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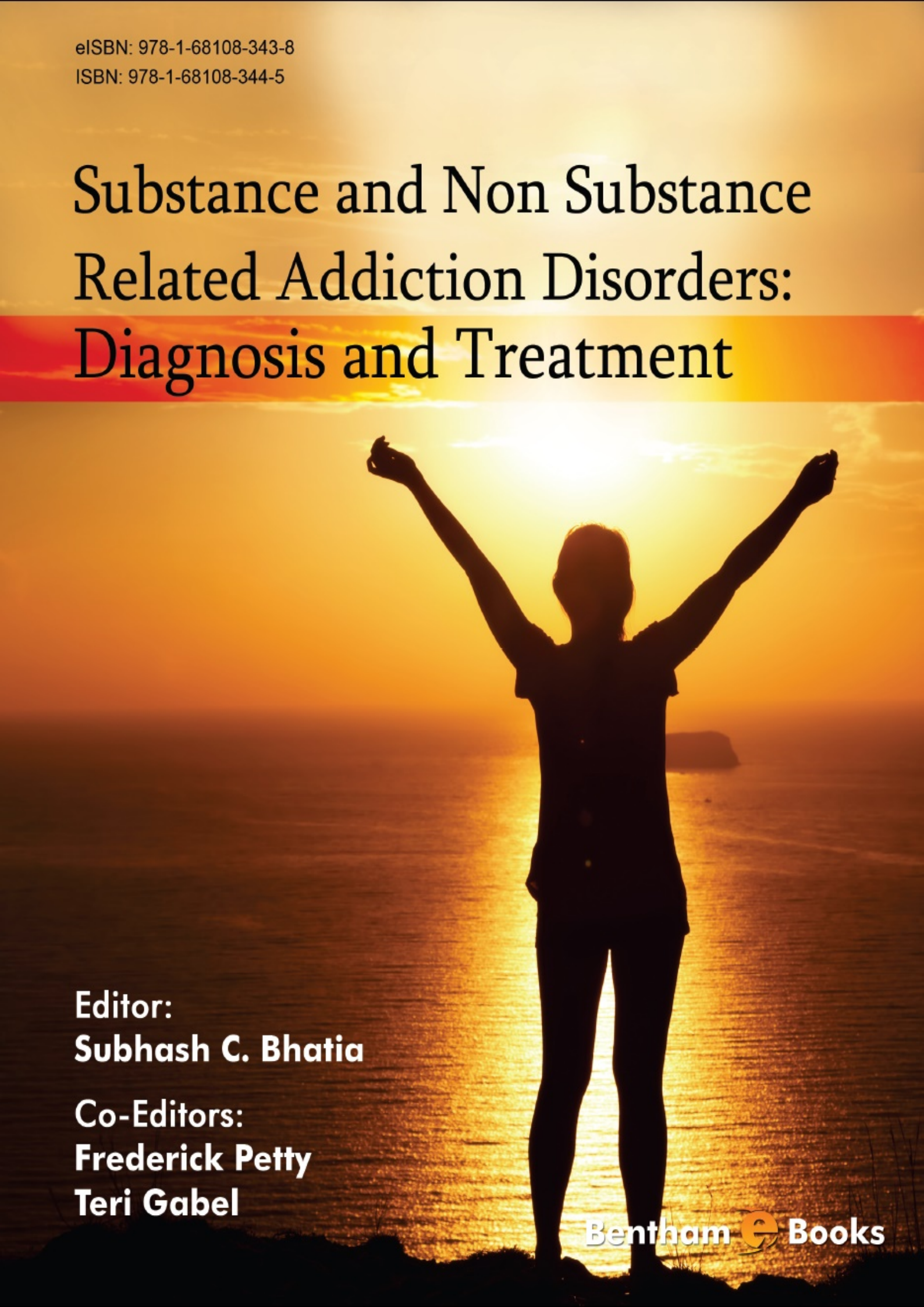
Substance and Non Substance Related Addiction Disorders: Diagnosis and Treatment



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Substance and Non Substance Related Addiction Disorders: Diagnosis and Treatment

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FOREWORD

About one person in three has a problem with potentially hazardous drug or alcohol use which often goes unrecognized. Excessive or hazardous use of drugs, including tobacco, and of alcohol, can have very negative biological, psychological and socio-economic consequences from the direct effect of the substances. In social realm addictive behaviors take a toll on relationships with friends and family. Also often harm can occur to the patient by failure to comply with medical or psychosocial treatment for abstinence or unsupervised withdrawal or through drug interactions. Thus, every practitioner should have knowledge regarding diagnosis and treatment of common substance use disorders.

The authors share with the readers wealth of information based on their experience about diagnosis and management of common substances of abuse as well as neurobiological underpinning of these disorders. Each chapter in section II features discussion of diagnosis, and approaches to treatment and highlights cases with approaches to the patient delineated.

The practitioners should find this volume useful, helpful, and interesting in helping to provide optimal health care to his or her patients.

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PREFACE

Substance use disorders are amongst the major causes of disease burden around the globe. In a World Drug Report by the United Nations Office on Drug and Crime it is estimated that 210 million individuals have used illicit drugs at least once and that these drugs are related to about 200,000 deaths. The economic burden of substance use disorders in the USA alone from health care costs, lost productivity, crime, incarceration and drug enforcement is estimated to be $524 billion.

Addiction is a brain disease where a person uses a drug compulsively despite negative consequences and drug use in turn causes persistent changes in the brain circuits which perpetuates its use. In predisposed individual's addiction starts during adolescent years. Fortunately addictions are preventable through public awareness and education and are treatable through contemporary medications, individual, group or family therapy as a well as self-help groups. Biopsychosocial intervention can mitigate life time suffering of the patient, family, and friends. Treatment also improves the quality of their lives. Moreover it can prevent tragic loss of life as well . Extended abstinence predicts long-term recovery. Drug addiction is a chronic disease and its relapse rate is comparable to hypertension, diabetes or asthma.

Recently one notable development has been publication of DSM-5 . Our publication provides information on the diagnosis of the additive disorders consistent with this new version of DSM.

The book is titled *Substance and Non Substance Related Addiction Disorders: Diagnosis and Treatment* and is divided in to three sections.

Section I addresses basic general topics related to scientific underpinnings of addictive disorders including the neurobiology and addiction neural reward pathways, genetics and psychosocial basis of addictions; urine drug screens in diagnosis and management of substance use disorders, co-occurring psychiatric and substance use disorders and pharmacological treatment of comorbid psychiatric disorders and motivational interviewing. Each chapter has key learning points, references, a patient education hand out .

Section II provides updated information about individual drug related addictive disorder. Each chapter in addition to key learning points and a patient education handout, describes a case vignette and its discussion related to specific drug, its diagnosis, medical and biopsychosocial interventions. In addition these chapters include

neurobiology, epidemiology summary and updated references with resources for more information.

Section III presents information about non-substance related addiction disorders, a vignette and its discussion, diagnosis and interdisciplinary treatment strategies. The chapter in this section is primarily devoted to gambling addiction; other non-substance related addictions are also mentioned.

This book is by multiple authors with experience in addictions and is designed to meet the clinical practice needs of internists, family physicians, nurse practitioners, physician assistants, addiction therapists, psychiatry and primary care residents, graduate students and other health care professionals interested in the care of patients with substance use and addiction disorders. A concise format for each chapter is used to maintain its user friendliness for quick review.

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This book is dedicated to our Teachers, Parents and Persons with Substance use Disorders.

Section I: General Topics

CHAPTER 1

Neurobiology and Psycho-Social Basis for Addiction and Related Disorders

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Abstract: Addictive disorders are diseases of the brain. Addictions like chronic illness may have remissions and relapses. These are caused by genetic, biological, psychological, social and economic factors. Reward pathways for all substance and non-substance related addictive behavior (gambling, sex and food addiction *etc.*) are similar and are mediated through nucleus accumbens and associated circuits. Negative preexisting emotional state or due to withdrawal from substance and self-medication to seek relief may perpetuate addictive behavior. Substance or non-substance related addictive behavior-pleasure-reinforcement-reuse paradigm perpetuates addictive behavior. Environmental cues and memories associated with addiction related activities contribute to craving and relapse. Dopamine neurotransmitter plays major role in addictive behaviors. Treatment consideration should factor in all of these biopsychosocial factors.

Keywords: Addiction reward pathways, Cues and craving, Dopamine, Nucleus accumbens, Operant conditioning, Self-medication theory.

KEY LEARNING POINTS

1. Addictive disorders have complex biopsychosocial underpinnings for both causation and treatment.

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2. Dopamine is the crucial neurotransmitter in reward circuits for all substance and non-substance related addictive disorders. Chronic use causes down regulation of dopamine receptors which accounts for tolerance.
3. Ventral tegmental area, nucleus accumbens, prefrontal cortex, hippocampus, amygdala and basal ganglia all contribute to impulsive and compulsive drug use as well as reward and cue driven craving.
4. Psychosocial stressors as epigenetic factor may change the genotype and may increase propensity to addiction.
5. Association of behaviors leading to reward is part of the operant conditioning paradigm and perpetuates drug use.
6. The self-medication hypothesis to treat negative emotional states is reported to be involved with addiction.
7. Adverse childhood experiences such as physical, sexual, emotional abuse, physical or emotional neglect, domestic violence and drug misuse or mental illness in the family, incarceration of a family member and parental separation and divorce may increase the risk of illicit drug use 2 to 4 times. This drug use may be viewed as self-soothing behavior and may persist through life.

NEUROBIOLOGY OF ADDICTION AND REWARD PATHWAYS

The neurobiology of substance and non-substance addiction and related disorders is complex but follows a common reward pathway. These disorders are chronic relapsing illnesses, a brain disease, characterized by engaging in the compulsive use of substances despite negative consequences. The drug use starts out with liking, which is a non-problematic use, followed by wanting and craving respectively leading to abuse and dependence. The intense craving is mediated by withdrawal effects, or after due to pleasurable effects of drug and/or environmental cues. The motivation to repeatedly re-experiencing pleasurable effects or to avoid aversive effects of drug withdrawal [1, 2]. This compels the individual to seek the drug. The following information provides a simplified summary version using an example of narcotic addiction.

For addictions, self-administration mimics binding of a substance directly to specific endogenous receptors resulting in reinforcing effects. For example in opiate addiction mu receptor activation in addition to causing analgesia, nausea,

reduced bowel motility, miosis (constricted pupils), sedation, reduced blood pressure and decreased respiration is also associated with euphoria [3]. Both substance and behavioral addictions are mediated through dopamine (DA) neurotransmission. DA is a primary neurotransmitter in reward pathways. DA is also responsible for emotion, cognition, motivation and euphoria and dysregulation of reward pathways and is considered the cause for addiction [4]. The dopamine neurotransmission is basis for addiction and related disorders through mesocortocolimbic dopamine projections from the ventral tegmental area (VTA) to the nucleus accumbens (NAc) [5].

Acute positive reinforcement, euphoria or the "high" is through the effect of DA and local opioid peptides through the common reward pathways *i.e.* VTA to nucleus accumbens (NAc) - amygdala reward system (5). Repeated replication of this positive reinforcement forms the basis of addiction.

Chronic substance use leads to neuroadaptation through decreased VTA mesolimbic and NAc DA neurotransmission [6]. Repeated use and excessive production of dopamine leads to down regulation of dopamine receptor sites. To experience the same level of euphoria again, an individual needs higher amounts. This forms the basis for tolerance. Also, stress results in increased production of corticotrophin releasing factor (CRF). This activates the hypothalamic-pituitar--adrenal axis (HPA) and other stress system like the amygdala [7]. This forms the basis for negative emotional states like dysphoria and anxiety. Individuals use substances to deal with these negative emotional states which promote addictive process. CRF adaptation may also explain role of stress and emotional states in craving for drug use (6).

Dysfunction of ventro-medial prefrontal cortex circuitry is the cause for impulsivity expressed as a sense of urgency, lack of evaluative and rational decision making processes [8]. This contributes to impulsive drug use.

Environmental cue-induced craving is mediated through hippocampus and basolateral amygdala [6].

