New Developments in Addiction Treatment

This ACADEMIC HIGHLIGHTS section of The Journal of Clinical Psychiatry *presents the highlights of the series of planning teleconferences "New Developments in Addiction Treatment," which was held in July 2006. This report was prepared by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Cephalon, Inc.*

The planning teleconferences were chaired by ***Charles P. O'Brien****, M.D., Ph.D., Department of Psychiatry, University of Pennsylvania and the Philadelphia VA Medical Center, Philadelphia. The faculty were* ***George F. Koob****, Ph.D., Committee on the Neurobiology of Addictive Disorders, the Scripps Research Institute and Pearson Center for Alcoholism and Addiction Research, La Jolla, Calif.;* ***David Mee-Lee****, M.D., American Society of Addiction Medicine, Chevy Chase, Md; and* ***Richard N. Rosenthal****, M.D., Department of Psychiatry, Columbia University and St. Luke's-Roosevelt Hospital Center, New York, N.Y.*

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Neurobiology of Addiction and Its Impact on the Development of Future Treatments

George F. Koob, Ph.D., began his presentation by identifying the neurobiology of addiction as the conceptual framework necessary to understand the medications developed for substance dependence. From this perspective, addiction may include positive and negative reinforcement as motivation for drug-seeking behavior, which may become exacerbated with the severity of the addiction.[1] For example, impulse-control disorders are motivated by positive reinforcement—feeling tension and arousal, completing the impulsive act, receiving immediate gratification, experiencing guilt or reproach, then starting the cycle over. Conversely, compulsive disorders are motivated by negative reinforcement—uncontrollable anxiety and stress, performing repetitive behaviors, experiencing relief, focusing on the obsession, then starting the cycle over. The collapsed cycles of impulse control and compulsive disorders form the 3 basic stages of addiction: preoccupation/anticipation, binge/intoxication, and withdrawal/negative affect (Figure 1).[1] The conceptualization of these 3 stages is particularly relevant in understanding the neurobiology of addiction from the perspective of medications development.

Animal Models

Valid animal models for each stage of the addiction cycle may predict the underlying neurobiology of addiction and may accurately represent the human condition during each phase. For example, animals will self-administer drugs in large amounts or binge, develop negative emotional states during withdrawal, and anticipate and reinstate the administration of substances after extinction. Further, animal models have been developed to demonstrate the transition from use to addiction.

Animal models of excessive alcohol intake include binge drinking, schedule-induced drinking, drinking in the dark, dependence-induced drinking, and intragastric self-administration in ethanol-dependent rats and mice. Dr. Koob noted that a majority of these animal models have been the basis for potential medication treatment for patients with alcohol dependence, such as naltrexone and acamprosate. The notable differences between the 2 drugs are that the opioid antagonist naltrexone has been shown to decrease baseline drinking,[2] while the *N*-methyl-D-aspartate (NMDA) receptor modulator acamprosate is more likely to decrease dependence-induced drinking.[3]

The Neurobiology of Addiction

Through animal models, the basic neurobiological circuitry of substance abuse has been established, which involves 2 key elements in the brain. One is the basal forebrain, where several neurotransmitters converge on or have connections with the extended amygdala, such as dopamine, opioid peptides, γ-aminobutyric acid (GABA), and glutamate.[1] This area also includes the nucleus accumbens. The other is the ventral tegmental area, the origin of the dopamine system, which is thought to be heavily involved in the motivation and responses to incentives.[4] Dr. Koob emphasized that a crucial aspect of this neurobiology is that several neurotransmitters interact with the reward system independently of dopamine, including opioid peptides, GABA, and possibly endocannabinoids.

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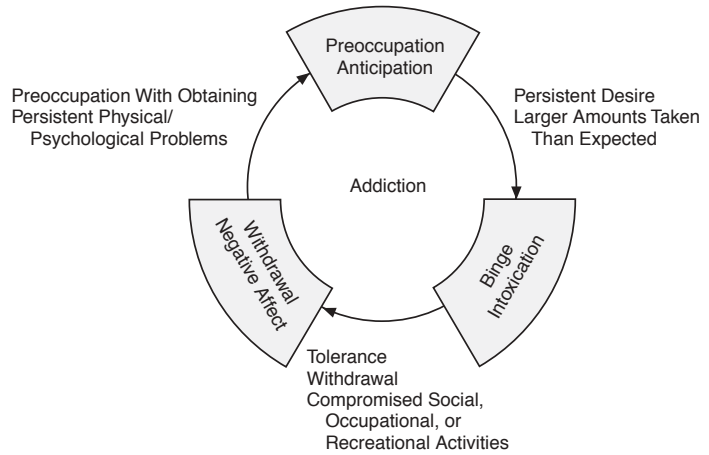
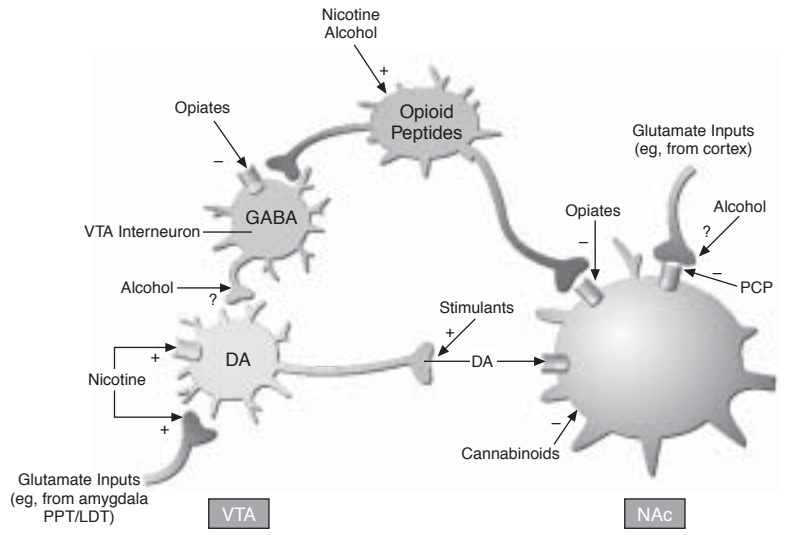
Figure 1. Compressed Stages of the Addiction Cycle With DSM-IV Criteria[a]



