

Adverse health consequences of cocaine abuse

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World Health Organization
Geneva
1987

ISBN 92 4 156107 6

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PRINTED IN ENGLAND

87/7162-Clays-5000

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Preface

Cocaine, despite its high cost to the consumer, is becoming the preferred drug of an increasing number of affluent drug-users in North and South America and in Europe. The increased production of cocaine with an associated reduction in market price has meant that cocaine is now within the reach of a large number of new users. In the Andean area of South America, the traditional practice of coca-leaf chewing continues among rural populations. Causing concern is the relatively new phenomenon of coca-paste smoking, which is rapidly spreading among the younger generation, particularly in urban populations, in many countries of South America.

The use of coca paste and cocaine is no longer confined to the American continent, but has spread, not only to Europe but also to many countries in other continents. There is no doubt about the seriousness of the problem; coca-paste and free-base smoking, sniffing, and the intravenous injection of cocaine hydrochloride are known to be particularly hazardous habits. Those countries that have not yet experienced any public health problems associated with the use of cocaine are likely to do so in the near future.

Resolution WHA37.23 of the 37th World Health Assembly (May 1984) recognized the dramatic global increase in the abuse of drugs, in general, and of cocaine in particular and also acknowledged the need to continue to seek improved methods of prevention and treatment of drug dependence, epidemiological surveillance, and dissemination of information. In response to Resolution WHA37.23, the WHO project on the adverse health consequences of cocaine and coca-paste smoking, was implemented; this book is published as part of that project.

The purpose of this book is to update existing knowledge on the problem of cocaine dependence by assessing the global situation and by considering the extent and magnitude of the problem and the associated adverse health consequences. The book also reviews current approaches to treatment and prevention and ongoing and needed research. It is based on material gathered during the course of the WHO project on Adverse Health Consequences of Cocaine and Coca-paste Smoking, and presented at a meeting of the Advisory Group held in Bogotá, Colombia, in September 1984. The project was supported by the United Nations Fund for Drug Abuse Control. Special thanks are due to Professor G. Edwards, Addiction Research Unit, Institute of Psychiatry, London, England, for his invaluable help in producing this publication. The following also deserve special mention for their assistance and contributions: Dr C. N. Cagliotti, Ministry of Social Welfare, Buenos Aires, Argentina; Dr N. Clarke, Ministry of Health, Nassau, Bahamas; Dr S. Cohen, Neuropsychiatric Institute, University of California at Los Angeles, Los Angeles, CA, USA; Dr C. E. Climent, Department of Psychiatry, University del Valle, Cali, Colombia; Dr K. Edmondson, Australian Institute of Health, Canberra, Australia; Dr G. Hernandez, Department of Psychiatry, School of Medicine, Javeriana University,

Glossary

Coca. This refers to the leaves of *Erythroxylon coca* or *E. novgranatense*, which are chewed by indigenous populations of north-western South America for their anti-fatigue and anti-hunger effects. A tea is made of coca leaves to treat mountain sickness. Coca contains 0.5–1.5% cocaine.

Coca paste (pasta, basuco). Coca paste is the first extraction product during the manufacture of cocaine. It is prepared by adding macerated coca leaves to sulfuric acid, kerosene or gasoline. The dried paste contains 40–90% cocaine sulfate, coca alkaloids, alkalis, and other substances. It is mixed with either tobacco or cannabis and smoked in a cigarette.

Cocaine (coke, snow). When coca paste is treated with hydrochloric acid and the product refined, cocaine hydrochloride of 98% or better purity is obtained; this is called cocaine. It appears on the illicit market at 12–75% purity after having been diluted with sugars, local anaesthetics such as procaine, amphetamine, or caffeine. The term cocaine is sometimes used generically to include all potent cocaine products, such as coca paste and cocaine free base.

Free base (cocaine base, cocaine alkaloid, base). Cocaine hydrochloride is converted to its alkaloid by treatment with an alkali. A variety of methods are used. Some involve extraction with a solvent followed by evaporation, others simply involve the addition of baking soda or other alkali. Free base contains some of the adulterants found in the illicit cocaine. It has a lower vaporizing point than cocaine hydrochloride, and thus less is lost when it is heated and inhaled.

Cocaine and its misuse: historical background

In South and Central America, chewing of the leaf of the coca plant dates back to very ancient times. News of this plant and its properties was brought back to Europe by the early explorers and references to coca can be found in European medical texts dating from the 17th century. However, it was not until the 19th century that scientific and medical interest in the drug became well developed. In 1860 the German chemist, Dr Albert Neimann, isolated cocaine in the pure alkaloid form from leaves brought to Europe. During the following twenty years or so, cocaine was used extensively by the medical profession as a stimulant, a local anaesthetic, and as a “cure” for morphine dependence.

This era of unrestrained medical enthusiasm was short-lived, however, and by the end of the 19th century it had become very clear that the dangers of dependence developing with this drug had been greatly underestimated. There were many reports from both Europe and North America of physicians and nurses who had become dependent and of cases of cocaine dependence, associated with its use in treatment.

In the early part of the 20th century it also became clear that as a result of the uncontrolled availability of this drug it was being used, in certain circles, as a “recreational” drug. The extent of this recreational use, at that time, is difficult to ascertain, but it was certainly extensive enough to arouse concern and to stimulate calls for legislative control—the fact that cocaine is a drug with potential for misuse had become very firmly established.

The middle decades of the 20th century might be viewed as a rather quiescent period as far as cocaine is concerned—coca leaves continued to be chewed in the geographical areas traditionally associated with their use and there was a continuing low-level problem of cocaine misuse in the developed world. This period, however, saw an almost explosive increase in the misuse of synthetic stimulants (amphetamine and phenmetrazine) in many countries. The experiences of the countries where these “epidemics” of misuse occurred gave ample confirmation of the threat to public health posed by any type of central nervous system stimulant. Today it is the use of cocaine that threatens to erupt into just such an epidemic.

Central nervous system stimulants are very popular as drugs of misuse; new drug misusers are likely to be rapidly recruited, and stimulant use can be a substitute for, or be combined with, narcotic misuse. Furthermore, in the aftermath of a stimulant epidemic, the established demand may be easily transferred to opiates.

The dangers of cocaine were initially underestimated and this mistake should not be repeated. The early experiences with cocaine and the problems of stimulant misuse in the middle of this century provide a warning of the potential public health problems associated with the

misuse of cocaine-type drugs. What is more, the present level of cocaine misuse signals a resurgence of stimulant misuse in epidemic proportions with all the associated dangers.