The compulsive drug-seeking behavior is hypothesized to be driven by ventral striatal-ventral pallidum-thalamic-cortical loops [7]. Drug seeking behavior

CHAPTER 2

Urine Drug Screening (UDS) in the Management of Substance Use Disorders

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Abstract: Urine drug screens can add accountability to a patient's recovery plan. An upfront discussion of the role of the urine drug screen in treatment is important for a solid provider client therapeutic relationship. Substance use disorders are relapsing and remitting disorders. The goal of treatment is to extend the duration of sobriety until it is life-long, a lifestyle. The role of the urine drug screen in a treatment program should be therapeutic not penalizing. Understanding what a drug screen can and can not do in providing information is important. Using a consistent screen and appropriately certified laboratory is a must. This chapter covers the types of drug screens, the substances identified in a standard urine dug screen and provides guidance on when other substances may need to be requested during screening. Some substances such as "bath salts" are not identified in current urine drug screens. In clinical situations it will be important to confirm any positive results found on a urine drug screen. Common agents and medications that cause false positive or negative results are identified in the chapter. Proper process for obtaining and handling the urine sample including proper chain of custody are presented.

Keywords: Adulteration, Bath salts, Chain of custody, False negative, False positive.

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KEY LEARNING POINTS

1. Most urine drug screens test for 5 common agents *i.e.* amphetamines, cocaine, PCP, Opiates (codeine and morphine), marijuana. Other substances to be tested must be added to the test request.
2. Urine drug screens do not identify certain substances like "Bath Salts".
3. Urine drug screen positive results must be confirmed before their use in any clinical decision making.
4. Certain medications can interfere with the results of a urine drug screen.
5. For legal reasons chain of custody of obtained samples must be maintained.
6. Urine samples must be evaluated for pH, temperature, specific gravity and adulteration.
7. Know the issues regarding the urine drug screen performed at your facility – what is tested for routinely, what false positives may occur with the process utilized.

CLINICAL VIGNETTE

Charles works in a high stress job with a large company that has a random drug screening program. His most recent urine drug screen was positive for phencyclidine (PCP). Charles is in danger of being fired from his job. Looking at his medical record, Charles is being treated for high blood pressure, high cholesterol and anxiety. His medications are simvastatin, venlafaxine, propranolol and a multiple vitamin.

DIAGNOSTIC CONSIDERATION

In this patient a drug screen may have value for clinical management acutely and for follow up. A legal issue may also surface if this patient is actually fired. Charles is being treated with venlafaxine which can yield a false positive for PCP with some immunoassay urine screens. The confirmation test should verify the false positive. Based on that Charles would be in no danger of losing his job.

REASONS FOR OBTAINING AN UDS

1. Medical: UDS may be beneficial when the patient is presenting with unusual symptoms or acting in a strange fashion. In instances of emergency

presentation for overdose, seizure, or other situations a UDS can be of immense importance.

2. Legal: UDS may be required for employment, probation or other legal issues.
3. Therapeutic: UDS can assist in the clarification of a diagnosis as part of the work up of a differential diagnosis. Once diagnosed with a substance use disorder the use of urine drug screens can be useful in monitoring compliance with treatment and sobriety.

It is important to consider the reason for UDS and its usefulness as in the vignette above. It is interesting to note at times UDS adds a piece of the puzzle not a diagnostic conclusion [1].

Depending on the substance involved, the results of the UDS may impact treatment both in the acute and follow up phase. This may also provide a tool to help identify reasons for relapse from psychiatric illness or help correlate with triggers for reuse of illicit drugs.

With alcohol use disorders medications such as naltrexone and acamprosate may be continued in light of a confirmed positive urine drug screen for ethanol. Alcohol is not included in a routine UDS and must be requested in addition to the baseline urine drug screen. Should the UDS show positive for other substances, treatment may need to be adjusted to address the clinical needs of the patient.

When used with a narcotic treatment contract and contingency management the results of a confirmed positive or negative result for the opioid/opiate adds value to assist with sobriety from drugs. A positive UDS for another substance of abuse may result in termination of the narcotic agent depending on the contract. UDS for opioids are relatively unreliable, many do not test for the desired agent and like alcohol it is important to request they test for the specific agent being prescribed [4 - 6].

URINE DRUG SCREENS

It is recommended that urine drug screens be performed by a laboratory that is certified by the Department of Health and Human Services (DHHS). This guarantees the use of standardized testing processes and procedures to provide

CHAPTER 3

Genetics of Addiction

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Abstract: Addictive disorders are complex diseases influenced by both genetic and environmental factors. Heritability of these disorders is moderate to high. Genes that increase the risk of addiction to a substance actually increase the risk of addiction to other substances. This means it is mainly through broad externalizing pathways that genes increase the risk of addiction. The current level of our knowledge in genetics is less than enough to have clinical applications. Probably, in the near future, we will be able to provide our patients with individualized report about their susceptibility to addiction.

Keywords: Environment, Genes, Genotype, Heritability, Phenotype, Risk, Susceptibility.

KEY LEARNING POINTS

1. Addictive disorders are complex diseases where genes, environment, stage of development and race play a part.
2. Based on twin studies heritability varies with the type of drug addiction.
3. Because of the co-occurrence of addictions and mental disorders it is possible that common genetic mechanisms play a part in both.

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4. Some specific genes have been identified *e.g.* for alcohol addiction protection, nicotine addiction.
5. Due to rapid advances in the field of genetics the answer to the association of genes and addiction is within our reach in the near future.

GENETICS OF ADDICTION

Both the environment and the genes contribute to degree of risk of developing these diseases.

The risk of heritability of addictive disorders is moderate to high and it is not the same among different substances. Moreover, factors like age, developmental stage, sex and race affect the degree of that risk [1].

Behaviors that are considered addictive are heterogeneous in their genetic origins and in their manifestations, which makes it more difficult to understand the heritability of these behaviors [1].

Twin studies help with quantifying the heritability of different addictive disorders. The heritability for nicotine dependence is 33-71% [2], alcohol dependence 48-66% [3], cannabis addiction 51-59% [4], cocaine use disorder 42-79% [5], opioid addiction 23% [6] and disordered gambling 49% [7]. Overall heritability for addiction to various substances of abuse is about 30% to 60% [1].

Twin studies suggest that specific genetic factors predispose some individuals to develop addictive disorders that co-occur with mental health disorders [1].

There is still a lot of a discussion about the use of the terms substance abuse, dependence and addiction. These terms are often used interchangeably.

Developing studies that help understand how genes influence addiction is difficult when the above terms are poorly delineated [1].

Recent publication of the DSM- 5 could have an impact on future studies, as the diagnosis of substance abuse and the diagnosis of substance dependence were removed from DSM-5 and replaced with the diagnoses of substance use disorder and non-substance use disorders or behavioral addictions, like gambling, have

been added [8].

Researchers have discovered few specific genes that protect against or increase the risk of developing specific addictive disorders. For example, the (ALDH2) gene is protective against alcohol dependence because it decreases the ability of metabolizing acetaldehyde. The build up with acetaldehyde causes symptoms, like flushed face, anxiety, nausea and vomiting. This leads to decrease in alcohol use, which results in decreased risk of developing alcohol dependence [9].

Gene cluster CHRNA5/A3/B4, which is found on chromosome 15 is amongst the most replicated for association with nicotine addiction [10]. Interestingly, this gene cluster on chromosome 15 is also associated with cocaine addiction. No consistent association has been reported for cannabinoid receptor 1 gene. The gene encoding the mu-opiod receptor OPRM1 has been extensively studied as to its role in opioid addiction but this relationship has not been consistently replicated. For disordered gambling dopamine 1 receptor encoding gene (DRD1) was reported to be associated with this disorder but a recent study did not support this association [11].

Some of the most important genes for substance addiction are the dopaminergic genes, especially the D2 receptor genes, mainly because of the important role of dopamine in the reward system [1].

While providing education to patients, we need to avoid conveying the idea that alcohol dependence is genetic as we know that a significant portion of the risk is actually environmental [1].

SUMMARY

Addictive disorders have genetic basis with heritability risk ranging from 23 to 79%. A few susceptibility and protective genes have been identified.

PATIENT EDUCATION SHEET

What is the Relationship of Genes and Addictions?

Addictions are complex diseases like diabetes. Genes, age, sex, development stage

CHAPTER 4

Dual Diagnosis

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Abstract: Dual diagnosis exists when there is a substance use disorder occurring in conjunction with another non-substance mental health diagnosis. The presence of dual diagnosis is common and poses significant challenges to health care providers, due to both the increased severity and poorer treatment outcomes compared to when there is a single condition. Substance use disorders may develop in response to a mental health condition, although this is not always the case. A key diagnostic task is to conduct a thorough assessment that considers a full range of issues. Treatment should attempt to address both aspects of a dual diagnosis in an integrated and coordinated manner. If this is not possible, treatment for both conditions should at least be concurrent. This is in contrast to past perspectives embracing a sequential approach. Treatments for dual diagnoses are effective and may include a variety of interventions including psychotherapy, pharmacotherapy, and community self-help groups. The current chapter utilizes a case example to illustrate many of the relevant issues.

Keywords: Assessment, Comorbid conditions, Comorbidity, Dual diagnoses, Dual diagnosis, Substance use disorder, Treatment.

KEY LEARNING POINTS

1. Dual diagnoses occur when a person suffers from both a substance use disorder and another mental health diagnosis.
2. Dual diagnoses are very common.
3. A thorough assessment is crucial to identify comorbid disorders.

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4. Treatment options include pharmacotherapy, psychotherapy, and use of community supports (*e.g.* 12-step groups).
5. Treatment should target both conditions in a concurrent or integrated manner.

CLINICAL VIGNETTE

Ms. Q is a 34-year-old Caucasian woman who presents to your clinic complaining of sleep problems and feeling "overwhelmed". She states that her mood has been "down" for nearly a year since about the time of her separation from her fiancé with whom she lived. She has had significant difficulty maintaining contacts with friends and family and has little motivation to engage in activities she used to enjoy. She has grown increasingly isolated and her work is suffering due to problems with attendance and concentration.

An inquiry into current substance use patterns reveals daily alcohol use. She drinks approximately 4-6 shots of vodka most nights, which she says helps her sleep. She notes increasing tolerance over time and several failed efforts to quit. More recently, she has found herself taking a drink in the morning "to avoid the shakes". She began drinking heavily near the end of her last relationship and has continued to drink despite being charged with a DUI.

Further discussion reveals a significant preoccupation with safety and beliefs about the world being "totally dangerous." She reports walking in her neighborhood only when accompanied by her large dog and repeatedly patrolling her house with the dog at her side to ensure that all doors and windows are locked. Sleep is a significant problem for Ms. Q, and she states that she cannot easily fall asleep unless she is intoxicated. Even when intoxicated she is only able to sleep for 4-5 hours per night, partly because she is plagued by nightmares. The content of the nightmares is related to episodes of domestic violence that occurred during her relationship. The worst episode involved her partner brandishing a knife and threatening to slash Ms. Q's throat. This event was terrifying and eventually led to Ms. Q's flight from the relationship. Images of the violent episodes (particularly the threats at knifepoint) frequently intrude into her consciousness and cause emotional and physical agitation. She currently feels jumpy and easily irritated. She also reports having a sense that her future will somehow be cut short. She has never told anyone about the abuse and she makes significant efforts to avoid

reminders of the relationship.

BACKGROUND

The term dual diagnosis is defined in this chapter as the presence of a substance use disorder (of a substance other than nicotine and caffeine) in conjunction with at least one other non-substance mental health diagnosis. Mental health issues commonly seen in dual diagnoses include mood disorders, such as major depressive disorder and bipolar disorders, anxiety or trauma- and stressor-related disorders including posttraumatic stress disorder (PTSD), and psychotic illnesses such as schizophrenia. A broad definition of dual diagnosis is used in the current chapter rather than the more restrictive definition requiring the presence of a severe and persistent mental illness (*e.g.* bipolar or psychotic disorder). The term dual diagnosis as used in this chapter also excludes the presence of multiple mental health conditions without an associated substance use problem.

The presence of dual diagnoses poses a significant challenge to healthcare providers. Patients with dual diagnoses may not respond as well to mental health treatment, experience higher relapse rates, and have poorer treatment compliance. Additionally, symptoms in this population may be more severe than for those with just one condition [10, 11]. These factors, in addition to others such as likely increased functional impairments make caring for the dually diagnosed more complex.

Dual diagnoses are common. Large epidemiological studies such as the National Comorbidity Study, have found that over 40% of those who were diagnosed with a substance use disorder in the past 12 months also had another non-substance mental health disorder during the same time period. Lifetime comorbidities are even greater, with rates of 41-65% of those who have had a substance use disorder also having had a mental health problem at some point in their lives [8]. The disorders with the greatest likelihoods of lifetime prevalence in conjunction with alcohol use problems are conduct disorder and antisocial personality disorder, followed by anxiety and affective disorders [7]. More recent large-scale studies confirm the high incidence of current and lifetime comorbidity for substance use disorders and mental health issues [3, 5, 6].