[a]Adapted with permission from Koob.[1]

Figure 2. Converging Acute Actions of Drugs of Abuse on the Ventral Tegmental Area and Nucleus Accumbens[a]



[a]Reprinted with permission from Nestler.[5]
Abbreviations: DA = dopamine, GABA = γ-aminobutyric acid, LDT = laterodorsal tegmentum, NAc = nucleus accumbens, PCP = phencyclidine, PPT = pedunculopontine tegmentum, VTA = ventral tegmental area.

Drug interaction with each neurotransmitter is contingent on the substance of abuse (Figure 2).[5] The ventral tegmental area interacts with substances such as alcohol, nicotine, and opiates; the nucleus accumbens interacts with substances such as alcohol, opiates, cannabinoids, and phencyclidine (PCP); and the amygdala interacts with substances such as alcohol, nicotine, cocaine, and amphetamines.[5] Increases in synaptic activity of the neurotransmitters dopamine, opioid peptides, serotonin, GABA, and glutamate during substance use activate the positive hedonic effects of the reward system, which project to the lateral hypothalamus and the brain stem, producing the euphoric and anxiolytic effects of ethanol.[1] Decreases in these neurotransmitters during substance withdrawal can cause negative hedonic effects (antireward), such as dysphoria, pain, anxiety, and panic attacks.[1] Further, increases in other neurotransmitters such as dynorphin, corticotropin-releasing factor (CRF), norepinephrine, and glutamate during withdrawal may cause the dysregulation of emotions, producing a negative affective state, dysphoria, stress, and hyperexcitability.[1]

Dr. Koob stated that recent advancements in the neurobiology of addiction suggest that the CRF system may play an important role in the reward system by controlling the body's behavioral response to stress through the pituitary-adrenal axis, which is activated by acute and chronic ethanol intake, and in the antireward system by activation of extrahypothalamic stress systems.[1] In an animal study,[6] blockade of the CRF system was shown to selectively decrease high alcohol intake (i.e., most importantly, the antagonist has no effect in nondependent animals).[7] The blocking of excessive alcohol intake by CRF manipulation is mediated by the central nucleus of the amygdala, which is activated during drug withdrawal. Thus, the administration of a CRF antagonist reduces anxiety,[8] in effect reversing the negative reinforcement associated with excessive alcohol intake.

Positive Reinforcement and Protracted Abstinence

Dr. Koob described 2 types of craving: conditioned positive reinforcement and protracted abstinence/stress-induced reinstatement. Conditioned positive reinforcement involves the pairing of stimuli such as environmental cues with ethanol self-administration to elicit response for the drug. An animal model of this type of craving is cue-induced reinstatement after response for the drug has been extinguished.[9] Upon reintroduction of the conditioned stimuli, animals will readily self-administer ethanol, effectively responding to the stimuli and not to the substance.

The second type of craving is the state of protracted abstinence in which

residual anxiety and dysphoria persist for weeks to months after substance use termination and which can be activated by acute administration of a stressor (stress-induced reinstatement). Although difficult to measure in animals, this alcohol deprivation effect has been observed in rats as a substantial increase in ethanol intake, even at inappropriate times.[10] For example, one animal model[10] exposed ethanol-dependent rats to chronic alcohol use followed by a 2-week ethanol vapor administration and a 2-week abstinence period. Upon readmission into the chronic alcohol use environment, alcohol ingestion substantially increased by 30% to 100% for 4 to 8 weeks after the acute withdrawal period. The chronic administration of acamprosate has been shown to decrease ethanol intake after protracted abstinence and alcohol deprivation[11] through blocking residual hyperexcitability caused by an increase in the neurotransmitter glutamate.[12] Also, this hyperexcitability and residual stress-like state can be blocked by CRF antagonists during protracted abstinence and upon reintroduction into the substance use environment, signifying interaction within the CRF system as well.

Studies[13,14] have shown naltrexone to block this ethanol-cued reinstatement, thereby maintaining minimal ethanol use after stimuli reintroduction. However, naltrexone does not block stress-induced reinstatement, as does the CRF antagonist D-Phe-CRF.[9,15] This evidence suggests that the CRF system is the main component in stress-induced reinstatement, whereas the primary factor of cue-induced reinstatement may be an endogenous release of opioid peptides.

Conclusion

Animal models developed for the various stages of the substance addiction cycle can provide a rationale for medication development for the treatment of patients with drug addiction. Animal models of reinstatement may be a valid approach to understanding human behavior, but require further validation. Dr. Koob reiterated that different medications for the treatment of alcohol dependence such as naltrexone and acamprosate have been proven to be effective, and new developments in treatments are targeting several neural substrates, including CRF, to create medications to decrease the use of substances of dependence.

Selecting Appropriate Pharmacotherapy for Specific Patients

Alcohol addiction is an illness caused by the repeated use of a substance that activates the brain's easily conditioned reward system. Charles P. O'Brien, M.D., Ph.D., stated that this disease should be treated as a chronic disorder, not as an acute disorder that can be remedied through short-term rehabilitation programs. Effective treatment of alcohol addiction includes medication management, which is necessary to control synaptic activity associated with conditioned responses within the brain. Dr. O'Brien stressed that long-term treatment with medications should be coupled with psychotherapy and support groups in order for patients to resist these conditioned responses associated with substance use and to ultimately prevent relapse into previous, compulsive, drug-seeking behavior.