Preparations and routes of administration

Reference has already been made to the historical and indigenous use of chewed cocaine in South America. The preparation of the pure alkaloid form of cocaine meant that many very different techniques of administration became possible, each with their attendant dangers. During recent years, the use of smoked cocaine base and “free-basing” have emerged. The major modes of administration in current use are described below.

(a) *Chewing.* A wad of coca leaves, to which lime is often added, is placed in the cheek. This technique provides a slow sustained release of the drug with buccal absorption. The blood levels of cocaine attained are likely to be low, dependence risk is similarly small, and there is unlikely to be any psychological or social impairment or threat to health. It is possible that there are some adverse consequences of such endemic use, but of all the routes of administration this seems to be the least dangerous.

(b) *Sniffing.* Powdered cocaine (cocaine hydrochloride) can be sniffed to achieve nasal absorption. This method can cause direct damage to the nasal septum and can give rise to many of the health problems listed in Chapter 5. However, the risk of dependence developing is probably less than with smoking or injection of the drug.

(c) *Injection.* Cocaine hydrochloride may be injected intravenously with all the attendant dangers of such injection practices, and with a high risk of dependence developing. At times, the combined injection of cocaine and heroin has been popular.

(d) *Free-basing.* Cocaine free base is the cocaine alkaloid or benzoylmethylecgonine. It is also known as base, cocaine base, or free base. Cocaine free base differs from cocaine hydrochloride, in that it is not readily soluble in the nasal mucous membranes or in the blood, but it has a low melting point and can be readily volatilized and inhaled during smoking. Cocaine free base is almost always smoked in a water pipe, which is usually made of glass.

(e) *Smoking of coca paste.* Coca paste is a white, semi-solid or solid preparation containing cocaine sulfate, coca alkaloids, ecgonine, benzoic acid, methanol, kerosene, alkaline compounds, sulfuric acid, and many impurities. It is usually smoked mixed with tobacco or cannabis.

Global extent and assessment of the problem

Overall trends

Cocaine misuse has reached epidemic levels in large areas of North and South America. While the countries experiencing the most severe consequences of the epidemic are Bolivia, Colombia, Peru, and the United States of America, evidence exists that cocaine abuse is rapidly increasing in parts of Canada, Europe, and South-East Asia.

There are historical records of past periods of dramatic increase in cocaine abuse that have subsequently declined, often without explanation. The present epidemic differs from previous episodes, firstly, because of the unprecedented availability of cocaine as a result of the massive increase in coca-leaf production and secondly, because of the global health problems associated with new methods of consumption of the drug.

With the possible exception of traditional coca-leaf chewing among rural Andean populations and the limited use of cocaine by affluent populations, cocaine use was not recognized as a major public health concern until the late 1970s. Before that time, cocaine, which was generally consumed via nasal sniffing, was considered to be a drug with a low abuse potential and few health consequences. Today the situation is vastly different. The drug is readily available, at a price that no longer limits its use to the affluent. New methods of consumption have led to new patterns of use and associated adverse health consequences. Far from being the safe drug it was once believed to be, cocaine is now recognized as one of the most reinforcing of all psychoactive drugs; its use leads to uncontrolled compulsive behaviour in an undefinable but probably large and growing percentage of consumers.

Extent of the problem

USA

Data from the national household survey carried out by the National Institute on Drug Abuse (NIDA) in the USA (23) indicate that the prevalence of cocaine use has increased substantially since the 1970s. Between 1974 and 1982, the number of people reported to have tried cocaine at least once increased from 5.4 million to 21.6 million. During the same period the number of current users of cocaine rose from 1.6 million to 4.2 million. Similarly, among high school seniors in the United States, only 9.0% had ever tried cocaine in 1975 and 1.9% were current users, but by 1983 the percentage of students having tried the drug had increased to 16.2% and the number of current users to 4.9% (24).

The effects of the dramatic increases in the late 1970s are becoming

increasingly evident as both the demand for treatment and the incidence of medical crises associated with cocaine use grow. Between 1976 and 1981, the number of emergency admissions for cocaine-related medical crises increased by 300%. Similarly, from 1975 to 1982 the number of cocaine-related deaths increased by approximately 300%. More recent data indicate that these trends are continuing. For example, approximately 2 000 cocaine-related emergency hospital admissions were recorded in the first quarter of 1984, a figure that equals the total number of such crises for 1978. Treatment data reflect similar increases. Hospital admissions for treatment in which cocaine was reported as the primary drug problem increased from 1.2% of admissions for drug abuse in 1976 to 5.8% in 1981 and 9% in 1982 (23).

In the United States, the dramatic increases in treatment, admissions, emergency care, and death associated with cocaine use are believed to reflect not only the growth in the number of users, but also the effect of new ways of taking the drug. There has been a major shift from sniffing or snorting cocaine to smoking of free base and to intravenous injection. The phenomenon of the smoking of cocaine base first appeared in the United States in 1974 and was mostly confined to the state of California. The first hospital admission for a problem related to free-basing was in 1975, the year in which extraction kits and smoking accessories became commercially available. In 1978, distribution of these accessories or paraphernalia spread from California throughout the United States. In 1979, only 1% of cocaine-related hospital admissions involved the use of free base, but by 1982 this figure had increased to 7%.

The most recent surveys of cocaine prevalence in the United States indicate that, among those under the age of 26 years, cocaine use has begun to stabilize (24).

Canada

Canadian data indicate that rates of cocaine use there are lower than those in the United States. However, both countries are experiencing increasing trends in levels of use. For example, in 1977 only 3.8% of students, grades 7–13, had used cocaine in the month prior to the survey, but by 1983 this percentage had increased to 4.1%. Similarly, in 1978 the percentage of Canadians aged 18 years and older who had ever used cocaine was 2.7%, but by 1984 this figure had increased to 3.3% (31).

Latin America

The cultivation of coca plants in Latin American countries has increased more than sixfold since the early 1970s. The majority of coca plants are grown in Bolivia, Colombia, and Peru. Estimates of the worldwide consumption of cocaine were 35–45 tonnes in 1981, 45–54 tonnes in 1982, and between 50 and 61 tonnes by 1983. There is no indication of any decline in this trend in consumption. Along with the increase in coca

production, there has been a related increase in drug use in Latin America. Crude refinement procedures can be used now to produce an inexpensive coca paste that is being widely smoked by Latin American youths. In Colombia, for example, a study of high school students in five different schools confirmed that coca-paste smoking is as widespread as the use of marijuana (8).