CHAPTER 5

Pharmacologic Treatment for Psychiatric Disorders Associated with Substance Use Disorders: An Overview

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Abstract: Management of substance use disorders is challenging, there are no medications that directly treat the use disorders, substitution therapy in opioid use disorders and potential anti-craving medications for alcohol use disorder are the closest available. Successful management of withdrawal syndromes and craving can improve the chances of sobriety. The presence of underlying medical and psychiatric disorders can derail attempts at long term sobriety if not managed. This chapter provides information on medications commonly used in the management of withdrawal symptoms and co-morbid psychiatric disorders, such as depression and anxiety, in the dually diagnosed patient. Tables of medications from the following classes are included: benzodiazepines and other antianxiety agents, antidepressants, mood stabilizers, anticonvulsants and antipsychotic medications. Key points in the patient specific selection, dosing and monitoring of these medications and management of their side effects are identified. Insomnia can derail sobriety and needs to be addressed. Information on sleep hygiene and medications for insomnia are also presented. Information on the individualization of treatment is also discussed. It is important to note that many of the medications presented in this chapter are being used for both US FDA labeled and off-label indications.

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Keywords: Anticonvulsants, Antidepressants, Antipsychotic, Anxiety, Benzodiazepines, Depression, Insomnia, Mood stabilizers, Psychotic symptoms.

KEY LEARNING POINTS

1. Co-morbid psychiatric and medical diagnoses need to be adequately treated.
2. Medications do not treat substance use disorders but manage associated symptoms.
3. Effectively managing the symptoms of withdrawal and craving can improve outcomes.
4. Medication choice must be carefully matched to the individual.
5. Many medications are used off-label in the management of substance use disorders and their symptoms.

INTRODUCTION

In the management of substance use disorders, pharmacologic interventions are generally used for symptomatic treatment of withdrawal and intoxication states or the management of underlying or co-morbid psychiatric diagnoses. Very few substance use disorders have FDA approved medications that can be used to decrease craving and/or assist with sobriety, the exception is opioid abuse, which has substitution therapies that are FDA approved [1]. Therefore, many medications listed below are used off-label in an attempt to assist the patient in their relapsing and remitting battle with substance use or managing symptoms due to anxiety, mood, psychotic or sleep disorders.

Benzodiazepines (Table 1)

Targets: intoxication, withdrawal states, agitation

- Ongoing use of benzodiazepines in patients with substance use disorders should be avoided if possible. In situations of acute intoxication or withdrawal the use of benzodiazepines may be indicated for a short period of time.
- For acute use, lorazepam is generally the medication of choice. In some situations, a longer acting agent such as clonazepam, chlordiazepoxide or diazepam may be indicated. Choice is determined by reason for use, the required route of administration and the presence of active metabolites resulting in a

longer duration of action.

Table 1. Selected benzodiazepines.

Agent	Equivalent Dose*	Pharmacokinetics/Pharmacology	Dosing Routes Available
Chlordiazepoxide	25mg	Onset: Slow (45-60 min) Half-life: 24-96+ hours 4-5 active metabolites	Oral IM: absorption is erratic and use is not recommended
Clonazepam	0.5mg	Onset: Intermediate (30 min) Half-life: 24 hours Insignificant active metabolites	Oral
Diazepam	5mg	Onset: Rapid (15 min) Half-life: 20-89+ hours 2-3 Active metabolites	Oral IV (max rate 5mg/minute) IM: absorption is adequate in the deltoid only
Lorazepam	1mg	Onset: Intermediate (30 min) Half-life: 12 hours NO active metabolites	Oral IV (max rate 2mg/minute) IM: good absorption anywhere

*Monitor the patient, conflicting data exists here. Adapted from references [2, 3]

Antidepressants

Targets: Depression, Anxiety, Impulsivity

- Medication selection will depend on patient and medication variables. Patients with preexisting depression and/or anxiety should continue to be treated during treatment for addictive disorders. Depression and anxiety can also develop during treatment and as a side effect of medications such as naltrexone and acamprosate, and needs to be addressed.
- All antidepressants carry a Black Box Warning regarding new onset suicidal ideation and behavior in children, adolescents, and young adults (<25yrs). Use of antidepressants must balance risk *versus* benefit.
- The Selective Serotonin Re-uptake Inhibitors (SSRI) and the Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) are used in the treatment of both depression and anxiety with good effectiveness and safety profiles and generic versions are available.
- Mirtazapine an agent with a different mechanism of action, alpha-2 auto-receptor blockade which results in elevated levels of serotonin and

CHAPTER 6

Motivational Interviewing

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Abstract: Motivational interviewing (MI) is to motivate patients with addictive and non-addictive disorders like noncompliant patients, to help them develop skills to find intrinsic motivation for change through resolution of ambivalence . Ambivalence may lead to arguments against change referred to as sustain talk. Strategies to decrease sustain talk may promote change talk. These strategies include: straight reflection, amplified reflection, double sided reflection, emphasizing autonomy, agreeing with a twist, reframing, running head start, and coming along side. Five principles for creating condition for change are: expressing empathy, avoiding confrontation, supporting self-efficacy, rolling with resistance, and developing discrepancy between the patient's behavior and his/her own goals and values. Key skills needed for MI include: open ended questioning, reflective listening, affirmations, periodic summarization of the content of the session, and informing and advising with permission of patient. The successful therapeutic process for MI involves: establishing rapport, setting the agenda, assessing readiness for change, sharpening the focus to what the patient truly wants to change, identifying ambivalence, eliciting self-motivating statements, handling resistance, and shifting focus of conversation to get around resistance. The stages of change model is distinct from MI but naturally fit together. MI helps patients move from one stage of change to another *e.g.* from pre-contemplation, contemplation, preparation, action, to maintenance.

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Keywords: Affirmation, Ambivalence, Change talk, Commitment, Developing discrepancy, Empathy, Motivational interviewing, Open-ended questions, Reflective listening, Rolling with resistance, Self-motivating statements, Stages of change, Summarization, Sustain talk.

KEY LEARNING POINTS

1. Motivational Interviewing uses non-judgmental, non-confrontational, and a non-adversarial approach to help patient mobilize motivation to change behavior.
2. This change is through a focused and goal directed counseling by exploration and resolution of ambivalence.
3. This counseling involves open ended questioning, reflective listening, affirmations and periodic summarization of sessions.
4. The patient is made aware of behaviors and their consequences, is engaged in change talk and helped to mobilize intrinsic, not imposed, motivation for such a change.

BACKGROUND

Miller and Rollnick provide a technical definition of Motivational Interviewing (MI) where MI is considered a specific type of communication that is goal oriented and collaborative in nature with emphasis on language that leads to change. MI is intended to support personal drive for and commitment to change in a particular way by provoking and examining the individual's specific motivation for change, and it is conducted in a way that conveys empathy and nonjudgmental acceptance [1]. Even though this technique was specifically developed for patients with addictive disorders, it can be adapted for situations outside the field of addiction, for example, to increase patients' motivation for adherence to medical or mental health treatments, health promotion, problem gambling and dual diagnosis *etc*. This is supported by over 200 randomized clinical trials [2]. Highly interactive MI groups can also mobilize motivation to change [3].

PROCESS

MI theorists hold that MI is about aiding people resolve their ambivalence

(indecision or fluctuation where one feels two ways about an idea, feeling or action) in a specific trend of change. When a therapist pushes for change with an ambivalent individual, it results in the other person providing opposite arguments. Arguments against change are referred to as *sustain talk*. That is why, in MI, the interviewer tries to elicit *change talk* (self-motivating speech) from within the individual, and to strengthen that change talk. People are more likely to get convinced by what they themselves say. MI is not about forcing or tricking people to change. In other words, MI is a facilitative style to communication that induces natural change [1].

As part of MI, sustain talk is a normal aspect of ambivalence and should not be considered as resistance [1]. One can respond to sustain talk in ways that could increase or decrease it. There are various ways to respond to sustain talk that could result in its decrease and may promote change talk [1]. The strategies to accomplish this may include: (a) *straight reflection*, simple or complex reflective statements can sometimes promote change talk (b) *amplified reflection,* the reflective statement with the intention to exaggerate what the individual has said (c) *double sided reflection*, reflective statement recognizes both the sustain talk and change talk that was previously expressed by the individual (d) *emphasizing autonomy* which makes it easier for people to choose change, (e) *reframing* or providing a different perspective for what the patient is sharing (f) *agreeing with a twist*, a combination of both reflection and reframing (g) *running head start*: The purpose here is to hear out the main drives for motivations for unwillingness when change talk is not provided, and then to ask about the negative attributes of the current situation and the benefits of changing the target behavior (h) *coming along side*: this is used when all attempts fail to elicit change talk. Joining with the individual's sustain talk will occasionally induce some change talk.

There are five principles for creating condition for change. These are:

1. Express empathy by sharing an informed understanding of a person's ambivalence and reasons for hesitation.
2. Avoid arguments or confrontation and allow patient to hear themselves. This will decrease resistance to change.
3. Support self-efficacy by encouraging the patient to make positive statements

Section II: Substance-Related Addiction Disorders (Alphabetical)

CHAPTER 7

Alcohol Use Disorders

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Abstract: This chapter reviews the epidemiology and pathophysiology of alcohol use disorders. No two patients with alcohol use disorders are the same and recognition of these patients in our practice is the first priority. Diagnostic indicators and the CAGE questions that can be used to assist in the identification of patients with alcohol use disorders are presented. Non-drug therapies are integral and include lifestyle changes, group therapies (alcoholics anonymous), and individual therapies (*i.e.*, cognitive behavioral therapy). These and other non-drug treatment options are discussed in this chapter. Medication options for the management of outpatient alcohol withdrawal are discussed and include benzodiazepines and anticonvulsant agents (off-label use). Medications to assist in maintaining sobriety and reduce craving should be offered to all patients. Medications discussed in this chapter include acamprosate, naltrexone and disulfiram. The information presented includes discussion of patient specific characteristics such as renal and hepatic function and underlying psychiatric issues such as anxiety, depression and insomnia that may affect medication selection and outcome. This chapter includes key learning points and a patient vignette to assist the learner. A patient education sheet on alcohol use disorders and additional patient resources accompanies the chapter.

Keywords: Acamprosate, Alcohol withdrawal, CAGE, Craving, Disulfiram, Naltrexone.

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KEY POINTS

1. No two patients with alcohol dependence are the same.
2. Non-drug therapies are an integral part of treatment.
3. Medications to assist in sobriety and reduce craving should be offered to all patients.
4. Acamprosate may target relief drinking.
5. Naltrexone may target impulse drinking.
6. Disulfiram is most effective when used in a program that observes individuals taking the medication.
7. Desire to quit affects the success of medication and treatment.

CLINICAL VIGNETTE

Karen is a 32 year old female that presented to her primary care physician with complaints of "stomach pain" and problems with "nervousness and insomnia". Further questioning reveals Karen has recently separated from her husband and about 6 weeks ago was fired from her job because of being under the influence of alcohol while at work.

Karen reports she started using alcohol at age 17 and received two "minor in possession" citations and was required to attend mandatory chemical dependency treatment at age 18. Karen states her parents allowed her to use alcohol during her teen years and reported both parents struggled with alcoholism. By age 25 Karen received 2 driving under the influence charges, and had lost 3 jobs because of alcohol consumption, and the subsequent hangovers which led to excessive absenteeism. Karen reports her husband has been encouraging her to seek treatment and he finally separated from her because he reports she is an "angry drunk".

Karen began drinking beer daily, but over the past 2 years she has been drinking about a 1/5th of vodka every day.

Karen now believes her alcohol use is a problem because her husband has left her, citing her alcohol use as the reason. Karen reports she stopped drinking about one

week ago and notes the tremors and anxiety have decreased, but she continues to have problems with insomnia, anxiety and cravings for alcohol.

Karen's physical exam revealed an enlarged liver and lab work revealed elevated liver enzymes and a mean corpuscular volume greater than 100fl in an otherwise healthy appearing female.

The physician educated Karen regarding the undesirable effects of excessive alcohol use on mood, sleep, and anxiety, and also acknowledged and supported Karen's recent sobriety. The physician reviewed with Karen the risks and benefits of the available pharmacological treatments for alcoholism. This discussion included the risks of using medications during pregnancy and breast feeding. Karen was started on acamprosate and encouraged to attend Alcoholic Anonymous meetings on a daily basis.