Medications for Alcohol Dependence

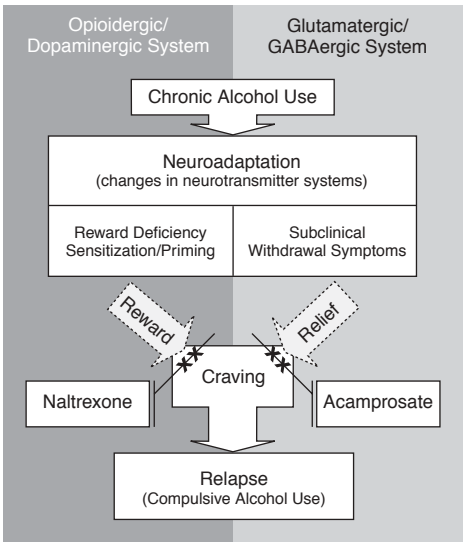
Alcohol is a substance that affects several neurotransmitter systems including dopamine, serotonin, endogenous opioids, NMDA, and GABA. Alcohol addiction medications may regulate these neurotransmitters during the withdrawal phase of treatment, helping to facilitate effective treatment interventions and to prevent relapse. Currently, 4 treatments have been approved by the U.S. Food and Drug Administration to treat patients with alcohol dependence: disulfiram, naltrexone, naltrexone for extended-release injectable suspension, and acamprosate.

Disulfiram. Disulfiram blocks the metabolism of alcohol through acetaldehyde dehydrogenase inhibition,[16] causing the accumulation of noxious metabolites upon alcohol ingestion. This medication is not a cure for alcoholism, but, instead, discourages alcohol consumption through unpleasant side effects, such as vomiting, anxiety, headache, and breathing difficulty.[17] Disulfiram has been shown to be efficacious, but many patients are nonadherent[16] unless the medication is administered under special circumstances, e.g., a spouse, employer, or court order ensures that the medication is taken regularly.[17,18]

Naltrexone. Alcohol activates the opioid peptide system, and the administration of naltrexone effectively reduces alcohol intake by blocking opiate receptors, which inhibits the euphoric effect produced by alcohol.[17] Research has shown that naltrexone decreases alcohol intake,[19–21] alcohol craving,[16] and overall number of relapses,[16,18] especially in patients who have high alcohol craving or those who have a family history of alcoholism. Genotype studies[22,23] of alcohol-dependent individuals have found an association between the presence of A118G, a variant of the μ-opiate receptor gene, and alcohol dependence, suggesting a sensitive endogenous opioid system in patients with this variant. Dr. O'Brien stated that this notion corresponds with studies[24,25] that show people with a strong family history of alcoholism have an increased plasma β-endorphin response to alcohol than people with a negative family history, which may signify a genetic predisposition to alcoholism. Additionally, naltrexone was shown to produce greater treatment response rates in patients with the A118G receptor variant as compared with patients without this receptor variant.[23] This genetic variant has also been found to be associated with greater stimulation from alcohol when given in the laboratory to nonalcoholics.[26] Thus it appears that those who get more reward from alcohol have the best response to naltrexone.

Naltrexone for extended-release injectable suspension. Naltrexone for extended-release injectable suspension has the same mechanism of action as the conventional form of naltrexone in that it inhibits the rewarding effects of alcohol by blocking the opiate receptors in the brain. Naltrexone for extended-release injectable suspension may improve adherence because it is long-acting and thus is administered only once every 4 weeks by a health care professional. It has been shown to be efficacious and well-tolerated.[27–29] Studies have reported significant differences for time to first drinking day,[29] fewer drinking days,[29,30] fewer heavy drinking days,[28] and better abstinence rates[29,30] compared with placebo when taking naltrexone for extended-release injectable suspension. Patients should be told that injection site reactions including pain, tenderness, induration, or pruritus may occur.[30]

Figure 3. A Representation of the Neuroadaptive Model of Craving and Possible Mechanisms of Action of Naltrexone and Acamprosate[a]



[a]Reprinted with permission from Jung and Namkoong.[17]
Abbreviation: GABA = γ-aminobutyric acid.

Acamprosate. Acamprosate is believed to interact with the NMDA/glutamate neurotransmitter system, which may be altered during prolonged alcohol withdrawal.[17] This medication has been shown to reduce alcohol intake[32] and alcohol craving,[33] increase alcohol abstinence,[18,33–35] and alleviate anxiety associated with the negative reinforcement of alcohol dependence.[36] Studies[37,38] have indicated that acamprosate is effective in treating patients who have severe, chronic alcoholism or those who have been fully detoxified and have had a period of inpatient care.

Adjunctive Administration of Medications for Alcohol Dependence

Although disulfiram, naltrexone, and acamprosate exhibit different interactions at the synaptic level, no adverse interaction among these medications has been reported.[17,39,40] Dr. O'Brien noted that the administration of 2 or more medications does not cause toxicity as a result of drug interactions and that, disulfiram, naltrexone, and acamprosate can be given adjunctively to reduce patients' risk of relapse. No studies have yet been conducted with naltrexone for extended-release injectable suspension to determine if it is safe to administer in combination with other medications for alcohol dependence. Figure 3 represents the possible mechanisms of action of naltrexone and acamprosate in a representative model of neuroadaptive craving.[17]

Studies[20,41–45] of the adjunctive efficacy of naltrexone and acamprosate have produced varied results. For instance, some studies[41–44] have indicated that this combination is efficacious for the treatment of alcohol dependency, especially in patients who were unresponsive to naltrexone or acamprosate monotherapy.[43] Further, Feeney et al.[44] found that the combination produced greater overall improvements in patients who were administered the naltrexone and acamprosate combination as opposed to one medication alone. Conversely, other studies[20,45] have failed to show an advantage for the combination.