Coca-paste use began in Bolivia and Peru in the early 1970s, first in the capital cities and then in other towns and rural areas. In a few years its use had spread to Argentina, Brazil, Colombia, Ecuador, and some Mexican cities near the border with the United States.

Epidemiological studies carried out in schools, universities, psychiatric hospitals, and in house surveys have shown that in Bolivia, Colombia, Ecuador, and Peru, coca-paste smoking has reached epidemic proportions and affects many thousands of individuals. Hospitals in these countries cannot respond to the demands for treatment from coca-paste smokers. The Antioquia Mental Hospital in Colombia is treating as many as 200 coca-paste smokers per month; this represents a threefold increase in the number of such patients between 1981 and 1983.¹ An outpatient clinic in Cali, Colombia, has reported that 4.4% of its patients are coca-paste smokers.²

The great increase in the numbers of patients has imposed a heavy burden on countries that have limited resources and few trained health professionals. In Peru, for example, about 30% of private and state psychiatric facilities are occupied by coca-paste smokers. In 1979 there were approximately 39 000 coca-paste smokers in Lima and 156 000 in the whole country (estimated from the population at risk—12–45 years of age). The numbers now are probably much higher because the habit has spread to an age range of 8–75 years in all areas of the country. Consequently, there are many thousands of coca-paste smokers who do not have access to treatment facilities. In Colombia, among inpatients treated in drug dependence centres, the proportion smoking this preparation rocketed from 1% in 1977 to 89.4% in 1984.

Of 48 304 Colombian university students studied, 5% used coca paste and 4.1% cocaine hydrochloride. In the city of Medellín, 4.1% of the population had smoked coca paste at least once. In Cali, 4.4% of outpatients in a psychiatric facility were coca-paste smokers. In another

¹ VELASQUEZ DE PABÓN, E. *Problemas del comportamiento de dependencia en adolescentes y jóvenes en relación al abuso del alcohol, drogas, cigarrillo y trastornos del peso*. WHO Study Group on Young People and Health for All by the Year 2000, Geneva, 4–8 June 1984.

² CLIMENT, C. & DE ARAGON, L. V. *Clinical aspects of coca-paste smoking (basuco) in Colombia*. Dept. of Psychiatry, Universidad del Valle. Presented at the Advisory Group Meeting on the adverse health consequences of cocaine and coca-paste smoking, Bogotá, Colombia, 10–14 September 1984.

psychiatric hospital, in Bogotá, the prevalence of coca-paste “addiction” among the inpatients increased from 25% in 1981 to 57% in 1983. Similar data on increasing use have been reported by physicians from Bolivia and Ecuador.

Coca-paste smoking has extended to include all social classes in Bolivia, Colombia, Peru, and parts of Ecuador. It is evident, therefore, that present facilities are totally inadequate for the enormous numbers of people who require treatment. Alternative and less costly methods of management need to be developed, such as the use of comprehensive outpatient treatment, day hospitals, substitute homes, adoptive homes, and intermediate or halfway houses.

Bahamas

There has been no evidence to date to suggest that coca-paste use occurs in the Bahamas, and this country does not produce any cocaine. However, the Bahamas serves as a transshipment area for cocaine between South and North America, and those who are involved in the drug trafficking have access to the drugs and in some cases are paid with drugs. Furthermore, it is thought that, in some cases, drugs deposited on any of the numerous small islands and cays may be found by local residents.

A major change in the pattern of cocaine abuse is thought to have taken place around 1979 when the free-base method of use was introduced. At the time, cocaine was still relatively expensive, costing approximately US \$100 per gram, and its purchase was, therefore, beyond the means of many people. However, during the latter part of 1979 and early 1980, it was observed that the number of admissions to psychiatric hospitals for the treatment of cocaine dependence began to increase gradually, and that by the end of 1980 the increase had become much more dramatic.

The number of patients currently seeking help for cocaine dependence has increased to such an extent that the existing facilities are totally inadequate and unable to cope, and a waiting list system has been introduced. At the same time, the age range of persons treated for cocaine dependence has widened such that persons as young as 9 years of age and patients over the age of 40 years are increasingly being admitted for treatment.¹

Linked with these changes in patterns of use has been a decrease in the price of cocaine on the street together with an increase in the quantity of the drug available. Information obtained from drug abusers

¹ CLARKE, N. *Cocaine abuse in the Bahamas*. Ministry of Health, Nassau, Bahamas. Presented at the Advisory Group Meeting on the adverse health consequences of cocaine and coca-paste smoking, Bogotá, Colombia, 10–14 September 1984.

undergoing therapy suggests that the price of cocaine that is available on the streets has dropped considerably, thus, a given quantity that would have cost US \$100 in 1980 could be purchased for US \$50 in 1984.

Europe

While there is considerable variation, available data indicate an increase in cocaine use in many European countries. A survey conducted in Bavaria, Federal Republic of Germany, showed a 4% prevalence of cocaine use in 1973; in 1980 the rate was 7% (6).

Most of the epidemiological studies conducted in European countries have assessed the problem at a particular time, so that data on trends are not available. In the Federal Republic of Germany, 4% of persons aged between 12 and 24 years in 1983 reported that they had used cocaine. In the Netherlands during the same period, 3% of a similar age group reported having used cocaine. Reports from Austria show that 1% of Austrian students are cocaine users, while in Switzerland in 1982 a sample of 420 young people aged from 15 to 24 years showed a cocaine use rate of 1.5% in males and 5.7% in females.¹

The use of cocaine has been reported in most European countries; France, Italy, Portugal, Spain, and the United Kingdom have all reported an increase in the availability of the drug. An indirect measure of availability is the amount of the drug confiscated by the authorities. In 1977, 59 kg of cocaine were reported to have been confiscated in European countries. By 1982 this figure was 398 kg and by 1983 it had risen to 952 kg.¹

In most European countries, the mass media have reported on the increasing problem caused by cocaine use and more health professionals are reporting health consequences related to the use of the drug. Public awareness is shifting from a rather permissive, to a more restrictive attitude, and cocaine tends to be viewed now as a dangerous drug.

South-East Asia and Pacific Region

With the exception of a few reports of cocaine use in Australia and the Philippines, this region remains relatively untouched by the cocaine epidemic. However, the amount of cocaine confiscated by authorities in Australia increased from 556 grams in 1977 to 8.9 kg in 1982; more than 4 kg were seized in the first 4 months of 1984. Similarly, seizures of cocaine have recently been reported in Hong Kong, the Philippines, and

¹ UCHTENHAGEN, A. *Global assessment and epidemiology of cocaine in Europe*. University of Zurich, Switzerland. Presented at the Advisory Group Meeting on the adverse health consequences of cocaine and coca-paste smoking, Bogotá, Colombia, 10-14 September 1984.