INTRODUCTION

Alcohol Use Disorders (AUDs) can be devastating conditions that negatively impact every aspect of a person’s life. Frequently, AUDs impair psychological, social, interpersonal, educational and occupational functioning. AUDs may also contribute to violence, legal problems, employment difficulties and significant family conflict. Furthermore, those individuals afflicted with AUDs suffer from increased medical and psychiatric morbidity.

AUDs are responsible for a remarkable toll on the United States economy. The overall annual cost related to AUDs approached $185 billion in 1998 [1]. Alcohol use has been attributed to more than 60 different medical conditions, and nearly 40 percent of hospitalized patients receive treatment for complications of alcohol misuse, which accounts for 15 percent of healthcare cost [2]. Individuals with alcohol-related medical illnesses have more frequent hospitalizations and longer hospital stays compared to individuals without AUDs [3]. Untreated alcoholic individuals have at least a 100 percent higher general health care cost compared to nonalcoholic individuals [4]. In 1998 expenditures for health care services to treat AUDs and the medical consequences of alcohol consumption was estimated to be $26.3 billion [5].

CHAPTER 8

Anabolic-Androgenic Steroids (AAS) Related Disorders

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Abstract: This chapter discusses epidemiologic, pathophysiology and diagnostic issues associated with long term none medical use of Anabolic Androgenic Steroids (AAS) .These agents are synthetic derivatives of the hormone testosterone with higher bioavailability and activity [1]. These drugs are used by athletes to gain muscle mass thereby gaining advantage. As a result many users often don't disclose their use to their doctors [2, 3]. Medical complications may include, hypertension, cardiomyopathy and hypogonadism. Psychiatric complications may include mood and psychotic disorders [4]. Withdrawal may lead to dysphoria and irritability. Patients usually do not consider themselves as addicted. They traditionally think that they are more knowledgeable about these drugs than their doctors [2, 3]. In USA, AAS are currently schedule class III drugs requiring prescription, however they can be easily obtained online from other countries.

KEY LEARNING POINTS

1. Illicit Anabolic steroid none medical use poses a worldwide public health problem.

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2. About 30% of Anabolic steroid users develop a clinical dependence syndrome with, chronic use despite adverse effects on physical, psychosocial, occupational or school functioning [5].
3. Dozens of formulations exist with different administrations routs (oral, IM and IV injection, and topically in the form of cream or gel. Amounts used may reach 10 to 100 times the usual therapeutic doses.
4. Medical morbidity with AAS use may include hypertension, dyslipidemia, cardiomyopathy, hypogonadism, hepatic dysfunction and HIV/AIDS hepatitis B and C due to sharing dirty needles.
5. AAS have been associated with the development of mania, hypomania, psychosis or uncontrolled anger ("roid rage"). AAS withdrawal symptoms are associated with craving, irritability, dysphoria, depression with or without suicidality.
6. AAS differ from classical drugs in that intoxication produce little immediate reward or "high", but instead has a delayed reward of muscle mass gain or "bulking".
7. Anabolic Steroids are classified in Schedule III. Among all the substances in Schedules II or III ASS are the only ones that are no identified with a specific use disorder in DSM- 5 [5].
8. AAS are illegal in the USA without a medical Prescription, But they are available over the counter in many countries, and are easily ordered online.
9. Anabolic steroid use can be a gateway drug to other substances including opioids [6].

CLINICAL VIGNETTE

A 17 year old male presented with his mother for a follow up appointment with his pediatrician. The lab results showed high LDL and low HDL, mild elevations of AST and ALT. blood pressure was 132/89. The initial reason for the visit was the treatment of acne on the upper back and chest that was resistant to over the counter treatment. The patient stated that he was currently a member of the high school football team, and that he had gained significant weight in the previous year. His mother complained that his gets easily angered, On one occasion she asked him to leave the house until he calms down. She noted that patient spent more time in the gym, He spends much less time with with his girlfriend or

playing his guitar with his friends as he used to do. His grades were falling and he was skipping school in order to go to the gym .

EPIDEMIOLOGY

Epidemiological survey in the US in the last 2 decades have estimated that 3% to 11% of male high school students have used AAS. The number of AAS users in the United States is estimated around 3 millions [7].

Anabolic steroid users are mostly none athletes who use the drugs for cosmetic reasons. A subset of this group suffers from an excessive a preoccupation by body image muscle dysmorphia (a subjective perception of being small and week) [8],

Research pointed out that Up to 6% of athletes abuse anabolic steroids to enhance performance in competitive sports or just a desire to increase physical attractiveness [7]. The 2004 Monitoring the Future report noted that that there was a decline in use among adolescents in grades 8 and 10 but not among 12^{th} graders.

About 30% of anabolic-androgenic steroids users appear to develop the classical picture of dependence syndrome.

2.7-2.9% of young American adults have taken AAS at least once in their lives [9].

DIAGNOSIS, AND CLINICAL PRESENTATION

DSM-5 does not have specific anabolic-androgenic steroid use disorder listed. However the symptoms and signs of these disorders can fit in the in one or more of the following categories.

Other (or unknown) Substance–Related Disorders, Other (or unknown) Substance Use Disorder, Other (unknown) Substance Withdrawal, Other (or unknown) Substance– Induced Disorders or Unspecified Other (or unknown) Substance–Related Disorder (non-substance use) disorder".

Individuals using ASS may present with well-developed muscularity of the upper body with on occasions needle marks in large muscles, acne, pigmented striae on skin, excessive facial body hair, obsession with weight training, dissatisfaction

CHAPTER 9

Caffeine Related Use Disorder

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Abstract: 80% of the World's population consumes caffeine. Its impact on mental health often goes unrecognized. Caffeine use has comorbidity with other substance use disorders. Caffeine is a methylxanthine and exerts its actions by inhibiting adenosine receptors. Caffeine is a stimulant, mild to moderate use has beneficial effects like improving attention and concentration, but problem use can mimic anxiety, sleep and mood disorders. High dose caffeine can even result in death. In this chapter, we discuss common presentations of caffeine use disorders, their recognition and management. Caffeine withdrawal can present with mood disturbance and headaches, instant alleviation of these symptoms with caffeine perpetuates its use. Caffeine withdrawal with abrupt cessation typically lasts 2-4 days. Calculating baseline consumption and gradually reducing the caffeine intake can address the impact of the withdrawal symptoms.

Keywords: Adenosine, Caffeine, Caffeine intoxication, Caffeine use disorders, Caffeine withdrawal, Methylxanthine.

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KEY LEARNING POINTS

1. Caffeine is the most commonly used psychoactive substance around the globe. It exerts its stimulant action by inhibiting adenosine receptors.
2. Caffeine is consumed mainly as coffee. Also it is consumed in tea and caffeinated sodas. In adolescents energy drinks with high amounts of caffeine is a popular way to consume caffeine.
3. Caffeine related disorders are caffeine intoxication and caffeine withdrawal. Caffeine can cause anxiety like symptoms as well as caffeine induced sleep disorder.
4. Caffeine at low to moderate doses, *i.e.* less than 300mg, may cause positive effects like increased arousal and energy. However at high doses, *i.e.* greater than 400mg, it can cause negative effects like restlessness, nervousness and psychomotor agitation.
5. Caffeine can also cause cross sensitization with nicotine related disorders.

CLINICAL VIGNETTE

A 25-year-old male patient was referred by his employer for a psychiatric evaluation as he was observed to be “hyper”. The patient reported that following departmental restructuring, he was taking on more responsibility. He reports experiencing poor sleep and anxiety about work. He reported being restless and exhibited pressured speech. He was sleeping only 4 hours and did not find sleep to be restful. He reported occasional panic attacks. He also reported seeing flashes of light occasionally. He has a history of smoking a pack of cigarettes a day but denied using illicit drugs. He reported drinking 5-6 cups of coffee and 2-3 energy drinks to promote alertness. He claimed that he tried to cut down on coffee. However on days he did not drink coffee he reported experiencing poor concentration, fatigue, headaches and depressed mood.

The patient reported recently he tried to cut down to 1-2 cups of coffee but had to increase his caffeine consumption to boost his energy to handle his increased work responsibilities and that it helped his fatigue and headaches also. He calculated his daily caffeine intake of 800-900 mg.

On physical examination, he had a pulse rate of 103. Urine toxicology screen was

negative for illicit drugs. With this history and physical examination the patient was diagnosed to have caffeine related disorder.

Following education and advice on the role of coffee in his recent symptoms and work related problems, he reduced his caffeine intake by 25% every week. Following reduction of his coffee intake, he noted a gradual improvement in sleep, concentration and fatigue.

DISCUSSION OF THE VIGNETTE

Recognition

Caffeine is the most commonly used psychoactive substance in the world [1]. Because of its common use, most patients do not associate its effects with any psychiatric problems. Excess coffee consumption can present with insomnia, restlessness, anxiety and excitement such as that experienced by the patient in this vignette [1]. The patient has been using increasing amounts of caffeine to improve his attention and concentration and work performance. This resulted in the development of tolerance. Tolerance to insomnia took longer to develop.

DIAGNOSTIC CONSIDERATIONS

In this vignette our patient escalates his coffee consumption to cope with increased work related stress due to increased work responsibilities. This escalation also coincided with onset of his symptoms. Specifically, the patient was using caffeine to improve his concentration. Chronic use of caffeine leads to tolerance requiring higher amounts of caffeine to achieve the same results at work. Because of this he exhibited symptoms of caffeine intoxication manifesting as restlessness, rambling speech, excitement, insomnia and tachycardia [2]. Other common symptoms associated with caffeine intoxication are nervousness, flushed face, diuresis, gastrointestinal disturbances, muscle twitching, inexhaustibility and psychomotor agitation. When 5 or more of these symptoms are present and cause clinically significant distress or impairment a diagnosis of caffeine intoxication can be made [2].

This patient also experienced caffeine withdrawal characterized by symptoms

CHAPTER 10

Cannabis and Cannabinoid Use Disorders

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Abstract: Cannabis or marijuana also called pot, grass, weed, herb *etc.* is derived from flowers, leaves, stem or seeds of cannabis sativa plant. It is consumed by smoking or mixing it with foods and beverages. Hashish is a resinous material made from cannabis plant . Cannabis and illicit synthetic THC compounds like "spice" K2" have similar psychoactive effects which are mediated through binding with cannabinoid receptor CB1. Whereas binding with CB2 receptors impacts immunity. Anandamides are the endogenous ligands for these receptors. THC is lipophilic and is deposited in fatty tissue and can be detected in the urine in chronic cannabis users for up to 30 days. THC synthetic compounds, Dronabinol (Marinol) and Nabilone (Cesamet) are approved for medicinal use in oncology, ophthalmology and AIDS. CB1 receptors binding in hippocampus causes short-term memory problems whereas binding in nucleus accumbens causes euphoria. Psychiatric disorders are mood and anxiety disorders. Psychosis is also reported. Genetic factors, as evidenced by twin studies, contribute from 30 to 80% variance to this risk. There are no pharmacological treatments approved for cannabis withdrawal. Short-term symptomatic treatment with non-benzodiazepine anxiolytics, antidepressants, or hypnotics may be considered. Cognitive-behavioral, motivational enhancement and family therapy, contingency management and self-help groups are valuable psychosocial treatment options.

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Key words: Anadamides, Cannabinoid receptors CB1 and CB2, Cannabis, Grass, Hashish, Hemp, Herb, Herbal Incense, K2, Marijuana, Pot, Spice, Synthetic Cannabinoids, THC, Weed.

KEY LEARNING POINTS

1. The main psychoactive substance in cannabis is delta-9-tetrahydrocannabinol (THC). It exerts its psychoactive effect through cannabinoid receptor CB1.
2. Cannabis is consumed in a variety of ways; smoking has a faster onset, with three times more potency than oral use and is the most common route of consumption.
3. Cannabis related disorders are: cannabis use disorder, cannabis intoxication, cannabis withdrawal and cannabis-induced psychosis, anxiety, sleep disturbance and delirium.
4. Cannabis- induced disorders are more prevalent in patients suffering from other psychiatric disorders.
5. Treatment options include treatment of comorbid psychiatric disorders, motivational enhancement therapy, cognitive-behavioral therapy, contingency management and family based interventions.
6. Synthetic cannabinoid agonists have been available in Europe since 2004 and are now available in most other countries, under the street brand names K2 and Spice.

