quality of care during early childhood, exposure to violence, and continued parental drug use are strong environmental factors influencing outcomes.[31,32]

Babies born to mothers who use cocaine during pregnancy are often prematurely delivered, have low birth weights and smaller head circumferences, and are shorter in length than babies born to mothers who do not use cocaine.[26,29,30] Dire predictions of reduced intelligence and social skills in babies born to mothers who used crack cocaine while pregnant during the 1980s—so-called "crack babies"—were grossly exaggerated. However, the fact that most of these children do not show serious overt deficits should not be overinterpreted to indicate that there is no cause for concern.

Using sophisticated technologies, scientists are now finding that exposure to cocaine during fetal development may lead to subtle, yet significant, later deficits in some children.[31,32] These include behavior problems (e.g., difficulties with self-regulation) and deficits in some aspects of cognitive performance, information processing, and sustained attention to tasks—abilities that are important for the realization of a child's full potential.[32,33] Some deficits persist into the later years, with prenatally exposed adolescents showing increased risk for subtle problems with language and memory.[34] Brain scans in teens suggests that at-rest functioning of some brain regions—including areas involved in attention, planning, and language—may differ from that of non-exposed peers.[35] More research is needed on the long-term effects of prenatal cocaine exposure.

How is cocaine addiction treated?

In 2013, cocaine accounted for almost 6 percent of all admissions to drug abuse treatment programs. The majority of individuals (68 percent in 2013) who seek treatment for cocaine use smoke crack and are likely to be polydrug users, meaning they use more than one substance.[36] Those who provide treatment for cocaine use should recognize that drug addiction is a complex disease involving changes in the brain as well as a wide range of social, familial, and other environmental factors; therefore, treatment of cocaine addiction must address this broad context as well as any other co-occurring mental disorders that require additional behavioral or pharmacological interventions.

Pharmacological Approaches

Presently, there are no medications approved by the U.S. Food and Drug Administration to treat cocaine addiction, though researchers are exploring a variety of neurobiological targets. Past research has primarily focused on dopamine, but scientists have also found that cocaine use induces changes in the brain related to other neurotransmitters—including serotonin, gamma-aminobutyric acid (GABA), norepinephrine, and glutamate.[37] Researchers are currently testing medications that act at the dopamine D_3 receptor, a subtype of dopamine receptor that is abundant in the emotion and reward centers of the brain.[38] Other research is testing compounds (e.g., *N*-acetylcysteine) that restore the balance between excitatory (glutamate) and inhibitory (GABA) neurotransmission, which is disrupted by long-term cocaine use.[39] Research in animals is also looking at medications (e.g., lorcaserin) that act at serotonin receptors.[40]

Several medications marketed for other diseases show promise in reducing cocaine use within controlled clinical trials. Among these, disulfiram, which is used to treat alcoholism, has shown the most promise. Scientists do not yet know exactly how disulfiram reduces cocaine use, though its effects may be related to its ability to inhibit an enzyme that converts dopamine to norepinephrine. However, disulfiram does not work for everyone. Pharmacogenetic studies are revealing variants in the gene that encodes

the DBH enzyme and seems to influence disulfiram's effectiveness in reducing cocaine use.[41–43] Knowing a patient's *DBH* genotype could help predict whether disulfiram would be an effective pharmacotherapy for cocaine dependence in that person.[41–43]

Finally, researchers have developed and conducted early tests on a cocaine vaccine that could help reduce the risk of relapse. The vaccine stimulates the immune system to create cocaine-specific antibodies that bind to cocaine, preventing it from getting into the brain.[44] In addition to showing the vaccine's safety, a clinical trial found that patients who attained high antibody levels significantly reduced cocaine use.[45] However, only 38 percent of the vaccinated subjects attained sufficient antibody levels and for only 2 months.[45]

Researchers are working to improve the cocaine vaccine by enhancing the strength of binding to cocaine and its ability to elicit antibodies.[44,46] New vaccine technologies, including gene transfer to boost the specificity and level of antibodies produced or enhance the metabolism of cocaine, may also improve the effectiveness of this treatment.[47] A pharmacogenetics study with a small number of patients suggests that individuals with a particular genotype respond well to the cocaine vaccine—an intriguing finding that requires more research.[48]

In addition to treatments for addiction, researchers are developing medical interventions to address the acute emergencies that result from cocaine overdose. One approach being explored is the use of genetically engineered human enzymes involved in the breakdown of cocaine, which would counter the behavioral and toxic effects of a cocaine overdose.[49] Currently, researchers are testing and refining these enzymes in animal research, with the ultimate goal of moving to clinical trials.[49]