Thailand. Therefore, even in this region there is no room for complacency.

Africa

There are no quantitative data on cocaine availability in African countries, but seizures of the drug have been reported in the past three years and there have been reports of cases of cocaine-dependent individuals from some African countries.

Some general epidemiological issues

Patterns of use

Epidemiological studies on cocaine typically include information on how cocaine is administered, how often it is used, at what doses, and in conjunction with which other drugs. However, to a great extent, these data are not comparable because of the absence of standardized methods of data collection.

Patterns of consumption have differed from place to place, and have also varied with time. In most areas, the sniffing of cocaine is now the predominant route of administration. The inhalation of cocaine alkaloid, or free base, is becoming more popular in North America while the smoking of coca paste, the first product of coca-leaf extraction, is the common method of use in South America.

There are also variations in the patterns of consumption in terms of frequency, regularity, and social setting of use, and dosage. The spectrum ranges from sporadic use at low doses to the daily use of high doses; from controlled use to compulsive use resulting in exhaustion; from collective recreational use to solitary use. The higher the frequency and dosage, the greater is the dependence liability. Cocaine injection, free-basing, and coca-paste smoking all fall into the category of high-dose use compared with cocaine sniffing, but the latter practice can also be excessive.

In almost all countries concerned, cocaine or coca paste is often used in combination, simultaneously or consecutively with other drugs. On the North American continent cocaine is mainly combined with alcohol and heroin, but sometimes with barbiturates or other sedatives. In South America coca paste is smoked with either marijuana or tobacco. In European countries, the predominant pattern of use exhibited by drug users who present for treatment, or are being sentenced, is one of multi-drug use including cocaine. The level of exclusive cocaine use is unknown since there may be many users who are not included in the available statistics because they have no contact with therapeutic, law enforcement, or other agencies. In Latin America there is some indication that coca-paste smoking may be replacing the use of other drugs.

With regard to the social setting of drug use, experimental and social/recreational use of cocaine is usually shared with another person. Heavy use may be solitary. Coca-paste smoking can be solitary, but there are also reports of group use in gangs of delinquent youths.

Populations at risk

Population surveys carried out in different regions and studies of consumption patterns have revealed certain risk factors for cocaine use. With few exceptions, men use cocaine or coca paste more often than women. In North America and Europe, it remains the case that adolescents and young adults are more likely to use cocaine than older individuals. However, recently there has been an increase in the number of middle-aged and elderly persons participating in treatment programmes in the Bahamas, Bolivia, Colombia, and Peru.

Other demographic variables are less consistent. Social class may be a risk factor in that, when the drug is expensive, the more affluent (and their offspring) are likely to be involved with cocaine use or with coca-paste smoking. As the drug becomes cheaper, the habit tends to spread to all social classes, involving particularly those young people with very underprivileged backgrounds—this sort of diffusion has recently been observed with coca-paste smoking in South America. In European countries data are available concerning clients of counselling centres, treatment programmes, and inmates of correctional and penal institutions. These data indicate a shift in cocaine use from higher social and educational levels of society to lower levels, while an increasing number of middle-class clients have been seen recently in treatment programmes.

Personality factors

Personality factors may be significant as predictors of risk. In general, disturbed or unconventional people will be attracted to any form of “rule breaking” or to membership of deviant groups, and hence these types of people may be especially likely to use cocaine. In the United States, for example, more unconventional attitudes to political and religious issues have been found among cocaine users than among the general population, but such findings may of course result from drug use or other associated happenings. It is quite possible for stable, mature individuals to become over-involved in cocaine use, if they have easy access to supplies. Thus, although attention to personality factors may often be important for the individual, there is little evidence that a consideration of personality factors will contribute much to studies at the epidemiological level.

Psychiatric illness must also be considered as a potential risk factor,

but there are discrepancies in the estimates of how many cocaine users have serious psychiatric illness in addition to their cocaine problem. Reported rates of psychiatric illness among cocaine users in the USA have ranged from 10% to over 50%. Estimates have differed widely not only between countries but also between different programmes in the same country. These variations may reflect true differences in prevalence or diagnostic difficulties that can lead to confusion with the effects or after-effects of the drug itself. The two most common psychiatric illnesses diagnosed among cocaine users are forms of depression and bipolar disorder, with a small percentage of attention-deficit disorders.

Family factors

The family background is another area that is frequently investigated during the analysis of data on users of cocaine and coca paste. Results from different regions tend to suggest that individuals from a broken home or an otherwise disrupted or inadequate family environment are numerically over-represented among cocaine users. But as with personality factors these findings should not be over-interpreted; cocaine or coca-paste use can and does occur in people with a stable home environment or from families with less obvious communication problems.

Peer-group and other environmental influences

Another risk factor invariably stressed is the contact with peers or other “influential” persons who are using cocaine or coca paste. This finding should be considered in different ways: the contacts with such people provide opportunities for being introduced to the habit and ensure availability of the drugs as well as being influential in providing models for cocaine-oriented lifestyles and careers. This risk factor is especially important when family and other controls do not offer attractive alternative life styles.

It is still debatable whether the risks associated with cocaine and coca paste act as a deterrent or in fact may stimulate some people to use the drugs. It has been found, for example, that a tendency towards risk-taking behaviour in other areas is associated with elevated figures for cocaine use among adolescents. The highest ratings of cocaine as a dangerous drug are found among ex-users. In adolescents and young adults risk-taking is part of a behavioural pattern that is frequently observed.

In addition, the absence of gratifying life prospects seems to promote use of drugs, including cocaine and coca paste, although this is not a direct finding in itself, but is rather an interpretation of certain observations such as the prevalence of hopelessness or boredom among these young people.

A factor that is, of course, of crucial importance is the actual availability of the drug, and its price. The number of users increases when more cocaine or coca paste is available on the market.

Initiation and discontinuation of use

Very little is known about the natural history of cocaine use and the extent to which any generalizations are possible. From what has been discussed in previous sections, it is evident that friends, social pressures, and curiosity about drugs may all encourage a non-user to experiment with cocaine, as may the imitation of admired role models, feelings of depression, and a deprived life style and other environmental factors. The degree to which perception of danger may militate against initiation is still uncertain; cocaine use may actually be attractive to some people as a form of "risk-taking". As regards the pathways out of cocaine use, the user's perception of mounting adverse consequences is often important. Impairment of physical and mental health, threatened loss of job or spouse, loss of ability to perform in school, and legal complications may all at times be relevant. The price of cocaine in the non-Latin American countries may become prohibitive, and even the cost of coca paste may eventually account for a major portion of a person's income, necessitating criminal activities to finance its continued use.

