus empowered, crime and death rates are sharply reduced and society’s quality of life improves along with the treated patient’s. To sum up, the therapeutic use of methadone does not produce or perpetuate any addictive condition; it is a cure for opiate addiction, meaning by “cure” a clinical check, of just the same kind as is observed when an anti-hypertensive drug is administered to a patient suffering from hypertension, or thyroxine is given to hypothyroid patients. So far no therapeutic approaches have been developed that are able to eradicate a chronic pathology, that is, cure it with no risk of relapse in treatment-free conditions. Medicines are now available, that are useful in alleviating pathologies previously regarded as untreatable. No medicine is equally effective on all patients who share the same diagnosis, and the best outcome such medicines can achieve is that of permitting the clinical control of symptoms, interference with the evolution of a pathological process, and the prevention of possible somatic complications. Methadone does exactly that: while it buffers withdrawal symptoms, it cuts the risk of infection and impulsive behaviours, in concomitance with which patients are likely to engage in law-breaking. In addition, it permits a condition of individual well-being, in terms of somatic comfort and mood stability, that is capable of restoring the individual’s productive potential, when that has previously been hampered by longlasting heroin use. Indeed, the therapeutic effect of methadone does not fade as a result of tolerance through time; nor has any social impairment been observed to develop. The dangers to society mentioned above, together with the core addictive pathology, are just those accounted for by the DSM-IV in defining an addictive disease. In order to achieve the objectives just indicated, a methadone programme should be worked out on the basis of a schedule that defines the criteria for eligibility, achievable objectives and methodology through different phases that act as milestones along the therapeutic path to recovery.

Patient enrolment

The subjects who are supposed to benefit most from methadone maintenance identify with those heroin abusers who find it awkward or almost impossible, to stop using heroin in the short term. Such individuals are likely to have repeatedly tried to get off the substance, but relapsed into using it in the short term, despite intervening periods of stable abstinence of variable length. Such attempts demonstrate the intention to stop using heroin, and may have been made either on the patient’s own initiative or under medical supervision; they may rely on opiate agonist tapering or on directly decreasing dosages of heroin itself, within natural environments or protected ones, such as hospitals or therapeutic communities. Methadone maintenance does not necessarily have to appeal to addicts with a long personal history of attachment to heroin, who are unable to handle their lives on their own. As to any kind of specific intervention, the earlier the phase of the targeted disease at the moment intervention starts, the greater its expected
effectiveness. The literature has not provided a great deal of evidence in support of this position, since cultural resistance to the spread of methadone treatment has strengthened the view that maintenance should be resorted to only in the case of patients who have “reached the bottom”. Concern over the AIDS epidemic and acknowledgements about viral hepatites have by now discredited that slogan. The impact of early-intervention measures on infective pathologies has been so strong that no intervention-delays policy appears to make sense any longer. Heroin addiction, as a disease, spontaneously tends to follow a chronic, relapsing course. A functional imbalance is set up, where the early withdrawal symptomatology - that is, the cluster of somatic vegetative alterations triggered by the absence of habitually consumed opiates - does not play a crucial role. In fact, other symptoms are also comprised within the opiate withdrawal phenomenon; these are masked in the early phase by overwhelming somatic alterations, but are bound to persist, and may recurrently and unpredictably intensify, so impairing most subjects’ ability to maintain abstinence, and pushing them towards a relapse into heroin use. These other symptoms comprise dysphoric mood, a heightened sensitivity to painful stimuli, and the incapacity to carry out tasks, even quite simple ones. These are subtle elements, but they can be intense enough to elicit relapses, and may escape recognition by clinicians; patients themselves are usually hardly aware of them. On grounds of diagnosis, a case of addiction is considered severe when repeated relapse into abuse of the same substance (heroin, in our case) is documented, despite an evident intention to stop using it, as demonstrated by repeated failures. Though any clinical treatment should meet the individual’s specific needs, most severely addicted patients, who happen to be the vast majority of heroin addicts, can best achieve recovery by a long-term methadone maintenance programme. Methadone maintenance guarantees a better outcome than no treatment at all, even when not associated with psychosocial support initiatives. Methadone is more effective in treating most heroin addicts than other therapeutic alternatives. More precisely, patients should be offered a well-structured programme, and be well informed about its mechanisms so as to best benefit from its advantages. The patient’s informed consent will actually correspond to a higher level of compliance as long as patients are aware of the aims and limitations of the approach chosen.

Objectives

A methadone maintenance treatment programme must pursue three fundamental objectives from the onset:
1. To free patients from their condition of suffering (resulting from a history of repeated failures, along with the consequent fear of being unable to achieve stable well-being at any time);
2. To block the effects of what may be self-administered heroin by the induction of a condition of tolerance to methadone (up to a full blocking dose, when necessary), which implies cross-tolerance to heroin. This second objective is crucial in achieving the third:
3. To suppress, rather than reduce, the craving for heroin, which may endure despite the
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achievement of a stable opiate blockade.