Because patients with alcohol dependence commonly have other comorbid psychiatric disorders, combinations with other medications may be effective.[46] For example, people with alcohol dependence frequently develop depression, and antidepressants in addition to naltrexone or acamprosate have been shown to be efficacious in individual cases.[46] However, Dr. O'Brien noted that few controlled studies have been conducted on adjunctive pharmacotherapy with antidepressants.[47]

Conclusion

Alcohol dependence is a chronic disorder that should be treated with medications as well as psychotherapy. Disulfiram, naltrexone, naltrexone for extended-release injectable suspension, and acamprosate have been shown to be efficacious in treating patients with alcohol dependence, although each medication is more effective than another in certain populations. For example, disulfiram has been shown to be effective in adherent patients, naltrexone has been shown to be effective in patients with high alcohol craving or family history of alcoholism, naltrexone for extended-release injectable suspension may be effective in patients who are not compliant with other forms of treatment, and acamprosate has been shown to be effective in patients with chronic alcohol dependence.

Dr. O'Brien also reiterated that all of these medications may be safely administered adjunctively, either with one another or with medications used to treat co-occurring disorders. However, naltrexone for extended-release injectable suspension has not been studied in combination with other medications.

Development and Implementation of the Patient Placement Criteria

The Patient Placement Criteria for the Treatment of Substance-Related Disorders[48] developed by the American Society for Addiction Medicine (ASAM) is an individualized, clinically driven addiction treatment strategy. In its first edition,[49] it integrated the Cleveland Admission, Discharge, and Transfer Criteria[50] and the National Association of Addiction Treatment Providers' Criteria.[51] The second edition of the Patient Placement Criteria[52] has been endorsed by the U.S. Department of Defense in its addiction programs worldwide, and in 1997 the U.S. Department of Veterans Health recommended the ASAM Criteria for use in its 171 hospitals nationwide. The Patient Placement Criteria have been approved in over 20 states across the nation.[53] The ASAM has developed Patient Placement Criteria for the purpose of establishing a national standard for addiction treatment for clinicians to use to ensure optimal patient outcomes.

Generations of Clinical Care

David Mee-Lee, M.D., began his presentation by explaining that clinical care has progressively become more patient-oriented. Patient placement in terms of addiction treatment has gone through a variety of generations, the most recent being a collaborative treatment process between the patient and physician. Four generations of clinical care have been defined: complications-driven treatment; diagnosis-driven treatment; individualized, clinically driven treatment; and clinical outcomes–driven treatment.[54]

Complications-driven treatment. In the first generation, patients are treated only for medical conditions resulting from the abuse of substances. For example, injuries sustained in a car accident while driving under the influence or depression or psychosis associated with substance abuse, cirrhosis, or other medical conditions are treated, but a definitive diagnosis of addiction is rarely made. Subsequently, patients are never treated specifically for the addiction disorder. Thus, patients continue on a cycle of having the complications of addiction treated but not the addiction disorder itself.

Diagnosis-driven treatment. The second generation of clinical care is diagnosis-driven treatment. Here, substance addiction is recognized and diagnosed, and patients are placed into treatment programs frequently with a fixed timeline, such as a 28-day rehabilitation program. Upon completion of the treatment program, patients are admitted into aftercare. However, if patients relapse during or after the addiction treatment program, they are often restarted in the same type of program, in which emphasis is more on completing the program than on treating their individual addiction disorder.

Individualized, clinically driven treatment. The third and current clinical care generation for the Patient Placement Criteria[48] focuses on individualized treatment in which an addiction diagnosis is necessary but is not a sufficient determinant of the treatment plan for a patient. Because addiction is a biopsychosocial disorder, treatment programs address a variety of patient modalities. These modalities may include interventions from differing schools of thought, including cognitive-behavioral therapy, medication approaches, and individual, group, and/or family therapy. The treatment plan is designed to match the service needs with a patient's severity of illness and level of function, which is then delivered in the least intensive, safest level of care. After a personalized treatment plan is executed, the patient's progress is evaluated to determine the current illness severity and level of function, and further assessments are made for future treatment options. This clinical-care generation is a continuous quality-improvement cycle of multidimensional assessments of patient functioning, evaluations with treatment priorities identified for treatment planning, progress evaluations to determine if the treatment is successful or not, and modifications of the treatment plan depending on the patient's progress.

Clinical outcomes–driven treatment. The last generation of clinical care and, as Dr. Mee-Lee affirmed, the future of the Patient Placement Criteria,[44] also involves developing an individualized treatment plan. However, the main focus of clinical outcomes–driven treatment is on using the multidimensional assessment to build an alliance between the physician and the patient. Starting with what the patient wants to achieve, e.g., abstinence or decreasing use or substance problems such as "I want to keep my job or marriage," the multidimensional assessment pinpoints factors that contribute most to positive patient outcomes. This generation of clinical care assesses the quality of the alliance with the patient, the degree to which the patient experiences hope and a positive expectation of treatment, and the degree to which the patient is engaged in treatment collaboration. In this model, emphasis is placed on collaborative treatment planning with the patient at the center of the process, which leads to the development of an individualized treatment plan. The level of care involves not only clinical interventions, but also other services as needed, such as child care, housing, transportation, and financial and vocational assistance, as well as working with patients' families. Additionally, other outcome instruments may be used to acquire immediate feedback to measure proximal patient outcomes and assess the need for changes if the treatment program is ineffective.[55]