Discontinuation of use can occur following experimental or infrequent recreational use without any therapeutic intervention. Compulsive use, whether in the form of sniffing, injecting or smoking cocaine free base or coca paste, may be far more difficult for the user himself to discontinue without medical or psychiatric intervention.

In conclusion, more information is needed to assess properly the global extent of the cocaine problem. The nature, extent, and trends of cocaine dependence are not known with any degree of certainty. Global prevalence studies are required and the epidemiological situation should be monitored periodically. The identification of susceptibility and risk factors, a scientific assessment of the social and health hazards, and a means of deterring destructive usage are needed before successful demand-reduction approaches can be initiated. Cocaine use is rapidly becoming a worldwide problem, requiring global collaboration.

Coca-paste smoking

This chapter describes the properties, use, effect, and consequences of coca-paste smoking.

Definition

Coca paste is a white powder which is produced when dried coca leaves are soaked in water and then treated with kerosene or gasoline, alkali, potassium permanganate, and sulfuric acid. This produces cocaine sulfate, but the paste also contains ecgonine, benzoylecgonine, hygrine, methylcocaine, methylecgonine, nicotine, benzoic acid, methanol, kerosene or gasoline, and sulfuric acid. When the paste is well dried, it can be mixed with tobacco or cannabis and smoked. Coca paste sold on the streets may also contain impurities added by the manufacturer. The cocaine content of coca paste may thus vary from 41% to 91%, but usually 1 kg of paste yields 0.5 kg of pure cocaine, when the paste is treated with hydrochloric acid (2, 12, 18, 26).

Some components of coca paste, such as methanol, kerosene, leaded gasoline, sulfuric acid, caustic soda, tobacco, and cannabis, can produce toxic effects in addition to the changes generated by cocaine sulfate. The caustic reactions associated with the local application of coca paste prevents its use by oral, intranasal, mucosal, intramuscular, intravenous or subcutaneous routes. Coca paste can only be smoked when combined with a very inflammable material such as tobacco or cannabis.

Effects of use

Coca-paste smoking produces considerable euphoria or central nervous system stimulation almost instantaneously, because of rapid cocaine penetration to the brain via the arteriole circulation of the lungs. These effects are accompanied by high plasma levels of cocaine. After a few seconds or minutes the euphoria is replaced by considerable anxiety, fear, depression or apathy. These unpleasant psychological changes (dysphoria) can be ameliorated by smoking more paste, so the person develops the need to use the drug continuously, for many hours, to feel relatively well again, although rarely will the user re-experience the initial high or euphoria. Users describe this type of reaction as anxiety, but really it is a complex state of anguish associated with a compulsive need to smoke more paste. The user may feel sad, aggressive, irritable, suspicious, or unpleasantly excited. If the individual continues to smoke, he or she may develop hallucinations, illusory perceptions, paranoid thinking or frank psychotic behaviour (17–19). There is no doubt that when people begin to use the drug, they can generally control their smoking to once or twice a week; however, for the majority, this

frequency increases progressively until they become intensive or compulsive daily users (16–19). Most subjects who volunteer, or are referred or brought to treatment, belong to this last group.

Consequences of use

The consequences of intensive use can be divided into physical, psychological, and social effects.

During the stages of euphoria and dysphoria, users experience numbness, dryness of the mouth, burning sensations of the eyes, sweating, palpitations, headache, muscle twitches, restlessness, dizziness, colicky pains, and a desire to urinate or defecate. On examination there is hyperhydrosis, hyperactivity, tremors, tachycardia, hypertension, mydriasis, fever, myoclonic jerks, and increased reflexes. At the same time users may experience apprehension, anxiety, suspiciousness, sadness, irritability or apathy (2, 4). Many users try to diminish these unpleasant sensations by drinking alcohol before resuming smoking.

If the person continues to smoke he or she may develop marked tachycardia, high blood pressure, fever, muscle spasms, multifocal myoclonus, cardiac arrhythmias, complex partial seizures, generalized convulsions, paranoid thinking, and visual, tactile, auditory, olfactory or sexual hallucinations. Finally, the user may develop manic or psychotic behaviour accompanied by the physical symptoms mentioned above. Death may occur as a result of status epilepticus, ventricular tachycardia, and heart or respiratory arrest. Some or all of these physical and psychological reactions can be observed in recent or intensive users, depending on the dose of drug smoked, the frequency of smoking sessions, or idiosyncratic predisposition. These reactions are more frequent in the compulsive, excessive or chronic smoker. Such persons tend, during the course of months or years, to lose weight, to develop anaemia, malnutrition, and immunodeficiencies, and to suffer from parasitic, bacterial, mycotic or viral infections. Bronchitis and other inflammatory changes of the respiratory tract are common.¹

A considerable number of recreational or situational coca-paste smokers may eventually show signs of psychological deterioration. They may develop brain syndromes including apathy, indifference, anhedonia, memory disturbances, inattention, thought deficiencies, chronic anxiety, chronic depression, suicidal ideation, irritability, impulsivity, compulsive behaviour, and psychopathic disorders. They lose interest in work,

¹ JERI, F. R. *Coca-paste smoking in Latin America: a review of a severe and unabated form of addiction*. University of San Marcos, Lima, Peru. Presented at the Advisory Group Meeting on the adverse health consequences of cocaine and coca-paste smoking, Bogotá, Colombia, 10–14 September 1984.

friendships, recreation, sports, sex, family and conjugal relationships. At this point, their overriding concern becomes the smoking of coca paste, as frequently and as intensively as possible (2, 25).

As a result of the physical and mental changes mentioned, the compulsive or chronic coca-paste smoker tends, at first, to associate with other drug-dependent persons, gradually losing contact with friends, colleagues, relatives, and even spouse and dependants.

The need to ensure regular supplies of the drug may mean that the person turns to crime to obtain the necessary money. Eventually, the person may lose his/her job, drop out of school, run away from home, or be expelled from the family circle, until finally the only contacts maintained are with the supplier of the drug.¹ The loss of skilled manpower for the country, resulting from the physical and psychological deterioration associated with habitual coca-paste smoking can be considerable.