If any craving, even if a minor one, is left, patients may resort to alcohol or psychotropics (depressants), as a surrogate for unavailable heroin, or for heroin made ineffective by a methadone-mediated opioid-blockade. Clinical experience has proved that these three objectives can easily be accomplished for most patients, so leading to the eradication of addictive practices and a resumption of patients’ previous lives. An individual’s potential and skills, which were progressively impaired as addiction developed, can be restored, partly as a direct result of addiction control, and partly as the outcome of rehabilitative intervention. Social and psychological remedies can be resorted to in order to optimize the results achieved by pharmacotherapy; they are especially useful for subjects who are afflicted with serious socio-environmental impairment. Behavioural changes witnessed in methadone-treated patients after the first few weeks are essentially due to the general, stable well-being made accessible by methadone itself - a state superseding the previous condition of affective and somatic instability. When tolerance to the administered methadone dosage has been achieved (so that there is no sign of narcosis, apart from a control of withdrawal that leads into a feeling of well-being), and when the patients show they have firmly broken away from addictive issues and environments, stabilization has been achieved.

Methodology

Early phase: Relief from global suffering

When patients ask for treatment, they are usually in a phase in which the only effect of daily heroin is that it buffers withdrawal, and surrogates such as sedatives and alcohol may as well be resorted to in order to soothe withdrawal-related discomfort. Addicts have learned that heroin is the best way to interrupt incipient withdrawal, and they have developed a stereotypical pattern of appetitive behaviour whose aim is that of finding the substance. As soon as withdrawal begins to escalate, when heroin is available in the environment, the addict’s behaviour becomes a craving-led one, which leaves no room for self-control, and it intensifies until the sought-after substance is found. At later phases of the disease, or when independent psychopathology is present, craving may lose its primary adaptive function and may no longer support inappropriate behaviour, such as aspecific acting-outs. One of the reasons for a heroin addict has for applying for methadone treatment may simply be to achieve relief, even if transient, from a state of discomfort. When the therapeutic programme is managed competently and with respect for patients, they will have the chance to realize that, as long as they stay in treatment, they will have no need to resort to street opiates (i.e. heroin) as a means to buffer discomfort. On the first day of treatment, dosages of methadone of 20 to 30 mg should be administered at first, possibly followed by supplementary charges if withdrawal does not diminish within 2-3 hrs. Additional dosages of 20-30 mg will then be administered every 3-4 hrs. (methadone blood level peaks at the 4th hr.), as long as its previous
administration, apart from not causing sedation, was not followed by a thorough resolution of withdrawal. No further dosage supplement will be administered in the absence of persistent or residual withdrawal. The total amount administered on the first day will be administered as a single dose on the following days. First-day doses higher than 30 mg may only be administered to patients, whose tolerance threshold is already known as quite high.

**Blockade of heroin effects and suppression of craving-related drug-seeking**

After 4-5 day of treatment, the methadone dosage will be gradually increased by 5-20 mg every 1-4 days, up to a value that is presumed to be enough to block the effect of injected street heroin, usually at least 60-70 mg. Patients receiving these doses continue to use heroin, but are unable to feel its effects any longer. This dilemma is crucial: on one hand heroin is ineffective, but on the other it is still sought after and craved by the subject. Thus, patients may take methadone at dosages lower than prescribed, in order to be able to feel the effect of injected heroin, or else try to increase heroin dosages to overcome the methadone blockade. As a further alternative, alcohol or psychotropics (especially benzodiazepines) may be used to elicit a narcotic effect from methadone, or psychostimulants may be resorted to. A strong risk of polyaddiction must therefore be taken into account. It should be remembered too that in normal individuals, behaviours tend to disappear if there is no reward for them. Blocking dosages of methadone suppress heroin-induced reinforcement, so the self-administration of heroin goes unrewarded and usually disappears. If it persists, or is replaced by alcohol or benzodiazepine use, the methadone dosage should be increased, and precautions should be taken to ensure that methadone is, in fact, taken at the prescribed dosages. Even when the oral dosages administered to different individuals are the same, methadone blood levels vary over a wide range. At oral dosages ranging between 80 and 120 mg/day, the definitive therapeutic objective - the cessation of heroin use - is usually achieved. A minority of patients, however, continue to consume heroin, and these require higher methadone dosages. Clinicians should always clarify whether any independent psychopathological condition is involved. A number of studies have tried to assess whether a value for methadone blood level can be defined as a marker of effectiveness for oral dosages. Effective methadone blood levels have been reported varying between 100 and 600 mg/ml. No threshold value for methadone blood levels has been identified. It is not good clinical practice to treat any individual at a single rigidly fixed standard dose. So too, it is not reasonable to fix a termination date for treatment. Putting a limit to methadone dosage or excluding some categories of addicts from treatment actually means leaving patients tied to their uncontrollable craving, which implies increasing the risks they incur of overdose, unsafe injections, polyaddiction, and HIV infection. The suppression of craving, that is, the compulsive appetitive drive, is the crucial therapeutic issue in the treatment of heroin addiction. The pharmacological properties of heroin reinforce heroin-directed search behaviours to a level of paroxysm. Once addicts find that the
effects of heroin have been blocked, their commitment to heroin is supposed to gradually fade to the point of extinction. This hypothesis, originally formulated by Wikler, provided the rationale for the use of long-lasting opiate antagonists in the treatment of heroin addiction. Antagonist treatments, however, are likely to be abandoned in the short term by most enrolled patients; in their case relapse occurs long before craving disappears. Like heroin antagonists, methadone too prevents heroin from inducing its effects; but, unlike the former, it cannot be discontinued abruptly, due to the persistence of heightened opioid tolerance. This characteristic, which is shared by all known opioid agonists, can be regarded as a drawback. On the other hand, therapeutic aims (e.g. retention in treatment) are favoured if patients know they cannot discontinue their therapy, without facing unpleasant consequences. In fact, compliance and retention rates are much higher in methadone maintenance programmes than in any other kind of approach. The retention rate is the most reliable index in assessing the effectiveness of any treatment approach to heroin addiction.