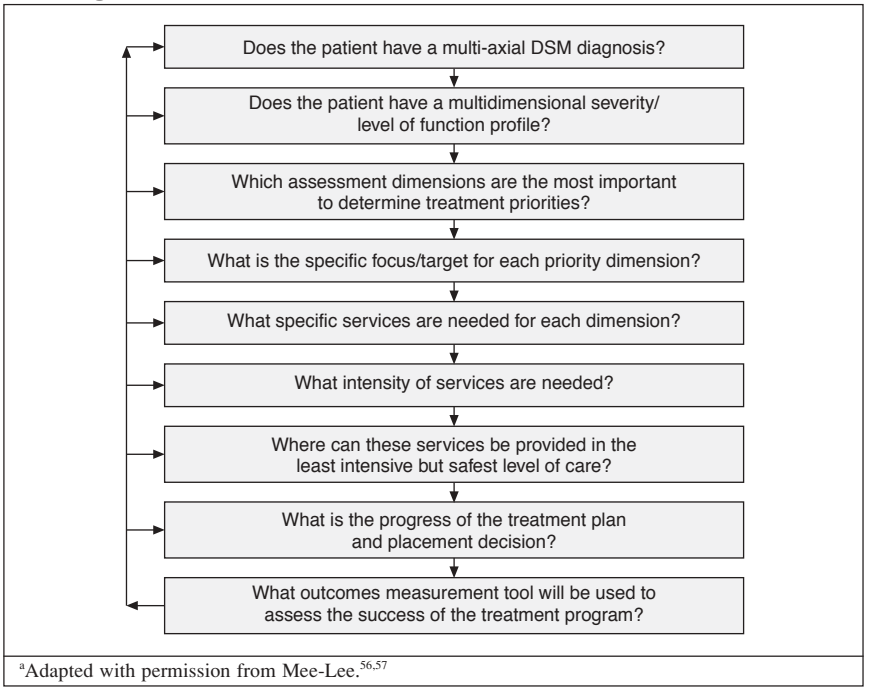
Table 1. Multidimensional Descriptions, Assessments, and Treatment Matches According to the Patient Placement Criteria[48]

Dimension	Description	Assessment	Treatment Match				
			Manage	Monitor	Medication	Meetings	Motivate
1	Acute intoxication and/or withdrawal potential	Patient detoxification service needs	✓	✓	✓		
2	Biomedical conditions and complications	Patient needs for biomedical and physical health services	✓	✓	✓	✓	
3	Emotional/behavioral/ cognitive conditions and complications	Degree of patient needs for formal mental health services for comorbid mental disorders	✓	✓	✓	✓	
4	Readiness to change	Degree of patient needs for clinical motivation–enhancement services	✓	✓		✓	✓
5	Relapse/continued use/ continued problem potential	Patient needs for relapse prevention services	✓	✓	✓	✓	
6	Recovery environment	Degree of patient needs for environmental support to recovery (child care, vocation, transportation, housing, family therapy)	✓	✓		✓	

A Multidimensional Assessment for Individualized Care

Dr. Mee-Lee reiterated that the Patient Placement Criteria emphasize a multidimensional assessment based on the biopsychosocial areas of addictive disorders. This assessment determines patients' illness severity and level of function, which leads to a treatment plan, or treatment match, with the appropriate intervention based on which dimensions are most needed at the time of the assessment (Table 1).[48] Dr. Mee-Lee expanded on dimension 3 (emotional/behavioral/cognitive conditions and complications) and stated that if a patient has addiction-related depression or anxiety, the problem may be treatable within the context of the addiction program. However, if a patient has a co-occurring mental illness, more collaboration and coordination with specific mental health care services will be necessary. Dimension 4 (readiness to change) examines the degree to which a patient needs clinical motivation–enhancement services to actively engage and attract the person in treatment planning for the addiction disorder and the co-occurring mental disorder. Dimension 5 (relapse/ continued use/continued problem potential) was recently revised because some patients may be prone to relapse due to co-occurring mental disorders. Such patients may require extra preventative measures to prevent relapse due to the co-occurring mental disorder. Dimension 6 (recovery environment) assesses a patient's daily life and support systems, such as family, significant others, vocation, transportation, housing, child care, and so on, and to what extent that environment is supportive or lacking thereof.

Figure 4. Specific Questions to Determine the Least Intensive, Safest Level of Care According to the Patient Placement Criteria[a]



[a]Adapted with permission from Mee-Lee.[56,57]

After assessments have been conducted, appropriate treatment modalities in collaboration with the patient are paired with each dimension to provide the optimum level of care. A need may exist for each modality to be matched to more than one dimension, and each dimension may include several modalities. For example, medication for the different dimensions of assessment may include detoxification medication for dimension 1, hypertension or diabetic medication for dimension 2, psychotropic medication for comorbid psychiatric disorders for dimension 3, and antiaddiction medications such as naltrexone, disulfiram,

Table 2. Example Model for Rating Patient Illness Severity and Level of Risk From the Patient Placement Criteria Appendix[a]

Risk Rating and Description	Types of Services and Modalities Needed	Intensity of Service/Level of Care/Setting
Risk rating 1–4: Various levels of functioning and severity and level of risk A higher number indicates a greater level of severity	Range of specific services needed in the treatment plan to match the patient's functioning and illness severity	Intensity rating 1–4: Intensity or level of service that can deliver the service plan safely and efficiently A higher number indicates a greater level of intensity

[a]Adapted with permission from Mee-Lee.[48]

acamprosate, methadone, or buprenorphine for dimension 5. Additionally, self-help or mutual-help meetings can facilitate recovery. Dr. Mee-Lee gave examples of a diabetes support group for dimension 2, or a Dual-Recovery Anonymous group for dimension 3, or Alcoholics Anonymous or Narcotics Anonymous for dimensions 4 and 5. Additionally, Al-Anon or Naranon are sources of support for family members of substance abusers, which addresses the recovery environment specified by dimension 6.