¹ JERI, F. R. See note 1, page 13.

Cocaine free-base smoking

The special phenomenon of cocaine free-base smoking is discussed in this chapter, including the preparation of the substance, doses, patterns of use, the acute and chronic effects of its use, and complications.

Cocaine free base was first smoked in California in the United States in 1974. The first hospital admission for a problem related to smoking of cocaine base was in 1975, and in the same year, extraction kits and smoking accessories became commercially available. In 1978, the distribution of these accessories spread from California throughout the United States. By 1979 cocaine free-base smoking had been reported in 15 states of the USA, the Bahamas and Puerto Rico. By 1980 its use was reported throughout the United States (30). Between 1980 and 1984 unpublished reports indicated rare cases of use in Canada and some European countries, including the Netherlands and the United Kingdom. Cocaine free-base use has also been reported from other countries, including Australia and Fiji.

Cocaine free base has recently achieved considerable popularity in the USA. Known as “crack”, it is sold in small amounts, and does not require any treatment before being smoked. The emergence of this substance has made cocaine available to a wider abuser population than ever before.

Preparation and purity

Cocaine free base (also known as cocaine base, base, or free base) is cocaine alkaloid or benzoylecgonine. During the early 1970s, cocaine users in North America became aware of the practice of smoking coca paste or *base* in South America. Confusing *base* with cocaine base, these users began experimenting with smoking cocaine free base extracted from the cocaine hydrochloride used intranasally and intravenously (30).

Cocaine free base is prepared by simple chemical procedures whereby the cocaine alkaloid is “freed” from the hydrochloride salt. The most common extraction methods used in the United States and the Bahamas involve the use of sodium bicarbonate (baking soda) while less common methods used in the United States and Colombia involve ammonia, ether, and other chemicals. Unlike cocaine hydrochloride, the free base is not readily soluble in nasal mucous membranes or in blood, but it does have a low melting point and can be readily volatilized and inhaled during smoking. As much as 84% of cocaine free base can survive the heat of combustion during smoking as compared with less than 1% of cocaine hydrochloride. Thus, the smoking of cocaine free base has largely replaced an earlier experimental practice of smoking cocaine hydrochloride in tobacco or marijuana cigarettes.

Methods of smoking

Cocaine free base is generally smoked in a water pipe, which is usually made of glass. Users place a small amount of cocaine on a steel or brass screen in the pipe bowl and apply heat from a torch (butane or propane), cigarette lighter, match or similar source. Deep inhalation techniques, similar to those used in smoking marijuana, are employed. Laboratory studies with smoking machines have demonstrated that because of the loss of cocaine through condensation in the pipe, melting, and escape through side-streams of smoke, only 5–6% of the cocaine free base is delivered to the mainstream of the smoke that is inhaled. None the less, individual variations in smoking techniques may increase the yield to 32% or more (27).

Dosage and absorption

The purity of cocaine free base is dependent on the purity of the cocaine hydrochloride from which it was extracted. In the United States, adulterants and diluents are often added to illicit supplies of cocaine hydrochloride. Some adulterants such as sugars, mannitol, and inositol, are removed to a large extent during the extraction process. Others, including the local anaesthetic lidocaine, and the stimulant ephedrine, survive both the extraction and smoking processes and can produce some psychoactive effects. In addition, even the smoking of pure cocaine free base results in the production of several pyrolysis products that have not been fully identified. None the less, cocaine free base is generally considered to be a purer and more potent cocaine preparation than coca paste, cocaine sulfate, or traditional *basuco* preparations.

The average amount of cocaine free base placed in the pipe bowl is 80–100 mg for a single “hit” or inhalation. Inhalations may be repeated every five minutes during smoking episodes (also called runs or binges), which may last from 30 minutes up to several days. Individual consumption may range from 9 to 30 g per 24-hour period, although individuals seeking treatment have reported smoking up to 150 g in 72 hours. In the United States the weekly consumption for individuals seeking treatment averaged approximately 9 g in one study and 28 g in another. In the Bahamas, individuals seeking treatment were reported to have consumed 3–4 g in 4-hour episodes; the use of 10 g in 2- or 3-day episodes has also been reported. Overall, such doses would result in plasma cocaine levels similar to those reported in users of coca paste.

Patterns of use

Regular smokers of cocaine free base may adopt one or more different patterns of chronic use. Some smoke with friends or acquaintances at parties or in social groups. In parts of the Bahamas and the United

States, locations known as “base houses” have been discovered by law enforcement authorities. These houses, similar to the opium dens of the last century, provide users with cocaine free base, pipes, and protected areas for smoking, all at costs that are lower than street prices. In the Bahamas other locations, known as “base camps”, are located on several islands where the cocaine free base can be easily obtained, often without cost. The widespread availability of low cost cocaine in the Bahamas results from its geographical position, i.e., in the main cocaine trafficking corridor between South and North America.

In addition to social patterns of use, regular users may adopt more intense, individually oriented patterns whereby they manifest a preoccupation with drug-seeking and drug-using behaviour. This pattern of cocaine free-base smoking appears to be limited only by individual tolerances and supplies. Such regular users may have smoked cocaine continuously for periods ranging from several months to several years.

Non-regular smokers of cocaine free base may either experiment occasionally with smoking or attempt to limit their use to infrequent smoking with other people. However, the urge is very strong to escalate to more individually oriented patterns of intense and compulsive use.

The smoking of cocaine free base is the most expensive form of cocaine use. Not only are large amounts of cocaine hydrochloride necessary to ensure good yields of cocaine free base, but inefficiencies in the smoking process itself, large doses, extended periods of smoking, and the rapid development of behavioural tolerance all combine to increase the quantity of supplies demanded.

Intoxication

The acute effects of cocaine free-base intoxication resemble other forms of cocaine intoxication, but they appear to be more intense. A characteristic intense feeling of euphoria and well-being, similar to that reported with intravenous use, is the effect most desired by users. Whereas intravenous users may experience this euphoria within 14 seconds, rapid absorption through the lungs enables smokers to experience this initial effect within 6 seconds. Repeated smoking appears to diminish greatly the intensity of this subjective effect.

Acute physical symptoms of intoxication include increased blood pressure and heart rate, increased muscle tension, tremors, nervousness or restlessness, palpitations, slurred speech, dysarthria, thirst, anorexia, coughing, mydriasis, blurred vision, insomnia, increased body temperature with sweating, headaches, dizziness, nausea, and diarrhoea. Psychological symptoms include, among many others, euphoria, grandiosity, feelings of increased abilities, hyperexcitability, hypervigilance, loquacity, increased sexual urges, paranoia, and hallucinations.