CLINICAL VIGNETTE

A 17-year-old male was brought to the clinic by his mother, following a recent history of poor academic performance. She feared that her son is depressed as he appeared more withdrawn, and had been sleeping and eating more. He had been missing school lately, and his grooming and hygiene had declined. On questioning, the patient admitted to yearlong difficulties with attention, concentration and memory. As a result, his grades have dropped from A's and B's to D's and F's. He denied any depression and reported feeling "great". His attention span and recall were impaired. He reported feeling anxious and had occasional panic attacks. He did not exhibit symptoms of psychosis. He denied

any illicit drug use.

Physical examination was positive for conjunctival injection and a pulse rate of 103. Urine toxicological screen tested positive for carboxy-tetrahydrocannabinol. When the patient was confronted with the positive urine drug screen for cannabis, he admitted to smoking marijuana about 2 hours ago. He stated that he had been smoking about 6-8 "joints" daily for a year. He did not feel that cannabis use was a problem. He admitted to experiencing irritability, nervousness; sleep problems and restlessness when he did not smoke "pot". A motivation enhancement approach was used, discussing the consequences of use with benefits of change. Relaxation exercises and distraction techniques were utilized to cope with withdrawal. Random urine drug screen for THC was instituted with a reward of his favorite comic book contingent on negative urine drug screen. During one year follow up patient reported using marijuana once.

DISCUSSION OF THE VIGNETTE

Recognition

Cannabis (also called marijuana) is the most widely used illicit drug in the United States. Owing to its illicit status, patients are often not truthful about this drug use. THC is lipophilic, and deposits in the adipose tissue with chronic use and is slowly released. Hence cannabis can be detected with routine urine drug screening for up to 30 days following cessation of chronic use, and up to 3 days following acute use. Acute intoxication, as noted in our patient, may cause conjunctival injection, tachycardia, and increased appetite; whereas withdrawal symptoms include irritability, nervousness, sleep problems and restlessness. The psychoactive effects of THC are mediated through binding with cannabinoid receptor CB1. Binding to cannabinoid receptors in the hippocampus causes short-term memory difficulties. This negatively impacts cognitive functioning causing impairment of academic achievement. The statement of feeling "great" in our patient was likely to be related to binding of THC with cannabinoid receptors in nucleus accumbens, a reward center in the brain.

CHAPTER 11

Ecstasy Substance Use Disorder

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Abstract: Ecstasy or 3, 4- methylenedioxymethamphetamine also called a club drug because of its use in "rave" parties has both stimulant and psychedelic effects. Stimulant effect which precedes psychedelic effect causes euphoria. In addition through release of oxytocin prosocial and empathic behavior as well as sense of intimacy is experienced. The psychedelic effect causes distortion of sensory perceptions. This drug is popular with adolescents and young adults and often associated with prolonged weekend "rave" parties. Its use causes depletion of serotonin which may cause depression and suicidal behavior. Depression may also be caused by "crash" from stimulant effect. With intoxication of ecstasy patient often experiences autonomic effects like elevated blood pressure, elevated temperature, cardiac arrhythmia, and panic attacks. In addition patient may experience headaches, vertigo, seizure and loss of consciousness. For intoxication treatment is supportive and symptomatic. There are no specific medications for its treatment. Psychosocial interventions like cognitive behavioral therapy, social and coping skills training and treatment of comorbid psychiatric disorder are very valuable options.

Keywords: Club drug, Ecstasy, MDMA, Oxytocin release, Pro social and pro empathy drug, Rave parties.

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KEY POINTS

1. Ecstasy or MDMA is an acronym for (3, 4-methylenedioxymethamphetamine) is so called "club drug". It has both stimulant and psychedelic properties. The former effect gives euphoria, interpersonal warmth and sense of intimacy and the later relates to distortion of sensory perceptions and time. It is also reported to provide enhanced pleasure through tactile experiences.
2. MDMA synthesized in 1900s in Germany. In 1970s some psychiatrists used MDMA as a psychotherapy tool without evidence of its benefits.
3. MDMA is considered empathomimetic due to its indirect activation of serotonin system and increased release of oxytocin.
4. In 1985 because of no medical benefits but significant abuse potential MDMA it was classified as schedule I drug. MDMA is an addictive drug and tolerance can happen too.
5. MDMA use became popular with adolescents and young adults in "rave", all night weekend nightclub parties. However its use has spread to other settings and demographics.
6. MDMA is neurotoxic to serotonin neurons and therefore can deplete serotonin leading to depression usually during early part of week when the effect of drug has worn off and person crashes which may increase suicidality so called "Tuesday Suicide".
7. Undesirable effects like anxiety, irritability, restlessness, sadness, impulsivity, aggression, sleep problems, reduced appetite and interest in sex and reduction in mental ability may last for up to o one week.
8. Intoxication and overdose with MDMA may cause elevated blood pressure, dizziness and fainting episodes, panic attacks, loss of consciousness and seizures.

CLINICAL VIGNETTE

A group of men brought a young man who appeared restless with heavy breathing to the local hospital ER in the early morning hours. A friend volunteered to report that they were in a rave party that lasted nine hours. He reported that his friend until half an hour ago seemed fine but started to complain of headache and became slow and sluggish and his speech became slow, also. The young man

reported that at this site of the party "they were selling the bottle of water for 6 dollars" and water from outside was not allowed. Therefore his consumption of fluids was limited. He added that his friend may have used Ecstasy and marijuana which he occasionally does. He was not sure however about the amount of Ecstasy the patient consumed. The vital signs were as follows: temperature 103, pulse rate 140, BP 148/92 and respiration rate 29, dry skin and tongue was suggestive of dehydration which was later confirmed by urine specific gravity. Patient was given IV saline to hydrate him. Gastric lavage with activated charcoal was done. Liver functions were normal. For sedation diazepam 5 mg was given orally.

DISCUSSION OF THE VIGNETTE

Based on history and urine drug screen Ecstasy use disorder was diagnosed. Gastric lavage with activated charcoal was performed. Elevated temperature was a symptom of Ecstasy use and dehydration. If untreated, this may progress to hyperthermia. Sodium level was normal. Agitation is treated with a benzodiazepine in this case diazepam which benefited agitation. Low potency neuroleptics like chlorpromazine should be avoided due to its intrinsic anticholinergic effects which can further elevate temperature. Due to the hepatotoxicity of MDMA hepatic functions should be evaluated which were normal in this patient. Blood pressure and elevated heart rate due to noradrenergic effects should be monitored.

NEUROPSYCHOPHARMACOLOGY

MDMA releases monoamine neurotransmitters (serotonin, norepinephrine and dopamine) in the brain [1] causes indirect activation of serotonergic system. Through 5HT 1A receptors MDMA increases release of oxytocin which promotes prosocial behavior [2, 3]. Oxytocin is typically released during hugging, sexual orgasm as well as child birth. Long term use of MDMA can cause neurotoxic effects on serotonin neurons causing depletion [4, 5] leading to depression and suicidal behavior. This is more often during mid-week [6]. Therapeutic effects of MDMA in Anxiety disorders are hypothesized to be due to increased oxytocin, increase in ventromedial prefrontal activity and as a result decrease in amygdala

CHAPTER 12

Hallucinogen-LSD Use Disorder

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Abstract: LSD is the most potent hallucinogen. This as well as other hallucinogens have been used for religious rituals by Native Americans for centuries. LSD chemical structure has similarity to serotonin and works through post synaptic 5-HT2A receptor agonistic effects. LSD was first synthesized in late nineteen thirties. LSD intoxication significantly increases central autonomic activity leading to panic states, tachycardia, increased blood pressure and body temperature, pupillary dilatation, piloerection, tremor and hyperreflexia. The panic states, perceptual disturbances and flashbacks are often referred to as "trips". Patient may experience these "trips" long after cessation of its use. Subjective effects of LSD start with somatic symptoms followed by perceptual disturbances, lability of mood, depersonalization, altered sense of time, visual distortions, mixing of sensations like "seeing" smells and "hearing" colors. This mixing of sensations is called synesthesia. LSD is not addictive but tolerance to behavioral effects and cross tolerance to other hallucinogens drugs are reported. Acute intoxication results in somatic, perceptual and psychic effects. Some patients also relive these experiences through flashbacks even long after cessation of its use. No withdrawal symptoms are reported. Long -Term effects of LSD use may include psychosis, depression, paranoid delusions and flashbacks. The treatment therefore will consist of targeting the specific clinical syndrome like with SSRIs for depression, antipsychotics like chlorpromazine for psychosis and bad "trips". As with acute effects safety of the user must be assured and may require inpatient admission. Comorbid mental disorder should be treated to improve outcome. Cognitive behavioral therapy, social skills enhancement training can help to improve adaptive functions.

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Keywords: DMT, Ergot derivative, Hallucinogen, LSD, LSD Trip, Lysergic Acid, MDA, Synesthesia.

KEY LEARNING POINTS

1. Hallucinogens include indole derivatives with structural similarities to serotonin. These are lysergic acid diethylamide (LSD), psilocybin, dimethyltryptamine (DMT). Other hallucinogens are substituted phenethylamines derivatives like mescaline, dimethoxymethylamphetamine (DOM), methylenedioxyamphetamine (MDA) and methyenedoxymethamphetamine (MDMA or Ecstasy). Phencyclidine (PCP) and cannabis. This chapter will primarily focus on LSD. PCP and cannabis are covered in other chapters.
2. LSD was first manufactured in 1938 from lysergic acid an ergot a fungus that grows on rye grain. In the USA its use became prevalent in the 1960's.
3. LSD is one of the most potent hallucinogens. Even 20 micrograms of the drug may manifest full behavioral effects; street doses range between 10-300 micrograms. Because of its high potency LSD it is applied to blotting paper and sold as pieces of it or applied to the back of postage stamps.
4. LSD is rapidly absorbed from the gastrointestinal track, easily crosses the blood brain barrier with behavioral effects manifesting within 60 minutes and peaking in 2-4 hours. The effects may last up to 12 hours.
5. The hallucinogenic activity of LSD and other serotonin class hallucinogens is possibly due to postsynaptic 5HT2A receptor agonism.
6. LSD significantly increases central autonomic activity. As a result the person may experience panic states, tachycardia, increased blood pressure and body temperature, pupillary dilatation, piloerection, tremor and hyperreflexia. The panic states, perceptual disturbances and flashbacks are often referred to as "trips". LSD is classified as Schedule I substance.
7. Subjective effects of LSD start with somatic symptoms followed by perceptual disturbances, changes in mood with lability, depersonalization, altered sense of time, visual distortions, mixing of sensations like "seeing" smells and "hearing" colors. This mixing of sensations is called synesthesia.

8. LSD is not considered an addictive drug. It lacks compulsive drug-seeking behavior.
9. With chronic use tolerance develops to behavioral effects but not to autonomic effects. Cross tolerance develops to mescaline and psilocybin but not to other drugs like PCP and cannabis.
10. There are no withdrawal symptoms following abrupt cessation of chronic use of LSD.

CLINICAL VIGNETTE

A twenty-one year old single white male presented to the office after discharge from the hospital. He stated that he has been having memory lapses. Prior to hospitalization he was found sitting on a residential patio. When residents of that house returned the person did not leave and therefore they called the police. He was arrested and ticked for trespassing. The police took him to the hospital rather than to the jail. When he woke up later that night in the hospital he stated he has no memory of that day. He had a similar experience about three months ago and doesn't recall what happened then either. On further questioning, he said he got into trouble at work last month because he missed a day of work and didn't realize it. He just got up one morning and went to work and was told he missed the day before and he couldn't remember the day before. It was just like it never happened. He is otherwise in good health. His Mini Mental Status Examination (MMSE) score today was 30/30. He was neurologically intact. Physical examination was normal. He worked as an electronics and computer sales person. He appears to be of average to above average intelligence. He denied the use of alcohol. He stopped using marijuana as his job performs random urine drugs screen. He stated he uses LSD frequently which he enjoys, it makes him hallucinate and provides him deeper insight about his own self. He first used LSD about four years ago. Since then he has used it every week or two. He denied craving about its use or spending lot of time in acquiring or using the drug. He stated that he has experienced LSD "trips" of variable intensity. He did not know the reason for variability in intensity or duration of "trips". He states he is a little "fuzzy" each time he comes "down" and that may be part of his memory problems. He denied illicit use of other drugs.