**Methadone treatment practice**

Like any other treatment, methadone maintenance should be adapted at all time, according to the ongoing clinical situation. During the first few months of therapy, patients are usually monitored daily. This is the so-called induction phase, during which the optimum methadone dose is worked out. No standard lowest effective dose has yet been determined, nor has any maximum dose ever been defined. So, it is unreasonable to increase the dose if addictive behaviours have been stably eradicated, or to raise the dose over a certain threshold if the response has been unsatisfactory. Methadone dosage should be tailored to the needs of each individual patient. Although most clinicians agree that the lowest effective dose is as high as 60 mg/day, and the average optimum value ranges between 80 and 120 mg/day, that knowledge must be read in statistical terms, which have been assessed with respect to retention in treatment, and to urinalysis results over the previous month or over a six-month interval. As a rule, the higher the standard dose used in the study, the higher the rate of responders to treatment. This correlation does not mean that all patients should be treated with high doses without allowing for any other differences. It means, rather, that it is unreasonable to put a limit either on methadone doses or on duration of treatment, as long as optimum results are being aimed at. Once stabilization dosages are reached, and the incipient reversal of addictive behaviour, as reflected in the restoration of social adaptation, is observed, psychosocial initiatives can be resorted to, as long as the maintenance phase continues. When behavioural changes are satisfactory and stable, patients can be allowed to attend the structure less often (but at least once a week). At this point, the controversial issue of take-home methadone dosages looms. It must be pointed out here that the transition from stricter to less strict supervision marks a necessary step towards recovery; there is also the psychological advantage of showing a patient who had lost control over his or her self-administration of a substance that treatment has given them a new capacity to
handle the medication. The feasibility of a take-home follow-up gives objective proof of restored self-control that has been achieved by therapeutic means, after previous authentication by a regular attendance at appointments for administration and the persistent negativity of urinalyses. The decision to allow a patient take-home rights also provides feedback to him or her arising from previous good compliance with treatment; it is the instrument of what we may call “methadone-mediated indirect behavioural conditioning”. Take-home is unsuitable for patients who have failed to display a positive therapeutic response, as it will end up working to favour unhealthy therapeutic relationships. Of course, physicians are allowed to make exceptions, when there are objective impediments to a patient’s daily attendance of the structure, as in the case of constraints arising from work or study needs, when these are important on rehabilitative grounds, or in that of more directly medical issues. However, patients should be made aware that they are not being given a privilege, but are being relied on in terms of responsibility. At first sight, it may seem too strict to require patients to attend the structure daily, but it goes against therapeutic logic to be indulgent to patients who are unable to achieve or maintain any stable balance outside that mode. Frequent contact with operators is also a source of therapeutic support, besides creating a chance for patients to benefit from counselling or psycho-educational facilities. With help from psychosocial operators, patients may start new jobs, or resume activities they had given up. Also, when take-home is allowed, patients should take their daily dose face to face with the operator on the day of weekly dose delivery, so as to prove they have maintained their tolerance level. When patients are suspected of having let their tolerance fall, they should be observed for a couple of hours after the oral administration of their supposed dose. If sedation develops, it means the patient has not been taking the supposed take-home dose regularly. In these circumstances, the patient must be confronted and asked for an explanation. It is quite likely that patients who have been put on to a take-home mode, because they had previously displayed stable abstinence, will reduce their daily dose, or split it over the 24-hour cycle, without saying anything about this to their physicians, to avoid facing disapproval. In any case, the clinical situation is the parameter that should determine decisions about the take-home option. Some patients may be allowed to attend less often than daily after the first few months, while for others this may take six months or longer, according to the single patient’s clinical situation (stable continuous administration, control of substance use and psychopathological balance). It is not strictly necessary to pass from daily administration to an alternate-day mode and then a twice-a-week mode, before allowing weekly take-home: some patients may be allowed to proceed directly to a weekly take-home mode. Even if methadone can be prescribed by GPs and provided by chemists, that solution would make it awkward for operators to check whether the patient actually takes the prescribed dose, if any, and does not seem to meet the requirements of patient monitoring. Patients may be directly provided with methadone by their GPs only in a condition of stable psychopathological balance, when they have no need for any psychosocial intervention, so that they can be trusted to manage the administration of their therapy. Nevertheless, GPs play an
important role in the programme, either when directly managing the therapy, or when in charge of long-stabilized patients. It must also be pointed out that the provision of take-home methadone by chemists directly to patients implies a lack of privacy.