Behavioral Interventions

Many behavioral treatments for cocaine addiction have proven to be effective in both residential and outpatient settings. Indeed, behavioral therapies are often the only available and effective treatments for many drug problems, including stimulant addictions. However, the integration of behavioral and

pharmacological treatments may ultimately prove to be the most effective approach.[50]

One form of behavioral therapy that is showing positive results in people with cocaine use disorders is contingency management (CM), also called motivational incentives. Programs use a voucher or prize-based system that rewards patients who abstain from cocaine and other drugs. On the basis of drug-free urine tests, the patients earn points, or chips, which can be exchanged for items that encourage healthy living, such as a gym membership, movie tickets, or dinner at a local restaurant. CM may be particularly useful for helping patients achieve initial abstinence from cocaine and stay in treatment.[39,50–52] This approach has recently been shown to be practical and effective in community treatment programs.[51]

Research indicates that CM benefits diverse populations of cocaine users. For example, studies show that cocaine-dependent pregnant women and women with young children who participated in a CM program as an adjunct to other substance use disorder treatment were able to stay abstinent longer than those who received an equivalent amount of vouchers with no behavioral requirements.[28] Patients participating in CM treatment for cocaine use who also experienced psychiatric symptoms—such as depression, emotional distress, and hostility—showed a significant reduction in these problems, probably related to reductions in cocaine use.[53]

Cognitive-behavioral therapy (CBT) is an effective approach for preventing relapse. This approach helps patients develop critical skills that support long-term abstinence—including the ability to recognize the situations in which they are most likely to use cocaine, avoid these situations, and cope more effectively with a range of problems associated with drug use. This therapy can also be used in conjunction with other treatments, thereby maximizing the benefits of both.[50]

Recently, researchers developed a computerized form of CBT (CBT4CBT) that patients use in a private room of a clinic.[54–56] This interactive multimedia program closely follows the key lessons and skill-development activities of in-person CBT in a series of modules. Movies present examples and information

that support the development of coping skills; quizzes, games, and homework assignments reinforce the lessons and provide opportunities to practice skills.[54–56] Studies have shown that adding CBT4CBT to weekly counseling boosted abstinence[54] and increased treatment success rates up to 6 months after treatment.[55]

Therapeutic communities (TCs)—drug-free residences in which people in recovery from substance use disorders help each other to understand and change their behaviors—can be an effective treatment for people who use drugs, including cocaine.[57] TCs may require a 6- to 12-month stay and can include onsite vocational rehabilitation and other supportive services that focus on successful re-integration of the individual into society. TCs can also provide support in other important areas—improving legal, employment, and mental health outcomes.[57,58]

Regardless of the specific type of substance use disorder treatment, it is important that patients receive services that match all of their treatment needs. For example, an unemployed patient would benefit from vocational rehabilitation or career counseling along with addiction treatment. Patients with marital problems may need couples counseling. Once inpatient treatment ends, ongoing support—also called aftercare—can help people avoid relapse. Research indicates that people who are committed to abstinence, engage in self-help behaviors, and believe that they have the ability to refrain from using cocaine (self-efficacy) are more likely to abstain.[59] Aftercare serves to reinforce these traits and address problems that may increase vulnerability to relapse, including depression and declining self-efficacy.[59]

Scientists have found promising results from telephone-based counseling as a low-cost method to deliver aftercare. For example, people who misused stimulants who participated in seven sessions of telephone counseling showed decreasing drug use during the first 3 months, whereas those who did not receive calls increased their use.[60] Voucher incentives can boost patients' willingness to participate in telephone aftercare, doubling the number of sessions received according to one study.[61]

Community-based recovery groups—such as Cocaine Anonymous—that use a

12-step program can also be helpful in maintaining abstinence. Participants may benefit from the supportive fellowship and from sharing with those experiencing common problems and issues.[62]

How is cutting-edge science helping us better understand addiction?

Two cutting-edge areas of science, genetics and brain imaging, are significantly advancing our understanding of cocaine addiction.