CHAPTER 13

Inhalant Use Disorders

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Abstract: Inhalation of volatile hydrocarbon-based substances produces intoxication and pleasurable effects. Use of inhalants usually starts in adolescence ages 12 to 17 often precedes use of tobacco, alcohol and illicit substances. It decreases gradually after the age of 20 years. These substances are lipophilic, cross the blood-brain barrier rapidly and cause CNS depressant effect mediated through gamma-aminobutyric acid (GABA) agonism or NMDA receptor antagonism. In addition to CNS toxicity these substances also have significant toxicity to other body organs like liver and kidneys. Prolonged use may lead to neurocognitive disorders, anxiety and even psychosis. Use of inhalants can lead to serious medical complications such as cardiac arrhythmias and seizures. Sudden heavy sniffing may lead to death due to asphyxiation. Intoxication syndrome includes euphoria, excitation, disinhibition, slurred speech, memory impairment and delirium and coma with high doses. Sudden discontinuation of inhalants may lead to a withdrawal syndrome similar to alcohol. However benzodiazepines, other CNS depressants and adrenergic drugs should be avoided. Psychosocial interventions are valuable.

Keywords: Asphyxiation, Choking, Cleaning fluids, Deodorant spray, GABA, Gases, Gasoline, Glues, Hair sprays, Nail polish remover, Neurotoxicity, Nitrites, NMDA, Spray paints, Volatile hydrocarbons.

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KEY LEARNING POINTS

1. Inhalants are volatile hydrocarbon-based substances when inhaled in a vapor form produce intoxication and pleasurable effect.
2. Inhalants are aerosols or volatile solvents like glues, gases, spray paints, nail polish remover, hair sprays, deodorants, gasoline, cleaning fluids, and nitrites. These don't include drugs that are sniffed or inhaled after burning like cannabis.
3. Most inhalants are central nervous system (CNS) depressants and can cause serious harm to vital organs including liver, heart, kidneys and brain.
4. Inhalants cause rapid high with excitation followed by drowsiness, disinhibition, light headedness and agitation. High amounts can produce confusion, delirium, anesthesia and loss of consciousness.
5. The effects may include diplopia, memory impairment, slurred speech, cardiac arrhythmias "sudden sniffing death" or death by asphyxiation, suffocation, seizures, coma, choking or motor vehicle accident.
6. Neurotoxic effects due to prolonged use may range from mild cognitive impairment to dementia.

CLINICAL VIGNETTE

A 14 year old male was brought to the emergency room (ER) by the ambulance. The patient was found unconscious by his mother with a rag soaked with gasoline in his hand. Pants and Underwear soaking wet, and smell like urine. On arrival at the emergency room he was confused and disoriented, with a gasoline odor on his breath. Examination also showed conjunctival injections, bilateral basal rales on auscultation, nystagmus, psychomotor retardation and Pulse: 53/Min. Complete blood count showed moderate leukocytosis and normocytic anemia, arterial blood gases showed mild hypercarbia.

DISCUSSION OF THE VIGNETTE

The vignette demonstrates a clinical history suggestive of acute intoxication with

gasoline, with neurologic, cardiac and pulmonary symptoms. Some of the neurologic symptoms and signs resembled alcohol intoxication. Patient was placed in a low stimulation environment. Most symptoms resolved within 2 hours with supportive interventions.

DIAGNOSTIC CONSIDERATIONS

The diagnostic criteria listed in DSM-5 for inhalant-related disorder are: presence of two out of 10 symptoms during 12 months period. These include use of large quantities inhalant use for more than intended period, tolerance, craving and inability to cut down their use, compulsive use despite health consequences, large amount of time spent to acquire or recover from their effects and as a result failure to meet social, occupational, recreational or role obligations. Specifiers include type of inhalant used, early or sustained remission [1]. With long-term use a withdrawal syndrome characterized by irritability, anxiety, restlessness, insomnia and tremor may manifest. In DSM-5 Inhalant -Related disorders are listed, as Inhalants use disorder, Inhalants Intoxication, Other Inhalants-Induced disorders and Unspecified Inhalants use disorders. The diagnosis is generally by history. Breath saliva or urine may aid in diagnosis of inhalant use or non-inhalant substance use disorder.

EPIDEMIOLOGY

Children and adolescents between 12-17 living in poverty, homelessness and from an ethnic minority are at higher risk. Inhalants are important gateway drug. 2011 Monitoring the Future (MTF) survey of 8^{th}, 10^{th} and 12^{th} graders revealed that 31.1 percent of 8^{th}-graders have used inhalants in current or past-year [2]. According to 2010 National Survey on Drug Use and Health (NSDUH) 793,000 individuals aged 12 and older used inhalants for the first time during the last 12 months; 68.4 percent were under the age of 18 [3]. The inhalant use disorder frequently remits after adolescence and therefore significantly declines after age 20.

CLINICAL PSYCHOPHARMACOLOGY

There are thousands of inhalant compounds that are easily accessible and legal to obtain for industrial and house hold uses. These products include adhesives,

CHAPTER 14

Opioid Use and Addictive Disorder

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Abstract: This chapter discusses epidemiologic, pathophysiology and diagnostic issues associated with opioid use disorders. Differentiation of the recreational user and the user who was prescribed narcotics for a diagnosed pain issue is an important variable in the approach to management. Absolute sobriety from opiates/opioids is difficult to achieve and a multifaceted approach is a necessity. This chapter also describes non-drug therapies used in the management of opioid use disorders, including narcotics anonymous, cognitive behavioral therapies and others. For many patients, substitution therapy may be necessary for the short or long term to prevent further issues with opioid use and a better outcome. Buprenorphine substitution therapy requires special provider training while methadone must be dispensed by a licensed opiate treatment program. Withdrawal from opioids is not life threatening but is subjectively very distressing. Management of opioid withdrawal can include treatment with buprenorphine or methadone resulting in relief of withdrawal symptoms and then slowly tapering off the medication. Alternatively non-opiate agents such as clonidine and other medications for symptom relief are used to ameliorate withdrawal. The chapter includes key points and a case vignette to assist the learner. A patient education sheet and further resources are included.

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Keywords: Buprenorphine, Clonidine, Methadone, Naloxone, Naltrexone, Suboxone, Substitution therapy, Subutex.

KEY LEARNING POINTS

1. The natural opiate products are morphine and codeine. These are made from opium which is extracted from the poppy plant.
2. Synthetic opioids include, heroin, hydromorphone, oxycodone, hydrocodone, meperidine, methadone and fentanyl.
3. Withdrawal from opioids is not dangerous but is subjectively very distressing.
4. Absolute sobriety from these drugs is rather difficult to achieve. Relapse is common, expect it, then get the patient back on the path to recovery.
5. Treatment of opioid use disorder is multifaceted. Treatment of comorbid psychiatric disorder(s) improves outcome.
6. Substitution therapy with buprenorphine or methadone or narcotic antagonist therapy is often required for a better outcome.

CLINICAL VIGNETTE

Sharon, a thirty-four year old married, ill-appearing white female, presents to your office stating that she is having a problem with her "pain pills." On further questioning, she provides the following information. She has been overusing the oxycodone (Oxycontin) that she has been getting for her chronic back pain. She says she is not even sure how much her back really hurts any more. She will also use hydrocodone (Vicodin) and oxycodone and acetaminophen (Percocet) because they are easier to get and she doesn't get questioned about these very often, but she worries about the acetaminophen content of these and possible liver damage. She prefers Oxycontin when she can get it, but finds it harder to obtain. She has gone to several different doctors and filled prescriptions at several different pharmacies so as to not raise any questions or arouse suspicion. She has friends that can help her get these medications on the street as well, and acknowledges that she has been doing this more over the past few months, at considerable expense. She has used as many as ten 80mg Oxycontin pills in a day. Most recently, she has been crushing these and snorting the powder to get a more immediate effect, instead of taking them orally. She reluctantly admits she has

also tried intravenous use after a couple of friends encouraged her to try this and showed her how to prepare and inject it. She then states "And I'm not very good at it" as she exposes her left anterior forearm to show you multiple infected injection sites and needle tracks.

Sharon provides the following history: She grew up with both parents, a brother and sister with no family history of drug or alcohol problems. She did very well in school and graduated from high school at age eighteen. She received an athletic scholarship to attend college and play volleyball. She went to college and majored in social work. She played volleyball for all four years and did well. She hurt her back in her third year however, and this lead to her first use of opioids. She was provided Vicodin and took this so she could continue to play even when her back hurt. She graduated and married when she was twenty-three. Her husband is three years older and is a civil engineer. They now have three children, ages 5, 9, and 10. Her husband is quite successful and as a result she has not had to work. Her husband is aware of the patient's problems, though probably not to the complete extent or the severity. She feels her husband is probably losing patience with her. She has tried to quit on several occasions. Her use has varied over the past years with rapid escalation over the past two years. She acknowledged some limited marijuana use while in college but has had no use since. Her alcohol use has been moderate since her late teens. She has been very active socially with her own and her husband's friends and families. She stated she usually works out in a gym daily where she has met her "using" friends. On examination, Sharon says she is "withdrawing", and feeling "sick" having not used any opioids for over eighteen hours. She says she wants help in quitting so she can get things together and "save my marriage and life". She stated "I love my family and this is no way to live". She stated she hurts all over, she is nauseous and has diarrhea. Her vital signs are blood pressure 155/95, pulse 105, respiratory rate 22 and body temperature 100.6F.

Sharon's opioid withdrawal is anticipated to worsen, but of immediate concern was the left forearm. CBC showed markedly elevated WBC. One abscess required incision and drainage. Culture showed the bacterial agent to be Methicillin Resistant Staphylococcus Aureus (MRSA). Sharon was hospitalized and treated with IV vancomycin. Opioid withdrawal was managed with clonidine 0.1 mg

CHAPTER 15

Phencyclidine (PCP) Use Disorder

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Abstract: PCP is highly lipophilic dissociative anesthetic and a hallucinogen. This has been available since early 1950s. Its recreational use started in 1960's. It is smoked, snorted or consumed orally. PCP works through NMDA receptor antagonism as well as through direct and indirect dopaminergic effects leading to psychosis. Intoxication with low to moderate dose produce numbness in the extremities, unsteady gait, slurred speech, bloodshot eyes, horizontal, vertical or rotator nystagmus, tachycardia, hypertension, elevation of body temperature, shallow breathing, dry skin, loss of balance, muscle rigidity, agitation, aggression false sense of invulnerability and superior strength leading to daring acts like jumping off of high building. A moderate dose may produce analgesia and anesthesia. High dose may cause drop in blood pressure, heart and respiratory rate, seizures, coma and death. The presence of nystagmus may assist in differentiating PCP psychosis from other causes of psychoses.. Long-term effects of PCP may include "flash-backs", similar to LSD, persistent speech problems, memory impairment, chronic anxiety, depression or psychosis. There is no specific PCP antagonist medication. Supportive care in an environment of reduced sensory stimulation, urine acidification, and sedation with benzodiazepines is recommended. For patients with psychosis antipsychotic medication may be warranted. Psychosocial interventions add significant value.

Keywords: Angel Dust, Dissociative Anesthetic, NMDA Receptor Antagonist, PCP, Phencyclidine, Psychotomimetic drug.

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KEY LEARNING POINTS

1. Phencyclidine (PCP) also known as Angel Dust was introduced in the early fifties as a "dissociative anesthetic" because it causes detachment (dissociation) from the environment and self. Its recreational use started in the 60s.
2. Users may experience feelings of superior strength and invulnerability, a numbing effect on the mind and its use is often associated with psychomotor agitation and aggression.
3. Long-term users of PCP may report memory loss, depression, disturbances of speech and thinking and weight loss.
4. PCP is addictive. Its repeated use causes craving and compulsive PCP-seeking behavior. It may be ingested, injected intravenously, inhaled or smoked by lacing cannabis with it or by dipping a cigarette in a fluid containing PCP.
5. PCP is primarily an NMDA receptor antagonist, but is also a dopamine agonist and an analgesic through effects on endorphin and enkephalin opioid receptors.
6. Chronic PCP use is associated with the development of psychosis indistinguishable from schizophrenia, possibly because PCP is a dopamine-2 receptor partial agonist and an inhibitor of dopamine reuptake.

CLINICAL VIGNETTE

An elderly couple contacted the emergency service frantically asking for help because their young neighbor broke into their apartment. They reported that "the young man is angry and is not making sense". They locked themselves in their bedroom until the police arrived. The individual was restless and incoherent; he grabbed a kitchen knife and charged towards a policeman who in turn shot him in the chest, a sad but true story.

DISCUSSION OF VIGNETTE

This person did not present to our clinic but from the news paper reports it is clear that patients with PCP intoxication often display unpredictable, belligerent, and assaultive behaviors.