Subpopulations of heroin addicts who should be given priority for enrolment in methadone programmes

Some categories of heroin addicts should be given priority in entering methadone treatments:

a) Pregnant addicts. Heroin addiction is unlikely to be compatible with healthy pregnancy. Methadone should be started without delay, and dosages should be reached that grant the mother a state of global well-being. Foetuses are just as much at risk as mothers by withdrawal, especially due to possible placenta disruption, and intoxication. It follows that no attempt to taper methadone, let alone interrupt its administration, should be performed during the last two months of pregnancy, when the placenta is losing its initial elasticity.

b) Parents of minors. Parenthood does benefit from the behavioural stabilization achievable with methadone, partly due to the improvement of family relationships.

c) HIV-positive/AIDS-affected heroin addicts or addicts with hepatitis. There is no incompatibility between methadone on one hand and antiviral therapies or therapy for the non-viral infective diseases of AIDS patients on the other. In addition, compliance with anti-infective therapies is far higher among methadone-maintained subjects. Special attention should be paid to the adjustment of methadone doses for patients who are also taking anti-retroviral drugs, due to the possibility of metabolic induction (e.g. nevirapine, efavirenz and lopinavir/ritonavir).

d) Jailed addicts. Adequate methadone treatment reduces the occurrence of self-injurious or violence acts among jailed addicts. Methadone tapering must not be performed too fast or earlier than reasonable, and must be assessed according to the patients’ symptomatology. Benzodiazepines should be avoided for as long as possible. If jailing is not expected to last long, it is reasonable to start a methadone maintenance programme, or at least maintain the dose previously administered. In this way, the risk of overdose after discharge from jail is minimized.

e) Heroin addicts with dual diagnosis. Heroin addicts suffering from additional psychiatric syndromes usually need higher dosages, possibly combined with other psychotropics, and take longer to reach stabilization. For those who were successfully stabilized, the outcome, in terms of retention rate and abuse of non-prescribed drugs, is equivalent, if not superior, to that of uncomplicated heroin addicts. Methadone treatment also favours the patient’s compliance with taking medications that target the associated psychopathology, and it improves their effectiveness.
The issue of programme monitoring

Within a well-conducted methadone programme, urinalyses should not be followed by sanctions, but should always be intended as a means to tailor treatment to each single patient’s needs. Moreover, urinary controls are helpful in deciding dosage changes. The response to pharmacotherapy is usually mirrored by:

1. the absence of morphine at urinalysis;
2. the absence of other abused substances;
3. quiet behaviour while physically present in the structure;
4. compliance with the schedule of administration and the rules of the programme;
5. positive changes in behaviour, detachment from the street environment, improvement of social and family contexts and involvement in new activities.

It is crucial to check that tolerance to opiates is maintained and stable. Patients who are stably maintained at a high tolerance level, like that induced by methadone stabilization, have no chance to feel the effects of heroin, at least at standard market dosages. As a result, possibly self-administered heroin cannot produce its toxic effect upon the brain. Other recommendations are that urinalysis checks be performed at random, and that checking samples should be correctly collected, so as to allow access to reliable information about the patient’s drug-taking behaviour. Other aspects should, however, also be taken into account, such as how a patient behaves while waiting for his or her turn at an administrative office or other facility, what relatives report about familial adaptation, information about school and work activities, and any other clues, circumstances or contexts which may help to spotlight behavioural changes. Whenever possible, physicians may directly ask patients questions about their knowledge of heroin abuse, especially when patients themselves report their personal experiences. In these circumstances, the physician in charge can directly weighup his decision while being acknowledged by the patient, so that adjustment, whether pharmacological or psychosocial, is granted immediately.