Continuum of Care

Dr. Mee-Lee stated that the Patient Placement Criteria provide a continuum of care with 4 broad levels. Beginning with the least intensive, the levels are outpatient treatment, intensive outpatient or partial hospitalization, residential inpatient treatment, and medically managed intensive inpatient treatment with 24-hour physician availability. At each level, a range of specific questions are used to determine the least intensive, safest level of care (Figure 4).[56,57] Moving through the levels ensures increased access to resources that will provide as much care as possible and ultimately improve the patient's overall outcome.

Nine studies of 3641 participants that tested the Patient Placement Criteria evaluated a computerized algorithm, which was created to help implement criteria with interrater reliability. A review[58] of the results of these studies indicated that the Patient Placement Criteria have valid clinical decision-making guidelines, good feasibility and reliability through standardized computer assessment instruments, and good concurrent validity in treating patients throughout the multidimensional assessments. Four independent studies[58] of varying samples, timeframes, and cultures signified that the Patient Placement Criteria have predictive validity in that they can be used to reliably determine which patients with different illness severities will prosper in what type of treatment environment. Dr. Mee-Lee stated that the most recent version of the Patient Placement Criteria[48] is poised to become a standard for intake and continued care to help identify the best use of resources, to increase access to care, and to hold treatment providers accountable through benchmarking.

Future directions for the criteria emphasize not only matching patients to levels of care, but also matching services to needs. The appendix of the current Patient Placement Criteria[44] features a model that rates patients' illness severity and level of risk on a scale of 0 to 4 in each of the 6 dimensions, with 4 being the greatest severity, and offers suggestions for needed services and appropriate treatment settings (Table 2).[48] A Patient Placement Criteria Supplement on pharmacotherapy for alcohol dependence is currently under development.

Conclusion

Dr. Mee-Lee reiterated that the Patient Placement Criteria developed by the ASAM helps guide and collaborate with an individual patient through treatment with assessments across 6 dimensions, including relapse, continued use, continued problem potential, and recovery environment. Further, once a patient has been properly assessed, an appropriate intensity level of treatment is matched to the patient's needs, which determine the level of care placement.

Standards of Care for Substance Abuse and Their Implementation Into Clinical Practice

In his presentation, Richard N. Rosenthal, M.D., proposed 6 overarching standards of care for treatment programs designed for patients with substance use disorders (Table 3).[59] These standards fall into 3 domains that correspond with what, by whom, where, and how care is delivered: treatment, which includes the effectiveness and specificity standards; provider, which includes the competence standard; and systems of care, which include the contextual, economic, and accessibility standards.

Treatment

Effectiveness standards. Dr. Rosenthal stated that treatment efficacy tends to be shown in randomized clinical trials with relatively homogenous samples that produce high internal validity. Because the samples are not heterogeneous, as patients are in nonresearch clinical settings, the generalizability of the studies decreases, thereby indicating a need for interventions that are not only statistically significant, but clinically significant as well.

To establish effective intervention standards, Dr. Rosenthal put forward that studies should protect against methodological bias. For example, study design and analysis should avoid schematic bias and inferential error and promote strong evidence.[60] Systematic reviews and meta-analyses of multiple randomized controlled trials are more reliable and generalizable than case

Table 3. Recommendations for Effective Standards of Care[59]

Domain	Standard of Care	Recommendation
Treatment	Effectiveness	Protect against methodological bias and promote strong, generalizable evidence
	Specificity	Use individualized, patient-oriented care that addresses the intensity and content of addiction services, as well as differential therapeutics of co-occurring mental disorders
Provider	Competence	Provide treatment in a competent manner through clinical integrity
Systems of care	Contextual	Improve care through patient-driven programs and address the nonlinearity of recovery
	Economic	Invest in addiction treatment, which will dramatically decrease expenditure on substance-related problems
	Accessibility	Make the appropriate means available to diagnose and treat patients

series or one clinician's experience.[61] However, the United States has not broadly adopted evidence-based interventions for substance use disorders but instead has used addiction treatments that are socially accepted and economically advantageous. For instance, commercially successful programs such as hypnosis or acupuncture for the treatment of nicotine use have not been proven to be more effective than placebo, yet they are commonly applied. Similarly, government insurance such as Medicaid has reimbursed inpatient detoxification for cocaine use despite evidence of a general lack of necessity for hospitalization. Conversely, methadone maintenance is a socially and politically unpopular intervention despite strong efficacy evidence that this type of intervention reduces the medical and social sequelae of opiate dependence.[62] Clearly, social and economic advantages should drive the rational use of this treatment in the United States.

Specificity standards. Although empirical validation is warranted, individualized patient-oriented care is clinically more effective than general care. Dr. Rosenthal cited the evolution of treatment for schizophrenia as an example of empirical change that led to an overall improvement in patient outcomes. In the early 20th century, schizophrenia was treated by packing patients in wet clothes and allowing the moisture to evaporate. This cooled the patient down, but was a very nonspecific treatment. Early pharmacotherapies consisted of bromides or other sedatives for agitation. In midcentury, patients' positive symptoms could be controlled with traditional neuroleptics. Today, schizophrenia is usually treated with atypical antipsychotic medication, which reduces positive, negative, and cognitive symptoms. Thus, with treatment becoming more specific, patient outcomes have dramatically improved. Recently, the research domain, including clinical outcome studies sponsored by the National Institutes of Health (NIH), has demanded specificity regarding sample populations, proper control groups, randomized clinical trials, treatment methodology, outcome standard definitions, and statistical methodology.