EPIDEMIOLOGY

In USA in 2007 nearly 6.1 million persons aged 12 or older reported that they had used PCP during their life time. Of these, 137,000 individuals used PCP in the last year. In 2006 50,000 more individuals in this age group used PCP, a rather unfavorable trend.

NEUROPSYCHOPHARMACOLOGY

PCP is classified as a dissociative anesthetic. It is an extremely lipid soluble substance and rapidly crosses the blood brain barrier. Most often the street dose of 5mg is consumed orally, by inhalation, smoking or even through topical application [1]. This dose results in a high enough serum concentration to manifest psychotic symptoms. Higher serum concentrations lead to unconsciousness and coma. The powder form of PCP is more popular. When the powder is sprinkled on marijuana, parsley, or mint and smoked or the powder is snorted, the effects are felt within 5 minutes and may last up to 6 hours [2]. PCP acts mainly through the antagonism of NMDA receptors similar to ketamine, another dissociate anesthetic. This hypoactivity of NMDA receptors may also contribute to psychosis [3]. PCP is also a partial agonist of D2 receptors as well as a dopamine reuptake blocker, these actions may be the reason for its psychotomimetic effects [4, 5]. In addition PCP acts on endorphin and enkephalin opioid receptors [6] a mechanism for its analgesic effects. PCP is known to cause tolerance and addiction. 10% of unaltered and 25-30% of conjugated metabolite of PCP is excreted in the urine and can be detected by urine test for up to 8 days [7]. Lamotrigine may cause false positive test.

PCP INTOXICATION

Low to moderate doses of PCP produce numbness in the extremities, intoxication characterized by an unsteady gait, slurred speech, bloodshot eyes, horizontal, vertical or rotator nystagmus, tachycardia, hypertension, elevation of body temperature, shallow breathing, dry skin, loss of balance, muscle rigidity, agitation and aggression. A moderate dose also produces analgesia and anesthesia. With high doses, blood pressure heart and respiratory rates drop. It may lead to seizures, coma and death often due to accidental injury or suicide. The presence of

CHAPTER 16

Sedative, Hypnotic or Anxiolytic-Related Disorders

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Abstract: Sedative Hypnotic Agents (SHAs) are prescribed across several medical disciplines, however, these carry a risk of addiction in small percentage of patients. SHA use for more than a month can result in tolerance and pharmacological dependence. This often requires dose escalation during the first 10-12 weeks of treatment . This pharmacological dependence should be distinguished from SHA use disorder. In this chapter we discuss the factors associated with risk and risk mitigation for SHA use disorder. Use of lowest possible effective dose for shorter period of time with close monitoring a valuable strategy to prevent addiction. Sudden SHA withdrawal specially from barbiturates may be fatal. We discuss the safe strategy for acute withdrawal by converting the drug of addiction to equivalent dose of a long half-life benzodiazepine or barbiturate. Stabilizing on that drug dose and gradually tapering from that. We also suggest treatment with adjunctive medications for comorbid psychiatric disorders. We conclude this chapter with a brief discussion of psychosocial strategies to promote abstinence and recovery.

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Keywords: Barbiturates, Benzodiazepines, Benzodiazepine daily equivalents, Dependence, Pharmacological dependence, Sedative Hypnotic use disorders, Withdrawal.

KEY LEARNING POINTS

1. Sedative, hypnotic or anxiolytic (SHA) medications at therapeutic doses are safe and effective in the management of anxiety and insomnia. They have anticonvulsant and muscle relaxant properties. Intoxication results in symptoms like slurred speech, lack of coordination, unsteady gait, and impaired performance while operating machinery or motor vehicles.
2. Chronic use of sedatives, hypnotics and anxiolytics cause pharmacological dependence. Sudden cessation or a significant reduction in dose can cause withdrawal symptoms like tachycardia, tremor, insomnia, anxiety, and agitation. Transient hallucinations and grand mal seizures can occur during severe withdrawal.
3. "Z-drugs" like eszopiclone, zaleplon and zolpidem, zolpidem-ER are nonbezodiazepine sedative hypnotics. These are safe and effective with intermittent and short-term use.
4. Barbiturates and related agents are prescribed infrequently. They cause more euphoria than benzodiazepines; thereby have a higher risk of abuse. Both barbiturate overdose and withdrawal is more dangerous than with other sedative medications.

CLINICAL VIGNETTE

A 27 year-old college student was diagnosed with panic disorder by her primary care physician and was treated with alprazolam 0.5mg three times a day. The dose was gradually increased to 2 mg three times a day over 2 months period. The patient was given monthly prescriptions, but she would call for bridge prescriptions between appointments, citing reasons like losing her prescription medication or accidentally flushing the medication. Her primary care provider assertively communicated to her about misuse of alprazolam, diagnosed her having alprazolam use disorder, and requested a psychiatric consultation.

Psychiatric history revealed that she has been suffering from panic attacks since

her teenage years. She had been coping with this anxiety with consumption of heavy amounts of alcohol that provided a temporary relief. She reported that she has been abstinent from alcohol for over a year. She also reported previous cannabis and methamphetamine use, but they made her anxiety and panic symptoms worse and therefore quit using those. Though she initially used alprazolam as prescribed, during her third visit she disclosed consuming at least 10-12 mg of alprazolam a day during the previous 6 months. She reported that dose reduction caused an exacerbation of anxiety symptoms, hand tremors and insomnia. She confided that she was obtaining alprazolam prescription from two different providers, using two different pharmacies. She shared her constant fear about running out of alprazolam. She reported that she felt tired during the day. Her supervisor reprimanded her for missing work, for poor work performance and for frequent work related errors.

For panic disorder, sertraline 25 mg/day was started that was increased to 50 mg/day in a week. The alprazolam dose of 12 mg a day was converted to equivalent benzodiazepine dose of clonazepam 6 mg a day given as 3 mg twice a day. In addition, she was prescribed alprazolam 0.5 mg as needed daily for breakthrough symptoms. The dose of clonazepam was reduced slowly by 0.5 mg every week to a target dose of 0.5 mg twice a day. Following this initial dose reduction regimen, clonazepam was tapered more gradually at 0.25 mg a week. With this slow taper over 9 weeks period, the patient did not experience any rebound or recurrence of symptoms. Along with the medication changes patient engaged in cognitive behavioral therapy to address both panic disorder and substance use disorder.

DISCUSSION OF THE VIGNETTE

Diagnostic Considerations

The patient in this vignette had a long-standing history of anxiety and panic disorder used alcohol to cope with it use disorder. Alcohol, cannabis and methamphetamine use were probable attempts to seek relief from her anxiety symptoms. Stimulant use or abstinence from alcohol increased anxiety and panic symptoms. Tolerance of high doses of alprazolam, withdrawal symptoms on dose

CHAPTER 17

Stimulant Use and Addictive Disorder: Amphetamine, Cocaine and Other Stimulants

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Abstract: Stimulant and cocaine use disorders are major public health problems. The prevalence of these disorders is on the rise around the globe and within in the US. Often more than one stimulant is used concurrently more often in patients with other psychiatric disorders like depression. These drugs are ingested, injected, smoked or snorted. Short-term effects lasts for about 40-60 minutes for cocaine and up to 12 hours for meth amphetamine, is characterized by initial "rush", increased energy, a general sense of wellbeing, euphoria, increased sex drive, increased self-confidence and decreased appetite, which typically lasts 40-60 minutes for cocaine and 6–12 hours for methamphetamine. Long-term use may result in psychosis and cognitive impairment. The economic, medical and societal impact of these disorders is substantial. The cost increases are due to 24 fold increase in myocardial infarction or infectious diseases like HIV and hepatitis in IV drug users, increased prevalence of psychosis and mood disorders as well as cost incurred by criminal justice system. Cognitive behavioral therapy has been extensively used for stimulant use disorders. Medication management with stimulants and anticonvulsants has shown modest improvement for relapse prevention. Contingency contracting coupled with medication management has resulted in improvement.

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Subhash C. Bhatia (Ed.)

Keywords: Bupropion, Cocaine, "Crack", "Crank", Disulfiram, "Freebase", "Meth", Modafinil, "Speed", Stimulants, Topiramate.

KEY LEARNING POINTS

1. Cocaine, amphetamines and other stimulant use is increasing worldwide with about 43 million people using either cocaine or stimulants.
2. Cocaine and stimulants are consumed in a variety of ways. Powdered form such as "speed," "meth," or "crank" can be snorted, injected, or dissolved in beverages. Freebase methamphetamine is smoked in a pipe or on aluminum foil. Cocaine is used as powder for intranasal or intravenous use, or smoked as crack.
3. It is not uncommon to find that more than one stimulant is used concurrently.
4. Stimulant related disorders are more common in patients with other psychiatric conditions such as depression.
5. Stimulant related disorders are: Stimulant Use Disorder, Stimulant Intoxication, Stimulant Withdrawal and Stimulant-Induced Disorder like Psychosis.
6. Myocardial infarction (MI) is a serious complication of cocaine use.
7. Treatment considerations include cognitive behavioral therapy, contingency management strategies and medications for detoxification and relapse prevention.

CLINICAL VIGNETTE

47 year old single African American male, presented to the Mental Health Clinic with history of relapse of cocaine use. He started to use cocaine at age of 14 years. He stated that he needed more cocaine to get the same "high". He spent a lot of time to procure and use cocaine, had traded sex to obtain cocaine and continued to use it despite knowing its harmful effects. His recent use started after being sober for two months. He used $6000 worth of cocaine in the past two months with the most recent use being three days prior to this visit. He stated he lost about 20 lbs. weight, and had experienced multiple episodes of chest pain during the course of the current relapse. He has not had an EKG recently. His longest sobriety from cocaine use was about four years ago which lasted for about 7 months. Even during early phase of cocaine remission, patient reported to have had an urge to use. Although guarded about history of using other stimulants, he revealed that he

also used methamphetamine about 9 years ago. At that time amount of methamphetamine use was contingent on availability of funds. Based on frequency, amount and duration of use and other behaviors at that time he met the diagnostic criteria for methamphetamine use disorder.

On this visit the patient reported depressed mood and poor concentration. He also reported hearing voices and was distressed because these voices were derogatory and occasionally commenting on his actions. He stated he wants treatment as he was "tired of drug use" and was frustrated with his inability to stop it. He also reported being afraid of medical consequences, particularly because of recent episodes of chest pain and weight loss.

His past psychiatric history was positive for major depressive disorder, recurrent type. He was being treated with bupropion and reported still having residual symptoms of depression. He had history of suicidal thoughts and attempts in the past. His last attempt was about 9 years ago. He has had psychotic symptoms even while not using stimulant(s) actively. He gave a history of physical, emotional and sexual trauma at age 8. He reported nightmares off and on related to his sexual trauma but denied having any flashbacks. He denied any OCD symptoms. His past medical history was positive for hepatitis C, human immunodeficiency virus, hypothyroidism and gastro esophageal reflux disease.

He was born and raised in California and supported himself financially with monthly social security disability check. He admitted to diverting his disability benefits for drug purchases. He was living in public housing by himself and was recently served an eviction notice due to nonpayment of rent. He had never married and did not have any children.

DISCUSSION OF THE VIGNETTE

Recognition

In this vignette, the patient presented three days after the last use of cocaine and did not have any short-term effects. He met the diagnostic criteria for stimulant use disorder and major depression. Generally short-term effects of stimulant use present as initial "rush", increased energy, a general sense of wellbeing, euphoria,

CHAPTER 18

Tobacco Use Disorders

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Abstract: Tobacco is one of the most widely used drugs of abuse, and represents the single most preventable cause of death. Physicians should take every opportunity to encourage their patients who smoke to quit. Most smokers are aware of the health hazards of smoking and want to quit. Smokers also need to be made aware of the health and economic benefits of a tobacco free life. Several pharmacological agents are available to help the patient who is committed to quitting. Nicotine replacement (patch, gum, lozenge, inhaler) is the most widely used, is available over the counter, and has a success rate about twice that of placebo. Bupropion (Zyban, Wellbutrin) has a slightly higher success rate, and can be used in conjunction with nicotine replacement. Varenicline (Chantix) probably provides the best success rates. Support and self-help groups are also a very useful resource for many patients.

Keywords: Bupropion, Nicotine, Nicotine replacement, Smoking, Tobacco, Varenicline.

KEY LEARNING POINTS

1. Quitting smoking is the single most positive action that your patients can take to improve their health.
2. Smokers lose 13-14 years of life expectancy.

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Subhash C. Bhatia (Ed.)