Medication tapering

Methadone tapering is the objective sought by everyone – patients, families and operators. Methadone maintenance actually aims to achieve tapering, but on time-scales and using modes which can be perceived as feasible and reasonable. Patients usually express their request for the completion of treatment after the first few months. It should be borne in mind that the reported condition of well-being, which supports the wish to terminate treatment, though genuine, is unlikely to correspond to an actual well-considered chance to remain abstinent in a drug-free condition. Follow-up studies on patients who had had their methadone tapered in the short term after stabilization have proved that treatment duration is crucial to making the treatment itself successful. Only after detachment from addictive behaviour has consolidated through time should any tapering be taken into consideration, let alone performed. A hypothesis of tapering
methadone should always take into account the clinical evaluation of the patient’s probability to maintaining on-drug achieved results in a drug-free condition. Skilled operators should favour the acceptance by patients of the time-scales necessary for a successful methadone programme, and, as a trend, try to retain the patients in treatment for prolonged periods. “The longer the patient attends the programme, the sounder and the more substantial are the results that can be achieved at the end of the treatment”. The tapering phase, to follow a long-term stabilization, is itself meant to last a long time, and tapering should not proceed, or be reversed, if the patient shows physical symptoms (e.g. somatization) or psychopathological ones. Tapering happens to be more awkward, and must be expected to last longer, in patients who have gone through repeated attempts at detoxification, rather than only one. Hence, a drug-free patient who underwent detoxification at some point in the past, and asks to be started again on methadone, should immediately be admitted to treatment.

Conclusions

At present, methadone treatment is regarded as the most effective and most popular treatment approach to heroin addiction. Administering an adequate dose of methadone may drastically improve the quality of life of subjects, who, due to the nature of their disease, have usually reached a high degree of somatic, psychic and social impairment. Methadone programmes must comprise a careful procedure involving increasing doses in order to achieve stabilization, which should then be maintained with a view to a long-lasting, slow tapering. In the meantime, other kinds of medical intervention, counselling and rehabilitative facilities should be provided.

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V Methadone and other substitutive Therapies

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Preamble

Throughout the 20th century, the right to health has become a reality and, in the course of the last decades, mental disorders and addictive behaviours have been increasingly considered as illnesses, gradually losing the social stigmas attached to them in the past. Thanks to these changes, psychiatric care services have progressively been integrated within health systems in general, and the universal right to health as well as the accessibility of care services have extended throughout European countries.

Even so, specifically in the case of doctors and in general health professionals, there are a series of factors that determine, paradoxically, that they are one of the most unattended populations, in terms of health.

In recent years, it has been discovered that health professionals in general, and especially doctors, do not act properly, in the majority of cases, as patients when they are ill. Moreover, it is important to keep in mind that mental and addictive illnesses still have a strong social stigma attached to them, even within the health collective, since there is a culture that prevents seeking help lest colleagues perceive the illness as weakness. Thus, many sick leaves, impairments and debarments are consequences of disorders for which there are effective treatments.

In the case of health professionals, and especially doctors that suffer from these types of problem, fear of detection by co-workers or by patients plays an important dissuasive role when it comes to seeking help and, therefore, to accessing the health system. In these cases, a strong tendency to experience these illnesses with a feeling of guilt and equally strong tendency to hide the illnesses, only retard the seeking of help and worsen the prognostic. This is not only an individual issue but also a general health issue.

In order to provide health professionals with access to health services, especially to mental health services, it is necessary that these programmes in all countries be based
Heroin Addiction and Related Clinical Problems

on the following:

Principles

1. Health systems should guarantee health professionals the same access to health facilities that the general population has.
2. Access to confidential treatment is considered important for all patients. Special arrangements would be required in order to assure this confidentiality for doctors and other health professionals when accessing treatment, especially when their condition involves mental or addictive disorders, which are still stigmatised.
3. It is necessary to create sufficient programmes and care services, so that sick professionals receive appropriate treatment in suitable conditions.
4. The relevant regulatory and professional bodies should have a supportive role in the organization, management and quality control of the care programmes created. Funding must be provided by the responsible institutions.
5. The objective of these programmes is not only to enhance the well-being of affected physicians, but also to maintain good health care delivery and safeguard patients.
6. These programmes should also have a preventive goal. They should attempt to provide all health professionals with the most favourable conditions, so that problems are detected and handled as precociously and effectively as possible.
7. Research in this field should be promoted, particularly on the effects of working conditions and other risk factors in mental health.
8. Ways of promoting health, including mental health, at an individual and an organizational level, should be encouraged.

Conclusions of the 1st European Conference PAIMM 2001

1. When health professionals, especially doctors, become ill, they do not go to the Health System like the rest of the population. Various studies have shown that in these cases, neither the doctor as patient nor the doctor as therapist, act in the same way as recommended to the rest of the population, which results in an inappropriate doctor-patient relationship being established.
   If, in addition, the health problem happens to be a mental disorder and/or an addiction, these sick people, almost systematically, conceal the problem, do not seek help and try to go on working regardless. This behaviour may well be due to the fact that these illnesses are still socially stigmatized, resulting in these sick professionals being afraid of being identified, thus losing their professional prestige vis-à-vis their patients, as well as the respect of their colleagues, and even their job.
   This situation dramatically affects their family and professional environment, causes them to be negligent and to fall into malpractice and can easily jeopardize the health of the patients attended by these professionals. All this can result in more serious complaints, malpractice suits and work-place conflicts. This then becomes
a public health problem with professional and social repercussions which need to be minimized or, if possible, prevented. These sick physicians have difficulty in exercising their rights to obtain health care as they do not seek appropriate treatment in the National Health System. They are then, paradoxically, among the least adequately attended populations.