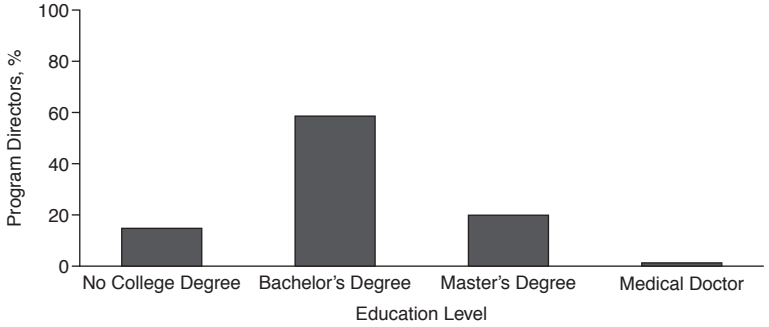
Patients with substance use disorders commonly have co-occurring mental illnesses, which are often underrecognized and undertreated, can increase relapse rates after substance abuse treatment, and can dramatically increase the use of health care services.[63–65] Therefore, specific guidelines for treatment should address the intensity and the content of services for addiction disorders, as well as the differential therapeutics of comorbid mental illnesses. Dr. Rosenthal explained that in the United States, general care is the normal standard of treatment. In examining the Epidemiologic Catchment Area (ECA) Study, Narrow et al.[66] found that of 186,000 patients receiving inpatient drug treatment, only 5.7% received care in a specialty addiction treatment unit, leaving 94.3% of patients to be treated with less addiction-specific treatment in inpatient general hospital units or other psychiatric units.

Many countries, including the United States, lack data on the effectiveness of specific addiction treatment interventions and programs, which should address treatment matching by age at onset, severity, functional impairment, comorbid psychopathology, and cognitive impairment. Dr. Rosenthal described the findings of one study[53] of the ASAM Patient Placement Criteria[48] in which patients who received a less-than-recommended level of care used nearly twice as many hospital beds over the next year for substance abuse treatment. Another treatment-matching study, Project Match,[67] found that cognitive-behavioral therapy, motivational enhancement, or 12-step facilitation treatment all reduced the percentage of drinking days for patients with alcohol dependence, although there was no ability to discriminate which patients would do better with which treatment intervention.

Provider

Competence standards. Dr. Rosenthal stressed that effective and specific treatment interventions must be provided in a competent manner through clinical integrity. The technology model of clinical integrity from psychotherapy research includes 2 components: fidelity and competency to deliver treatment.[68] Fidelity, or adherence to the specified treatment guidelines, can be seriously affected by "drift"—practitioners veering away from specified treatment guidelines as a result of the development of individual styles and idiosyncrasies. Drift can happen over time with pharmacotherapy as well as psychotherapy. Fidelity must be examined to identify unique and essential factors to a particular intervention, generalizable factors that can be shared with other interventions, acceptable but unnecessary treatments, and aspects proscribed to that intervention to specifically avoid.

Figure 5. Education Level of Addiction Program Directors According to the National Survey of Substance Abuse Treatment Services (N-SSATS)[a]



[a]Data from McLellan et al.[69]

Competence to deliver treatment deals with practitioners' skill in working with patients as well as education and training, which may be inadequate in many treatment facilities (Figure 5).[69] For physicians, education and training includes supervision in and out of residency training and continuing medical education (CME). Because the Accreditation Council for Graduate Medical Education (ACGME) only recently has required a month of addiction training for general psychiatry residencies, many practicing psychiatrists do not have formal training specific to addiction treatment; therefore, CME becomes the avenue to improve psychiatrists' repertoire for addiction interventions. In addition, the ACGME has established core competencies to improve medical training in all specialties. The 6 core competencies are medical knowledge, patient care, practice-based learning and improvement, systems-based practice, professionalism, and interpersonal and communication skills. Institutions such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the Commission on Accreditation of Rehabilitation Facilities (CARF) regulate the delivery of care on the inpatient and outpatient level, which have standards regarding the credentialing of practitioners.

Dr. Rosenthal expanded on institutional competency standards and stated that institutional policies and procedures can have a substantial impact on patient outcomes. For example, methadone maintenance programs that were executed competently, but had a maximum allowed dosage of 50 mg/day, resulted in ineffective treatment because the dosage was too low to be effective for many patients.[70] In alcohol treatment facilities, insufficient systems-level standards include poor screening and identification of alcohol problems, inadequate and deteriorating infrastructure, and inadequate diffusion of technological advances in treatment.

Systems of Care

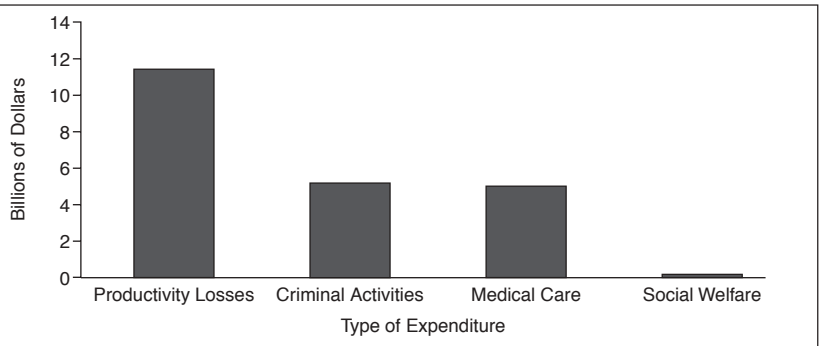
Contextual standards. The context or model of care standard states that care improves as the treatment model becomes patient-driven instead of program-driven through the increased specificity of intervention programs.[64] Additionally, Dr. Rosenthal reinforced that models of care need to be more accurate in addressing the nonlinearity of recovery and patients' episodic exacerbations, which are likely to occur.[64] The model of managed care[64] attempts to provide the least restrictive and most economically favorable care option with the goal of optimal patient outcomes. The result is an acute care model for a chronic illness, which is unlikely to have long-term impact because patients present the goodness-of-fit problem, or insufficient treatment match, of an acute care treatment plan. This lack of a comprehensive approach is also worsened by comorbid mental illnesses and medical conditions. Further, economic research has not yet demonstrated whether this model of care would be efficacious in practice.