The chronic physical effects include, among others, dry chapped lips and skin, chest pains, black sputum, hypertension, impaired vision, lethargy, tremors and shaking, and decreased dream sleep. Chronic psychological effects include dysphoria, irritability, attentional dysfunction, maladaptive behaviour, delirium, delusional disorders, and paranoid psychosis.

An important consideration is that smokers of cocaine free base, like users of coca paste, can progress acutely or chronically through a continuum of increasingly severe psychopathology. This continuum is marked by clinical syndromes of euphoria, dysphoria and, finally, by schizophreniform psychosis. Taken together these syndromes can constitute an organic mental disorder. Neither cocaine smoking (via coca paste or cocaine free base) nor intravenous use appear to be self-limiting, and may continue until either the supply of the drug or the user is exhausted (30).

Complications arising from smoking cocaine free base may include syncope, chest pains, lower back pains, myoclonic jerking, and seizures. Several published case studies have reported pulmonary dysfunction in users as well as isolated instances of barotrauma marked by pleuritic chest pain and dyspnoea (29, 35). Bronchitis and pneumonia due to cocaine free-base contaminants, such as ammonia, have also been reported. Deaths have occurred as a result of continuous seizures, cardiac arrhythmias, respiratory paralysis, and suicide.

Adverse health and social consequences

Although cocaine is often thought of as a harmless drug, clinical and research evidence indicates otherwise. Morbidity and mortality due to the pharmacological properties of cocaine, the manner of usage, its reinforcing effects, and the social consequences that may stem from its use, together provide an extensive catalogue of potential adverse consequences that give cause for considerable concern.

Animal experiments

In laboratory animals the intravenous injection of cocaine initiates and maintains the specific behaviour patterns that are required to obtain additional injections. Such repetitive behaviour is considered to be equivalent to the cocaine-seeking and compulsive-use patterns observed in man.

Animals will work more persistently at pressing a bar to obtain cocaine than for any other drug, including opiates. They will choose the bar that provides a higher dose and an electric shock in preference to one that offers a lower dose without a shock. They will continue to self-administer cocaine even when electric shocks are paired with the cocaine bolus (5). Hungry animals will preferentially press the bar for cocaine rather than for food (1). Male non-human primates will continue to work for cocaine despite the presence of a receptive female in their cage. Under conditions of unlimited access, monkeys will press the bar until exhausted or convulsing (10). If the animal recovers it will return to the task of acquiring more cocaine (33). In one experiment a monkey continued to press the bar despite the fact that it required 12 800 presses to obtain a single dose of the drug. After the conditioned response to cocaine has been extinguished, a single injection will re-establish the bar-pressing activity.

Under conditions of limited access, for example, when cocaine is available for a few hours a day, the laboratory animal is able to regulate its bar pressing so that a fairly consistent dose is acquired each day. There are many parallels between these cocaine-seeking animals and human compulsive users.

The basis of dependence on cocaine

Cocaine action appears to be the result of its ability to stimulate and potentiate the action of endogenous amines in the central nervous system. It inhibits the uptake of norepinephrine, dopamine, and serotonin, and releases norepinephrine from sympathetic terminals (11).

Cocaine is the most reinforcing drug known (28). Animals and people soon become compulsive users, especially when the rapid delivery systems, such as intravenous use or free-base or coca-paste smoking, are employed. The reward is immediate and the return to baseline mood

levels or below occurs rapidly. Both the intense euphoria and its disappearance drive the person to seek more cocaine. With nasal absorption the mood peak is lower, but compulsive patterns are known to develop with this technique as well.

It is clear that cocaine is a powerful reinforcer. While certain people, because of personality factors or life style may become more easily over-involved, it is likely that anyone with access to cocaine risks becoming a compulsive user (9). Instances where mature, stable, well-integrated individuals acquire a pervasive craving for cocaine are well known.

Laboratory animals and people, given access to opiate and stimulant drugs, frequently become compulsive users. Often, even after prolonged periods of abstinence, they persist in their drug-seeking behaviour. There is evidence to suggest that, in the absence of the drug, environmental stimuli previously associated with drug-taking might arouse a motivational state similar to that activated by the drug itself (22).

After a prolonged series of stimulations and dysphoric reactions to cocaine, sudden cessation can produce a stimulant-withdrawal syndrome characterized primarily by deep depression. In an effort to relieve the depression, self-treatment with cocaine is often restarted; this has little impact on the depressive process, but results in a relapse to compulsive use.

In the withdrawal phase, the dopamine neurotransmitters to the reward system have been exhausted and the receptor cells of the reward centres of the brain have become refractory, leaving the person unable to enjoy ordinary pleasures for days or weeks thereafter.

This combination of positive and negative conditioning—the intense euphoria associated with cocaine use, the effort to avoid dysphoria, the distressing post-cocaine depression and the painful anhedonic residual phase—makes it easy to understand why relapse occurs so frequently during treatment.

Problems resulting from the dependence potential of cocaine

The severity of the dependence syndrome that can develop with the use of this drug means that the person who has become cocaine-dependent may find it very difficult to break the habit, while anyone who has recently broken the habit may be very prone to a relapse.

The extreme compulsivity that may characterize an individual's need for this drug accounts for the frequent reports of the heavily dependent cocaine user putting the need to obtain the drug above all other considerations, and consequently neglecting ordinary family and social responsibilities. Crime may be perceived as the only way to meet the continuing cost of maintaining drug supplies. The dependent state

therefore makes the user vulnerable to many problems, both personal and social, while also exposing him to numerous psychological and physical risks, as discussed in the following sections.

Psychological hazards of cocaine use

The non-specific effects on personality and behaviour that commonly result from severe cocaine dependence are the most serious psychological hazards of cocaine use. This disruption of personality is closely related to some of the social problems discussed in the previous section. The dependent cocaine user may become irresponsible, moody, suspicious, unreliable, self-centred, irritable, and, in certain circumstances, violent or suicidal.

A more specific psychological consequence that can result from heavy cocaine use is cocaine psychosis, a condition closely resembling amphetamine psychosis. In its mildest form, this disturbance may be characterized by no more than rather minor and fleeting perceptual distortions and exaggerated suspiciousness, for example, lights may look especially bright or flickering, there may be a transient delusion that a stranger is a policeman. In its extreme form cocaine psychosis is a devastatingly florid and chaotic type of toxic psychosis characterized by a mass of delusional and hallucinatory experiences, and often by marked paranoid colouring. Complete recovery can usually be expected to occur within a few days, but even so this type of illness must be seen as potentially dangerous for both the user and those around him.