2. In view of this situation, it is clearly vital to create professional control procedures which ensure that these sick doctors receive the necessary aid and support and present no risk for their patients. And it is essential, too, to guarantee total respect for their right to confidentiality.

Some years ago, in the USA, Canada and some states in Australia, some special programmes and mechanisms were created in order to detect these cases and try to give them the right health care in confidential conditions.

In Europe, there are some countries, such as the United Kingdom and Sweden, which have recommendations from their Medical Councils about how to treat these sick physicians. However, there are no specific services which guarantee that the treatment is confidential, or programmes that monitor and control medical practice.

There are other countries, such as Germany, which have private hospitals where it is known that treatment is given for these cases, but they are private and without any participation from the Medical Councils. Finally, some other countries, such as France, Italy and Austria, do not fit any of these descriptions and it is not known what happens there.

3. In Spain, PAIMM (Integral Care Programme for Sick Physicians) and RETORN (Care Programme for Nurses’ Health), are preventive and care programmes, which have two essential aims: on one hand, to attend health professionals with mental problems and/or addictive behaviours, by means of specific and duly specialized services under conditions of strict confidentiality; and on the other hand, to assure the citizens, as far as possible, that health professionals, above all physicians, are able to exercise a good practice in optimum conditions. The Government of Generalitat of Catalonia and the regional Medical Council and Nursing Body take part in PAIMM and RETORN, these latter professional bodies are in charge of the management of the programmes in order to best ensure good professional practices.

PAIMM was created in Catalonia three years ago, and is gradually spreading to other professional bodies and health authorities in other autonomous regions of Spain. Progress, however, is slow, partly because of inadequate support from the corresponding health authorities.

It must be emphasized that outpatient treatment, which it is all that the majority of sick health professionals need, should be readily accessible and should not involve travelling over long distances. Inpatient services have to be centralized in one unit which covers a large territory. To be fully confidential and specialized, they need to have a size which justifies their cost and, for this reason, if a doctor has to be hospitalized for mental or addiction problem, the PAIMM facility in Barcelona is recommended. The professionals of this unit work closely with the professionals in all the regions to ensure that the patient recovers fully and can carry on his or her
professional rehabilitation. Some regional medical councils, such as Cordova, Cadis, the Balearic Isles and Navarre, thanks to their effort and determination are beginning to set up PAIMMs in their territories. In this way, they will be able to organize Council Procedures and set up specialized outpatient services under conditions of confidentiality.

4. Public health administrations are responsible for the health of the population in general, and for that of health professionals, in particular. The national health service, and above all, the autonomous authorities in Spain should participate in programmes such as PAIMM and RETORN. What is at stake is a question of public health, and the health of professionals in the system. The coming transfers of health services to the autonomous regions of Spain should foment effective collaboration in developing these programmes.

Public health administrations, especially the autonomous authorities, should finance treatment for these sick professionals, so that they can make use of their right of access to treatment. The professionals bodies should also participate in the financing and should take responsibility for regulating good professional practice and ensuring access to the appropriate treatment.

The Generalitat of Catalonia has participate in the incubation, development and financing of the PAIMM and RETORN programmes in Catalonia, being the first autonomous government in Spain to do so. Nowadays, there are other regional governments, e.g. the Balearic Isles and Navarre, which have decided to give economic support to their medical councils in order to achieve the same objectives. Other regional authorities, such as that of Madrid, have decided to await the coming transfers of health services, to finance to their medical council, and thus set up their regional programme.

5. By unanimity, it was concluded that, following the model initiated in Catalonia, similar programmes should be put in place in all Spain and Europe because it assures the two essential purposes of the programme.

The OMC, (Organization of Medical Councils of Spain), will make every effort to ensure that the provincial and regional medical councils lead the programme development in Spain, to guarantee that the incipient projects correspond to their original purposes.

The OMC will make the PAIMM project known to the Medical Associations and Bodies of Europe and will work towards the setting up of similar projects across the European Union.

Barcelona, 9th November 2002

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RENAISSANCE HOTEL, WASHINGTON, DC, USA

CALL FOR PRESENTATION

VI EUROPAI FORUM
DURING AATOD CONFERENCE

SUPPORTED BY

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AMERICAN ASSOCIATION FOR THE TREATMENT OF OPIOID DEPENDENCE

IN COLLABORATION WITH HEROIN ADDICTION AND RELATED CLINICAL PROBLEMS - PISA, ITALY, EU
Galicia document on problems related to addictive disorders in Europe

I European Symposium on Clinical Problems of Addictive Disorders
Santiago de Compostela, Spain, 2002

There is an increase in prevalence of substance abuse and dependence disorders in all European countries, and Addictive Disorders represent a heavy burden on the affected individuals, their families and on society across Europe. However, research is sparse and there is insufficient dialogue between different professional groups working in related areas. Major advances are occurring in our understanding in some of the areas of research but they are not integrated into the wider examination of addictive behaviours and evidence from research is not effectively translated into clinical practice and political decisions.