Researchers estimate that genetics contributes 42 to 79 percent of the risk for cocaine use and dependence.[63] Of course, with a complex disease such as addiction, many different genes are involved, and their expression can be influenced by the environment. There appears to be significant overlap in the genes that put people at risk for all addictive substances, perhaps indicating a common biological pathway for addiction regardless of the drug.[63]

In genome-wide association studies (GWAS), researchers examine whether certain gene variants are more frequently found in people with a substance use disorder, which eventually might help identify those at increased risk for drug addiction.[64,65] Identifying genes linked to addiction is only the first step. Candidate-gene research examines the links between substance use and specific genes that encode proteins that appear to be related to addiction. For example, researchers have found connections between various aspects of cocaine addiction and the genes that encode for particular dopamine receptors and the enzymes that break down this neurotransmitter.[63]

Because environmental factors typically shape the impact of genes on disease risk, researchers must also identify how particular gene-by-environment interactions influence the course of addiction.[63] Research in the field of *epigenetics* is uncovering how the environment induces long-term changes in gene expression—influencing the pattern of gene expression—without altering the DNA sequence.[66]

In animal research, scientists are determining how long-term cocaine exposure changes gene expression in the brain, particularly in the reward pathway. Studies have linked specific cocaine-induced epigenetic changes to neuroadaptations[67] and behavioral hallmarks of addiction, such as sensitivity to

cocaine's rewarding effects.[66,67] The epigenetic changes induced by cocaine can be passed to the next generation, even if the drug exposure does not occur prenatally.[68] Although much more genetic and epigenetic research is needed, understanding addiction at the molecular level offers great promise for improving diagnosis, for example by discovering biomarkers for disease severity or treatment response.[66]

Although more research is needed, brain-imaging might be used to detect biomarkers for drug addiction vulnerability, as these technologies have yielded insights into the processes underlying craving and how medications may quell the brain's response to cocaine cues.[69] A relatively new neuroimaging technology called default-mode or resting-state functional magnetic resonance imaging (rs-fMRI) reveals brain activity when people are alert but not performing a particular task; researchers use this technique to compare functional brain networks of people who have used cocaine for a long time and those who have not. These studies suggest that there is reduced connectivity between various brain circuits[70–72] and between the two hemispheres[73] among people with cocaine dependence. Researchers have also correlated reduced connectivity between particular brain circuits with important addiction-related behaviors, including risk for relapse[71] and impulsivity.[72]

Neuroimaging technologies are also documenting how the brains of cocaine users may recover after periods of abstinence. For example, these techniques indicate that years of cocaine use are associated with reduced grey matter in particular brain regions. However, people who maintained cocaine abstinence for approximately 9 months showed grey matter levels similar to or greater than those of people who had never used the drug.[74] Further analysis indicated that the increased grey matter occurred in regions other than the ones altered by cocaine use, suggesting that the neurobiological changes involved in recovery are more complex than simply reversing the changes related to addiction.[74] The researchers also found that increased grey matter volume in brain regions involved with behavioral control were associated with longer duration of abstinence.[74]

fMRI technologies have also revealed that abstinence from cocaine has important, restorative effects on the brain. Although current cocaine users demonstrated reduced brain activity in a brain circuit that mediates response

inhibition during a motor control task, individuals who had attained abstinence for an average of 8 months showed similar patterns of activation and levels of performance to those who had never used the drug.[75] The results suggest that abstinence helps restore the functioning of this brain circuit.

Researchers are engaged in several large-scale, collaborative projects to map the human connectome, which is the brain's network of interconnected circuits. For example, the National Institutes of Health supports the Human Connectome Project to generate maps of the developing, adult, and aging brain. By having a map of the typical brain, scientists will further understand how neural functioning differs in behavioral disorders—knowledge that will drive improved diagnostics and treatments.

Where can I get further information about cocaine?

To learn more about cocaine and other drugs of abuse, visit the NIDA website at www.drugabuse.gov or contact *DrugPubs* at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).

NIDA's website includes:

- Information on drugs of abuse and related health consequences
- NIDA publications, news, and events
- Resources for health care professionals, educators, and patients and families
- Information on NIDA research studies and clinical trials
- Funding information (including program announcements and deadlines)
- International activities
- Links to related websites (access to websites of many other organizations in the field)
- Information in Spanish (en español)

NIDA websites and webpages

- www.drugabuse.gov
- www.teens.drugabuse.gov
- www.easyread.drugabuse.gov
- www.drugabuse.gov/drugs-abuse/cocaine
- www.researchstudies.drugabuse.gov
- www.irp.drugabuse.gov

For physician information

- NIDAMED: www.drugabuse.gov/nidamed

Other websites

Information on cocaine abuse is also available through the following Web site:

- Substance Abuse and Mental Health Services Administration: www.samhsa.gov
- Drug Enforcement Administration: www.dea.gov
- Monitoring the Future: www.monitoringthefuture.org/
- The Partnership at Drug Free.org: www.drugfree.org/drug-guide

Mindful
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“This course was developed from the public domain document: Cocaine – National Institute on Drug Abuse (NIDA) - NIH (2016).”