The standards of contextual care have moved away from long-standing treatment strategies such as fixed-length inpatient programs because of high expense and a lack of efficacy. Newer models have been developed for inpatient, outpatient, and residential addiction treatment settings. For example, medically supervised inpatient detoxification is migrating toward outpatient settings in which public sector funding is following the commercial insurers. Further, outpatient programs have differentiated into low-intensity, high-intensity, and partial hospitalization levels of care. Dr. Rosenthal affirmed that institutions that have implemented these programs have lowered the average length of patient hospitalization as well as per patient costs.

Economic standard. The economic standard asks the question, "Is the treatment worth the investment?" Dr. Rosenthal averred that economic losses due to addiction should be offset by appropriate expenditures for addiction treatment. However, more persons are currently affected by substance use disorders than are being treated in the United States, at a considerable expense to the economy, reinforcing the need for economic standards in addiction treatment. For example, an estimated $11.5 billion of U.S. tax dollars were directed at substance use disorder treatment funding in 1990,[71] yet the cost of drug and alcohol problems, e.g., associated crime, property loss, lost work productivity, general health care costs, acquired immunodeficiency syndrome (AIDS), and fetal alcohol syndrome, during that year climbed to nearly $165.5 billion.[72] For heroin addiction alone, Mark et al.[73] estimated a $21.9 billion expenditure in 1996 (Figure 6).

Evidence has shown that treatment programs for addiction can be successful and can effectively reduce the amount of expenditure on substance-related problems. The National Institute on Drug Abuse (NIDA) reported

Figure 6. Estimated Total Expenditures on Heroin Addiction in the United States in 1996[a]



[a]Data from Mark et al.[73]

that every $1 invested in addiction treatment returns $4 to $7 through reductions in drug-related crimes and criminal costs alone.[74] For instance, the California Drug and Alcohol Treatment Assessment (CALDATA) study[75] of 1825 treatment participants revealed that in 1992, addiction treatment costs were $209 million. Subsequently, the savings for taxpayers were $1.5 billion, elucidating the economic benefits of implementing addiction programs. Similarly, another study[76] found that patients involved in early alcohol treatment interventions had fewer hospital days and fewer emergency department visits than the control group. These effects were maintained at the 4-year follow-up period, producing a $43,000 reduction in health care costs for every $10,000 spent on early alcohol treatment. The outcomes of the few studies that have been conducted on economic factors concerning addiction treatment programs are promising and warrant further study to validate the exact economic benefits of addiction treatment.

Accessibility standard. Untreated substance use disorder results in disability and poor quality of life. Dr. Rosenthal emphasized that people with substance use disorders should have the appropriate means to be clinically diagnosed and have access to care. In 2002, 18.2 to 18.6 million people met the criteria for alcohol abuse/dependence, of which only 1.9 to 2.7 million received any treatment, leaving at least 15.5 million people untreated.[77]

In addition to untreated populations, the number of addiction treatment facilities is inadequate. The World Health Organization Treatment Mapping Survey[78] found that nearly two thirds of countries polled signified a greater demand for addiction treatment services than were available, especially in countries with a high prevalence of substance abuse. The United States is no different; the 12-month prevalence for substance use disorders, is 16.7%,[79] of which only 19% of patients with alcohol dependence and 26% of patients with other substance dependence receive treatment.[68] Further, the National Survey of Substance Abuse Treatment Services (N-SSATS) examined the treatment settings for substance use disorders, and of 13,454 programs, less than one fifth were using antiaddiction medications.[80] Dr. Rosenthal reiterated that the treatment level in the United States does not necessarily use evidence-based interventions and that patients are clearly not receiving the appropriate access to medication.

Patients with substance use disorder are commonly misdiagnosed, thereby hindering the application of the appropriate treatment interventions. Ananth et al.[81] found that of 75 patients originally admitted for psychiatric inpatient treatment, 4 were initially diagnosed with a substance use disorder. Upon further investigation through clinical rounds, an additional 25 cases were diagnosed. After structured interviews were conducted, a total of 187 cases of substance use disorder were uncovered, with many patients meeting the criteria for more than one diagnosis. Dr. Rosenthal explained that he and his colleagues[82] used similar methods to discover an approximate 80% gap in multiple substance use disorder diagnoses between the initial admission and structured interviews of patients with schizophrenia being treated in an inpatient program.

The Treatment Outcome Prospective Study[83] reported that patients who were consistently exposed to methadone had a greatly reduced rate of heroin use compared with baseline, evidencing the importance of accessibility to an effective methadone program. Further, the highest retention program informed patients of their dosage to actively include them in treatment planning and provided easy access to high-quality services.

Conclusion

Dr. Rosenthal concluded that although clinical evidence supports both behavioral interventions, such as motivational enhancement, relapse prevention, and individual drug counseling,[84] and pharmacotherapeutic interventions in the treatment of substance use disorders, the field has been slow to adopt both classes of interventions. Other barriers to effective addiction treatment include a lack of specific standards for clinician and institutional competence, patient-driven treatment programs, and accessibility concerning those programs. Further, there are more people living with addictive disorders than are currently being treated, which has a considerable economic impact in the United States.

Drug names: acamprosate (Campral), buprenorphine (Suboxone, Subutex, and others), disulfiram (Antabuse), methadone (Methadose, Dolophine, and others), naltrexone (ReVia), naltrexone for extended-release injectable suspension (Vivitrol).

Disclosure of off-label usage: The chair has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside U.S. Food and Drug Administration–approved labeling has been presented in this activity.

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For the CME Posttest for this ACADEMIC HIGHLIGHTS, see pages 1824–1825.