Strengthened research of Addictive Disorders in the European context will lead to better understanding of the underlying problems, the development of more effective evidence-based treatments, and a model for improved integration of diverse perspectives influencing individual, developmental and wider societal and cultural influences on the emergence of drug problems and associated harms in Europe. This broader scope would cover, for example, new molecular genetic work, neurobiological and psychological investigations, comorbid psychopathology, and the interaction of these individual factors with socio-cultural influences including varying legal contexts.

There are already different institutions, organisations and scientific societies across Europe who are addressing partial aspects of this area. Our intention is not to replace or duplicate their work. Rather, it is our aim to add a comprehensive European dimension, bearing in mind also the enlargement of the EU, and to be a forum for fostering communication and cross-fertilisation between basic scientist and clinicians; epidemiology and public health, to help policy- and decision-makers. This would allow clarifying together differences and similarities across drugs, alcohol and tobacco; similarities and differences across European countries to facilitate cross-national research and to make possible the elaboration of effective and practical treatment protocols and guides.

We conclude that there is a need for a European College on Addiction Sciences to
establish a forum that facilitates and potentiates dialogue with other similar organisations inside and outside Europe. The foundation of a European multidisciplinary umbrella organisation with representation from well-established professional bodies and their specialist organs dealing with addictions as well as addictions scientific societies is needed to lobby for resources and exchange information that would maximise the efforts to tackle the problem. The proposed European College of Addictions Sciences would fulfil such a function without replicating the work of existing structures and organisations. It can help establish a proper framework to foster multi-centre research.

We invite all concerned scientists, working in the different areas related to Addictive Disorders to follow this discussion at the First European Congress on Addictive Disorders, 27th-29th March 2003 in Alicante (Spain).

The College’s aims would include:

A. Improving contribution of research:

- To provide a forum that would facilitate the communication of new advances in basic, naturalistic, clinical, and epidemiological research.
- To promote an evidence-based approach to interventions by:
  - Identifying and summarizing existing evidence.
  - Disseminating the evidence.
  - Facilitating the transfer of evidence into practice.
  - Facilitating multicentre experimental research.
- To promote research into cost effectiveness of interventions.
- To encourage research into the identification of factors which may affect effectiveness of interventions and thus help to improve quality of interventions.
- To establish a network of experts that could explore fund-raising opportunities across Europe to support common initiatives and multidisciplinary cross-national research.

B. Improvement of treatment services for addictive disorders in Europe:

- Whether in primary or specialised care, the scientific evidence base for the treatment approaches used is not always sufficient. New channels to dissemination of research findings into policy, services planning and practice will be promoted.
- More research will be promoted to provide options for services, in order to meet the needs of an increasingly heterogeneous population of substance misusers with psychiatric and somatic illnesses.
- To encourage research to provide treatment services and programmes with adequate evaluation systems, of processes and results, that would allow determining the effectiveness and efficacy of the implemented interventions.
- Ethical issues to be addressed include: patients´ choices; the accessibility and availability of suitably diversified services; aspects of mandatory and coercive treatments; the need to appreciate ethical issues in future research.

All the participants who met in Santiago de Compostela for the I European
Symposium on Clinic Problems of Addictive Disorders wish to express their gratitude to the Plan de Galicia sobre Drogas of the Conselleria de Sanidad of the Galician Government, to the Plan Nacional sobre Drogas of the Ministerio de Interior of the Spanish Government, and to the Sociedad Española de Toxicomanías (Spanish Society on Drug Addiction) for supporting and encouraging this discussion.

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5th Conference of the European Opiate Addiction
Treatment Association.
Maintenance Therapy

Evidence-based Practice & Integrated Treatment Approaches
Oslo, Norway, May 14th to 16th, 2002

The conference, held at the Rica Sjølyst congress centre in the fine city of Oslo, was attended by around 500 international delegates. All countries of Europe were represented and, as usual, we were delighted to welcome colleagues from other parts of the world including USA, Australia, New Zealand and Iran.

The conference was divided into three sections:
* Maintenance treatment in Europe
* Evidence-based practice
* Integrated treatment approaches

Following an introductory lecture on the neurobiological basis for opiate addiction from Mary Jane Kreek of Rockefeller University, USA the first afternoon was devoted to the examination of different national systems in Europe with papers from Scandinavia, The Netherlands, France and central Europe followed by an overview of the differences in European systems presented by Michael Farrell of the Addiction Research Centre, UK.

The second day featured the principles and practice of evidence based maintenance treatment and included recent study results of trials with methadone, buprenorphine, heroin, morphine sulphate, codeine and naltrexone.

Day three considered integrated treatment approaches examining the evidence for the use of psychosocial methods and ways of integrating maintenance and different therapeutic programs. Papers included: “Twelve steps programme and methadone treatment”, “Low threshold MMT-evidence for goal attainment” and “Evidence for superior efficacy for an integrated high-threshold programme”.

