

to substitute methamphetamine, antidepressants, and several second-generation atypical antipsychotic drugs as medical adjuncts in treating methamphetamine addiction. Pharmacological intervention, however, does not address the often complicated life circumstances that contribute to addiction.

Cognitive behavioral therapy helps patients appreciate the circumstances that often lead them to use methamphetamine, and helps them safely avoid these situations or effectively cope with them. Counselors are also trained to help patients modify their attitudes and behaviors about drug use and to teach effective life skills. Family therapy, in which abuse is confronted by the entire family of an adolescent methamphetamine user, may also be employed. In the future, special psychosocial interventions will likely be geared toward the unique backgrounds of diverse methamphetamine users, such as mothers, gay and bisexual men, criminally institutionalized users, users living in rural areas, and minorities.

The *Center for Substance Abuse Treatment's Tip #33: Treatment of Stimulant Abuse* is an important handbook for clinicians working with recovering methamphetamine users. Other approaches include the "Twelve-Step" program, which has been successful for treating other forms of substance abuse, and the "Matrix Model," a 16-week outpatient treatment approach for treating stimulant abuse. Studies examining these approaches and others are ongoing and have shown some positive short-term results, but have been inconclusive in the long term.

In any case, epidemiologists and other public health officials in North America and worldwide are currently focusing on the methamphetamine epidemic in an attempt to better characterize patterns of addiction. Treatment of methamphetamine abuse and strategies aimed at mitigating the harms of drug use, such as the transmission of HIV and other blood-borne disease, will remain an important area of focus in the future.

SEE ALSO: AIDS; Amphetamines; Club Drugs; Drug Abuse; Hepatitis; Rehabilitation.

BIBLIOGRAPHY. A.M. Barr, et al., "The Need for Speed: An Update on Methamphetamine Addiction," *Journal of Psychiatry and Neuroscience* (v.31/5, 2006); *Center for Substance Abuse Treatment Tip #33* (Chair, CSAT Consensus Panel) (Department of Health and Human Services, 1998);

J. C. Maxwell, "Emerging Research on Methamphetamine," *Current Opinion in Psychiatry* (v.18/3, 2005); R. Rawson, *Treatment of Stimulant Abuse*, NIDA Research Report—Methamphetamine Abuse and Addiction, <http://www.drugabuse.gov/PDF/RRMetham.pdf> (cited August 2006).

SCOTT E. HADLAND, M.D.

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

Methylation

Methylation refers to the replacement of a molecule or atom by a methyl (-CH₃) group. Various types of methylation are defined based upon the atom or molecule that is replaced. In genetics, methylation may refer to the silencing of one of the X chromosomes in females by adding a methyl groups to its cytosine bases by an enzyme called DNA methyltransferase. In biochemistry, methylation is the replacement of a hydrogen atom with a methyl group. Methylation reactions are usually catalyzed by enzymes.

Methylation serves specific purpose in systems; for example, it may be used to modify the structure of heavy metals, regulate the expression of genes, regulate the function of proteins, and also regulate the metabolism of RNA. There are two basic types of methylation: chemical and biological methylation.

Chemical methylation is studied in the area of organic chemistry, where the term alkylation is used to define the addition of a -CH₃ group. Alkylation is done using electrophilic (electron loving) compounds such as dimethyl sulfate and iodomethane, which react in a nucleophilic substitution. For example, ethers may be produced by methylation of alkoxides, and ketones may be produced by methylation of ketone enolates.

Biological methylation occurs in various ways. In epigenetic inheritance, methylation can occur as DNA methylation or protein methylation. In DNA methylation, there is an addition of a methyl group to a cytosine residue, causing cytosine to become 5-methylcytosine. DNA methylation occurs at CpG sites, that is, sites where a cytosine is immediately in front of a guanine. This type of methylation controls gene expression or activity. In protein methylation, a lysine amino acid or an arginine residue is methylat-

ed in the reaction. Arginine may be methylated once or twice, and lysine may be methylated once, twice or three times. Histones can also be methylated by an enzyme called histone methyltransferase, which transfers methyl groups from S-adenosyl methionine to the histone. Protein methylation is also used to control gene expression by activating or deactivating a gene.

Eukaryotic embryos also undergo methylation. Eukaryotic DNA is unmethylated from fertilization to 8-cell stage. It then undergoes *de novo* methylation from the 8-cell stage to morula, during which epigenetic information is modified and added to the genome. Methylation is complete by blastula stage. If embryonic methylation doesn't occur, the embryo dies. Methylation continues to occur in the postnatal development and plays an important role in the interaction of gene expression and environmental factors.

Methylation plays an important role in tumor formation. Tumors begin with abnormal localized hypermethylation, genome-wide hypomethylation, and increased expression of DNA methyltransferase. Research shows that genome-wide hypomethylation leads to increased mutation rates and instability of chromosomes. Furthermore, hypermethylation is one of the symptoms seen in prostate cancer.

Bacteria also use methylation as a tool for self-defense. Bacteria protect its DNA by methylation of adenosine bases. Foreign DNA that enters the bacteria remains unmethylated, thus, prone to destruction by the bacteria's restriction enzymes.

ALSO SEE: Biochemistry; Chromosome; DNA; Genetics.

BIBLIOGRAPHY. Robert L. Nussbaum, Roderick R. McInnes, and Huntington F. Willard, *Genetics in Medicine*, 6th ed. (Thompson & Thompson, 2001).

RAHUL GLADWIN, M.D.
UNIVERSITY OF HEALTH SCIENCES, ANTIGUA

Mexico

Prior to the arrival of the Spanish in 1519, the area of modern-day Mexico was occupied by the Aztecs and other peoples, who had established a highly de-

veloped sense of healthcare. Although most of their medical works were lost, some medical tracts from the Aztec period survive, indicating great advances they had achieved. Indeed the Conquistadors were so interested in the medical treatments of the Aztecs that King Philip II of Spain in 1570 was encouraged to send his doctor Francisco Hernandex to Mexico for seven years to record much of the information that might otherwise have been lost.

The arrival of the Spanish changed the whole healthcare system in the country. While most Indians continued to use herbal remedies, many succumbed to newly-introduced European diseases such as smallpox, cholera, typhoid, measles and influenza. The Spanish and other Europeans also suffered from new medical conditions such as venereal diseases and also from bites from poisonous snakes.

The healthcare system established by the Spanish was solely aimed at the Europeans, with the majority of Mexicans unable to access it. It was also largely located in major cities such as Mexico City and Vera Cruz. This did not stop epidemics such as that of smallpox in 1797 or Asiatic cholera in 1833.

Mexican independence was declared in 1810, and was recognized eleven years later, after which there was a series of wars which saw the United States take much territory from Mexico. Constant wars followed, with Emperor Maximilian ruling the country for three years, and then there were many presidents, some of whom had popular support. The Mexican Revolution of 1910 changed the political landscape, but instability still afflicted Mexico until the 1930s.

After independence in 1810, there were attempts to improve the healthcare system of the country, with the Mexican National Academy of Medicine established in 1864. During the presidency of Benito Juarez (1867–1872), there were attempts to provide healthcare to more of the native Indian population of the country.

Budgetary problems and fighting often prevented this, with great investment in the health services after the 1910 Mexican Revolution. Venustiano Carranza Garza, president of Mexico from 1914–1920, had been governor of Coahuila where he had improved many of the health facilities for the poor. He tried to do the same as president, but failed to introduce the much-needed reforms. Some of his successors also tried, and failed, in the same endeavor.