3. Medication for smoking cessation can result in over 1/3 of smokers quitting.

CLINICAL VIGNETTE

Mr. R was a 56 year old elementary school teacher, who was visiting his family physician for a routine health maintenance check up. He had a history of hypertension and dyslipidemia, both well controlled with medication. He was also about 20 pounds over his ideal body weight, but was otherwise in good health. During the clinic visit, his physician asked him if he was ready to stop smoking cigarettes. The patient was smoking about a pack of cigarettes per day, and has expressed some interest in quitting. He had stopped "cold turkey" for about a month fifteen years ago, after the birth of a child. He had also quit about ten years ago using bupropion (Wellbutrin, Zyban) plus nicotine replacement gum for several months, but returned to smoking after getting a new job and feeling under "stress." The patient had no significant other history of substance use disorder. He drank socially, never more than 6 drinks per week. He had never used marihuana, cocaine, amphetamine, or other drugs of abuse. The family physician provided brief behavioral counseling, and prescribed varenicline (Chantix), 2 mg twice a day. The patient quit successfully, and was still totally abstinent from cigarettes at a follow-up visit two months later.

RECOGNITION

Recognition of tobacco use disorder generally depends on self report. Since use of tobacco is legal, patients are less likely to give erroneous information than for illegal drugs of abuse. Also, use of tobacco does not generally have the social stigma associated with excessive alcohol use. Thus, the clinician can generally assume that a patient will be truthful about tobacco use. Excessive long term tobacco abuse can be associated with pulmonary and cardiovascular findings on the physical examination. There is a blood test which can be used to verify nicotine, serum cotinine, which is a metabolite of nicotine. However, it remains primarily a specialized or research test, and is not practical for everyday clinical use.

Tobacco used disorder is a chronic disease, and clinicians should offer every patient who smokes brief behavioral counseling. Further discussion of

psychological and behavioral interventions for tobacco addiction is presented below. It should be emphasized that most (70%) smokers would like to quit.

DIAGNOSTIC ELEMENTS PRESENTED

Tobacco use disorder is usually diagnosed by self report. In cases where smokers minimize their habit, or deny it altogether, it may be helpful to have a family conference. In addition to smoking, tobacco may be used orally, as chewing tobacco or snuff.

EPIDEMIOLOGY

Tobacco is a universally available drug of abuse. The percent of Americans who smoke is now about 21%. This represents a dramatic decrease since the 1950's, when almost 50% of Americans smoked. This decrease is probably due to a number of factors, not the least of which was the Surgeon General's report on smoking and health issued in 1964. Rates of smoking are higher in developing countries, and in lower socio-economic classes. In the USA, smoking rates are the highest among Native Americans (43%); intermediate in African-Americans (23%) and Caucasians (22%); and lowest in Hispanics (15%) and Asians (10%). Marketing to women has been successful, and rates of smoking, though still lower than men, have increased over the years. Rates of smoking also vary by state, with the highest rates in Kentucky (28%) and the lowest in Utah (12%). Most (90%) smokers begin by age 21 [1].

BACKGROUND

Smoking is the most preventable cause of death and disability, and the greatest cause of excess health care costs. In the USA, 1 in 5 deaths (440,000 deaths per year) are smoking related. The largest number of these are due to lung cancer (125,000), with heart disease (82,000), and COPD (65,000) also major sources of mortality. Cigarette smoking accounts for 30% of all deaths from cancer, and 50% of long term smokers die prematurely of smoking consequences. Smokers have a 3 times greater risk of MI, a 2 times greater risk of stroke, and a 10 times greater risk of peripheral vascular disease.

Rates of smoking are higher in all mental illnesses and psychiatric disorders.

Section III : Non Substance-Related Addiction Disorders

CHAPTER 19

Non-Substance-Related Addictive Disorders

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Abstract: Historically, since ancient times mankind around the globe has resorted to gambling behavior in one or other form, there is no specific cause for gambling addiction. Like other addictions genetic, biological, psychological and environmental causes play a part. Often competitive workaholics are drawn to gambling. Drugs like levodopa for parkinsonism may increase gambling behavior. Gambling is more common in younger individuals with no difference between sexes. Gambling has similar reward pathways as for other addictions and has impulsive and compulsive quality. These individuals show preoccupation with gambling, seek thrill from it, hide or lie about losses and at times experience remorse or guilt and try unsuccessfully to cut down and often chase their losses with a hope to "hit a big jackpot". Diagnosis is based on DSM-5 criteria. Certain scales can be used to assess its severity. There are no known proven preventive strategies for gambling. Also there are no approved pharmacological interventions, however research favors therapeutic value of SSRIs, mood stabilizers and opiate antagonists . Like for other addictions gambling and related disorders also benefit from motivational enhancement, individual, group, couple and family therapies as well as self-help groups like Gambling Anonymous (GA).

Keywords: Card game gambling, Casino gambling, Cockfight, Compulsive gambling, Dogfight betting, Horse race betting, Internet gaming and gambling, Lottery betting, Pathological gambling, Problem gambling, Slot machine gambling, Sports betting, Wagering.

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Subhash C. Bhatia (Ed.)

KEY LEARNING POINTS

1. Non-Substance-Related Addictive Disorders in literature also described as Behavioral Addictions or "Soft Addictions". Some of the examples of such addictions are: gambling, internet, sex, food, exercise, pornography and shopping *etc*.
2. Like substances these additive behaviors are persistent, repetitive, compulsive and problematic. These continue despite negative social, legal and occupational consequences.
3. Non- substance related addictions like substance related addictions are also mediated through brain reward circuits.
4. Because of available research data about epidemiology, clinical course and biological factors Gambling Disorder is included in DSM-5 chapter on addictive disorder. However Internet Gaming Disorder lacks such a data and therefore in DSM-5 it is part of the section on Conditions for Further Study.
5. For gambling disorder pharmacological interventions with SSRIs and opioid antagonists and psychological interventions with behavioral and cognitive behavioral therapy have data for efficacy.

CLINICAL VIGNETTE

Mr. A is a 36 year old Caucasian male a 7th grade mathematics teacher came with his wife, a registered nurse with symptoms of depression with suicidal intent and plan. He was also not able to function well at work. He admitted to craving about going to casino with a confidence that he will figure out a way to recuperate his losses. He stated that he wanted to die through a planned motor vehicle accident to mimic an accidental death in order for his family receiving life insurance benefits to cover his gambling debts as well as other financial obligations.

History revealed that for the last 10 years patient has been gambling excessively. He stated that at least 2 to 3 times a week he was either at casinos or horse race track. During this period, the patient has gambled away most of his savings including funds set aside for education of his 7 year old son. He recently has a

warrant against him for arrest for forging checks. His wife discovered notices from the bank for insufficient funds and financial penalties related to that. Mrs. A confronted her husband many a times and every time he had a different excuse or different lie. Recently in response to these confrontations Mr. A displayed remorse and guilt and at times was able to cut down on his gambling for short periods. A few times he also made contact with 12-step Gamblers Anonymous (GA). His wife stated that she was "fed up" with her husband's gambling behavior and had contacted a divorce attorney to file for separation.

In addition to Gambling Disorder, Mr. A was diagnosed to have major depression of moderate severity and was admitted to residential rehabilitation gambling addiction treatment program. Initially patient was in denial and felt that he is endowed with a gift to win and "it was just a matter of time for a big win and he will be able to compensate his losses". Early on the couple therapy sessions were stormy. With non confrontational supportive and empathic approach and motivational enhancement therapy in about 3 weeks he acknowledged some need for treatment and started to invest in his own recovery. He was prescribed an antidepressant sertraline 50 mg a daily in the morning and trazodone 100 mg at bed time. He also received cognitive behavioral therapy. His wife also decided to engage in couple therapy. While in the program, his depression gradually improved but he struggled with making a change in his gambling mind set. Patient was discharged from the residential rehabilitation program after a month. Soon after that he returned to work as a teacher. Patient continued outpatient cognitive behavioral therapy and antidepressant medication as well as participated in GA meetings. He also retained a sponsor. During a 12 month follow up period, patient denied have craving to return to casinos and was getting along better with his wife and colleagues at school. He also developed a restitution plan to retire his gambling debt.

Discussion of Vignette

This patient meets the DSM-5 diagnostic criteria for both gambling and major depressive disorder. This better outcome is possible because of better understanding of psychopathology and neurobiology of gambling and related disorders. The success of treatment in this patient was due to multimodal

CHAPTER 20

Cognitive-Behavioral Therapy and Other Psychosocial Interventions for Substance Use Disorders

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Abstract: The effectiveness of psychosocial evidenced-based behavioral interventions for substance and non-substance related disorders are comparable to their effectiveness for other psychiatric disorders . Cognitive behavioral therapy addresses the negative and dysfunctional thoughts and emotions related to these disorders and their reinforcing effects. This also helps develop cognitive skills to deal with cue driven craving leading to reengagement in addictive behaviors. Contingency management uses tangible rewards to support addiction free life style evidenced by negative drug screen participation in individual and group therapy. Behavioral self-control promotes goal setting and self-monitoring for harm reduction. Self-help 12-step programs promote acceptance, surrender to a higher power and self-governance through utilization of support from AA fellowship community. Motivational enhancement therapy is to help individuals to move higher on stages of change and to promote self-efficacy. Solution-based therapy helps patients find solutions while reinforcing their successes in solving those problems. All these therapies with or without pharmacotherapy have value in achieving addiction free life style.

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Keywords: AA, Behavioral self-control training (BSCT), CA, Cognitive-Behavioral Therapy (CBT), Contingency management (CM), GA, Motivational Enhancement Therapy (MET), NA, Relapse Prevention (RP), Voucher-based reinforcement (VBR).

KEY LEARNING POINTS

1. Cognitive Behavioral Therapy (CBT) for substance use disorder is based on the theory that substance and non-substance related maladaptive behaviors and dysfunctional emotions are learned through their powerfully reinforcing effects.
2. Cognitive strategy may include appreciating consequences of continued use, confronting thoughts to reuse substances and developing skills to discontinue such a use.
3. CBT can be utilized as an individual, couple, family or group approach in a variety of treatment settings such as acute inpatient, therapeutic community, residential programs or outpatient visits.
4. CBT includes social and coping skills training to enhance the person's capacity to verbally and nonverbally communicate, develop empathy and maintain relationships, and to be assertive.
5. CBT aids in identifying triggers and cravings, creating skills to deal with such, as well as crafting relapse prevention strategies.
6. Other psychosocial interventions include Motivation Enhancement Therapy (MET), Contingency Management (CM), and Relapse Prevention (RP) which assist in training to recognize and deal with cues to reuse.
7. Twelve-Step self-help programs like Alcoholics Anonymous (AA), Narcotics Anonymous (NA), Cocaine Anonymous (CA), and programs for non-substance related disorders like Gamblers Anonymous (GA) involve acceptance, surrender to a higher power, and self-governance.

PSYCHO-SOCIAL INTERVENTIONS FOR SUBSTANCE USE DISORDERS

"I tried to quit smoking many times, It won't work as long as my wife continues to smoke"

"Doctor I am at a point in where I am not looking for highs any more, I just

don't want to go through the withdrawal"

"For years I enjoyed my rolling joints, Since I stopped I don't know what to do with my fingers. I never thought that this will be a problem"

"Since I stopped drinking I stay home, All my friends drink, I know that it is too risky to go out with them"

These are real statements from real patients describing the complex bio-psychosocial interplay in substance use disorders, classical conditioning, positive and negative reinforcement, social learning, socio-economic status, access to care and cultural values are all important variables that influence development, complications and treatment outcomes of addictions.

The first part of the chapter reviews evidence based psychosocial treatment Approaches while the second part is dedicated to the American society of Addiction medicine placement criteria, A standardized tool to assess substance use needs and the corresponding treatment level.

Screening, Brief Interventions and Referral to Treatment

A brief intervention targeting harmful and risky use, that did not reach addiction threshold, the effectiveness of the intervention and the relatively limited cost and time resources, make it an appropriate tool in Primary care and ER settings. The duration may vary from 5-30 minutes. The goal of the intervention is to assess hazardous or harmful substance use, followed by a brief discussion, education and advice . The Acronym "FRAMES" refers to the components of the intervention. FRAMES:- Feedback, Responsibility, Advice, Menu of options, Empathy and Self efficacy (confidence for change).

Feedback

After performing assessment of substance use problems . Providing Feedback about the risks associated with current use risks and harms. It is useful to provide comparisons between the patient's pattern of use *vs.* average patterns in the population and problem patterns.

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Subhash C. Bhatia

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