In total 91 papers were presented by delegates from 25 different countries.

From www.europad.org
The EUROPAD Awards 2002
“Chimera Award”

“Dedicated to all those who dream of a better world for drug addicts”

Chimera was a monster in the Greek mythology: it had a lion head, a goat body and a dragon tail: being a monster, it can well represent drug addiction as a monster that must be defeated.

But, in the poetical language, the term “Chimera” means unrealizable dreams, impossible imaginations: and in this sense, it still well represents the attempt made by doctors of realizing their dream of helping drug addicts.

In both senses, therefore, we can say that some kind of physicians, those who try to treat drug addiction, run after “chimeras”, both to kill the monster, and to realize their dream of helping drug addicts.

Presented by Icro Maremmani and Marc Reisinger

The awards ceremony took place after the conference dinner on May 15.

The winners were:
Marc Auriacombe
Lubomir Okhrulica
Mercedes Lovrecic

Marc Auriacombe is working at the University Victor Segalen of Bordeaux, where he is the coordinator of the Drug Dependence Research Group in the Laboratory of Psychiatry. He is an expert for French National Agencies, WHO (World Health Organization) workgroups, EMCDDA (European Monitoring Centre for Drugs and Drug Addiction) expert groups. His main areas of interest in drug abuse research are methadone and buprenorphine treatments for maintenance of abstinence, quality of life impact and outcome research issue. Marc Auriacombe works in Bordeaux, in a group that started using buprenorphine for the treatment of heroin dependent individuals in 1986, with Dr. Daulouede and Prod. Tignol. This group is among those that have the largest clinical experience with buprenorphine in France.

Lubomir Okhrulica is director of the Institute and the Centre for Treatment of Drug Dependencies in Bratislava, Slovak Republic, since 1996. At present, he is also Chief Expert for Drug Dependencies at the Ministry of Health of the Slovak Republic, where he is working on the implementation of new health programmes on national level, especially in the field of risk reduction. The focus of his studies is the pharmacokinetics of opiates and especially of methadone, but also the evaluation of the programmes, the epidemiology of drugs, dual diagnosis associated with dependence, and even prevention.
Mercedes Lovrecic is a psychiatrist, who is working in Slovenia to promote access to the treatment for heroin addicts with psychiatric comorbidity. In 2002 she was a psychiatrist at the Health Centre of Izla, co-founding member and head of Psychiatry and Addiction Medicine Center. After being Director of the Health Center of Izola, Slovenia, where one of the first European Centres for Double Diagnosed Patients treated with methadone is active, at present she is “focal point” of the Institute of Public Health of the Slovenian Republic.

EUROPAD wish to thank The Norwegian Directorate for Health and Social Welfare, Alcohol and Drug Addiction Service/ City of Oslo and the University of Oslo for their valuable financial support and Schering-Plough, Reckitt Benckiser and Meda A/S for sponsoring some of the speakers.

Our particular thanks go to the local Programme Committee, Helge Waal, Olof Blix, Olav Espergren, Reidar Hole, Aud L Krook Gabrielle Welle-Strand and members of the Norwegian National Scientific committee and the International Scientific committee for their expertise and hard work which ensured that the conference was produced to the highest professional standards.

Finally, congratulations to Egil Haga and his administrative team from MARIO for arranging such a successful conference and the people of Oslo for providing such a friendly and efficient setting for our conference.
CALL FOR PRESENTATION

Europad will select up to ten papers (20 minutes each) to be presented during the AATCD Conference in a workshop provided by Jano Mascarenhas and Marco Rastagni.

The abstract will be photocopied and will appear in an abstract book exactly as typed. Therefore, please follow carefully the instructions given below:

1. The abstract must be written in English.

2. Type the abstract in one paragraph, single spaced, do not exceed one page (100-200 words). Keep within the indicated margins. Required dimensions are 15 cm (width) by 10 cm (height).

3. Use a typewriter or word processor and a good quality black ribbon. Please avoid corrections, erasures, smudges, and corrections to typewritten text. Symbols used in the typewritten or word processor should be hand-written in black ink.

4. The title should be written in CAPITAL LETTERS, followed by the name(s) and affiliation of the author(s). The name of the author presenting this paper should be underlined. Please provide address, phone, fax and e-mail of the presenter.

Abstracts with two copies should be mailed by November 1, 2003 to:
EUROPAD - Jano Mascarenhas, President
c/o AATCD office
Via XX Settembre 83 - 55100 Firenze, Italy
E-mail: janom@uol.com.br

- Electronic Submission:
Please e-mail the abstract to:
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marcordiglia@polito.polimi.it
as a text file, also as a Microsoft Word, Rich Text Format document or pdf document as an attachment to the e-mail.
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Bibliography must be ordered by authors’ names alphabetically. Start each reference with bibliography number; use these numbers, in parentheses, for in-text citations. Personal communications, unpublished manuscripts, manuscripts submitted but not yet accepted, and similar unpublished items should not appear in the reference list. Such citations may be noted in the text.

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