Adverse physical consequences of cocaine use

As with other drugs, adverse physical consequences may arise both from the direct toxic effects of cocaine and as a result of the method of self-administration.

As regards direct toxic physical complications, it should first be realized that cocaine overdose can be fatal, with the subject dying as a result of ventricular fibrillation, cardiac arrest, apnoea, or hyperthermia. Such fatalities are fortunately very rare, but several small case series have been reported.

Extreme and transient hypertension can be induced by the self-administration of cocaine, and a few cases have been reported of resulting cerebrovascular bleeding and stroke. Heavy administration of cocaine can cause epileptiform fits.

In addition, there are a variety of reports suggesting that other types of direct toxic damage may occur with cocaine use such as brain or liver damage. Until further research is carried out there is no firm evidence on which to judge these reports.

The adverse consequences that can result from the mode of administration include, of course, all the well known infectious and

embolic complications of intravenous infection of any drug. In addition, there are certain special dangers associated with the smoking of coca paste and free base. There is a possibility that the drug or certain contaminants may damage the alveolar linings of the lung. A well established but rather uncommon risk of sniffing cocaine is damage to, or perforation of, the nasal septum.

Complications due to the interaction between cocaine and other disorders and drugs

Patients with coronary insufficiency are at increased risk when using cocaine because of the resultant tachycardia, hypertension, vasoconstriction, and greater cardiac demand. Diabetics are also at risk when using cocaine because the drug sensitizes the body to epinephrine, which can raise blood sugar levels. Compulsive diabetic users may also give insufficient attention to their diet and to their prescribed antidiabetic medication.

All drugs that release epinephrine, including guanethidine, are incompatible with cocaine use. Heroin in combination with cocaine depresses the respiratory centre more readily than either drug alone. Occasionally an individual with a congenital lack of the enzyme cholinesterase, can die from as little as 20 mg of cocaine.

Public health and social consequences

Most families of a cocaine- or coca-paste-dependent user live in a state of turmoil.

The costs of cocaine or coca-paste dependence are such that it is often difficult to maintain continuing use without resorting to unlawful means of obtaining funds. Family, friends, and strangers may be robbed and the user may resort to drug-dealing and other illegal activities to support the habit.

Cocaine trafficking generates enormous sums of money, and often leads to corruption in many aspects of public life, to violence, and murder. It can cause major problems for governments and undermine traditional ethical and social values. Farmers may turn from food production to coca planting because of the great financial returns.

When large numbers of young people become over-involved in cocaine use, the loss to a nation can be immense because the productivity of these individuals is reduced or lost. In addition the total health costs of caring for compulsive cocaine users are enormous. The costs of associated chronic illness are still not known. The possibility exists that cocaine and coca-paste smokers may develop chronic pulmonary dysfunction or disease. Whether permanent damage occurs to other organs in long-term users remains unknown.

Thus, it is not only the individual who suffers as a result of cocaine dependence, but also his or her family, community, and country.

Treatment and management

General considerations

The treatment of cocaine abuse and dependence presents a number of complex problems, many of which have not yet been adequately investigated. This complexity arises from the variety of factors that influence the presentation, course, and outcome of the disorder, including: route of administration; form of cocaine used; frequency and intensity of use; simultaneous use of other drugs; presence of impurities in the drugs; presence of diagnosable psychiatric illness; social class of user. The treatments that have been described in the scientific literature are discussed in this chapter, as well as the way in which the factors listed above necessitate the modification of their treatments in various settings.

Several forms of cocaine misuse have been described: experimental, recreational, situational, intensive, and compulsive. Cases of acute intoxication have been documented following all of these forms of use; treatment has been detoxication and sedation with minor tranquillizers. Rare complications such as hallucinosis, psychosis, convulsions, respiratory distress, heart failure, or injuries suffered in accidents, fights, assaults or suicide attempts require emergency treatment or intensive care.

Some individuals use cocaine in specific situations or for self-medication. Evaluation of these individuals, after the intoxication phase has been controlled, may show that they suffer from stress reactions, reactive depression, character disorder, paranoid psychosis, latent or active schizophrenia, unipolar or bipolar affective disease, mild or moderate mental retardation, or other chronic brain disorders. These conditions should be treated in the appropriate way.

The majority of patients at treatment centres are compulsive, relapsing or chronic cocaine abusers. They may suffer from several of the conditions for which hospitalization is recommended: concurrent dependence on alcohol or other drugs; serious medical or psychiatric problems; severe psychological impairment; lack of motivation; lack of family or social support; and repeated outpatient failures. Consequently, these patients are generally treated as inpatients for a few weeks to one month. Treatment consists of detoxication, use of sedatives or neuroleptics, and supportive behavioural or dynamic psychotherapy. Economic and personal limitations often mean that such periods of hospitalization and psychotherapy are extremely brief. After discharge, a considerable number of relapses occur among this group. Follow-up studies in three centres have demonstrated relapse rates of 50%, 60.9%,

and 87.5% one year after discharge (21, 31).¹ These results have prompted some clinicians to use psychosurgery (bilateral anterior cingulotomy) for severe, chronic, and recidivistic patients. There are no reports in the scientific literature on this form of treatment, but preliminary results indicate only a 50% success rate after one year of follow-up. The majority of clinicians consider that at present there is no justification for psychosurgery because other methods of therapy, effective in severe multi-drug abusers, have not been properly employed for cocaine abusers.

Routes of administration and sequences/intensity of use

Severe problems can occur as a result of cocaine use, regardless of the route of administration—intranasal sniffing, intravenous injection, or smoking. However, it appears that those taking the drug by the last two routes are more likely to become heavily addicted earlier and apply for treatment sooner, and that a higher percentage of them will develop severe problems. Different routes of administration do not seem to demand different treatment approaches. It is not yet known whether the route of administration affects the outcome of treatment. However, the presence of other drugs or impurities, e.g., the presence of cannabis in *basuco*, may produce physical or psychological problems that need to be kept in mind during the acute treatment process.

Presence of diagnosable psychiatric illness

There is a great discrepancy among the estimates of how many cocaine abusers have serious psychiatric illness in addition to their cocaine problem. Rates reported have ranged from 10% ² to over 50% (21) and differ not only between countries but also between different programmes in the same country. Such divergence may represent true differences in prevalence or may reflect difficulties in making a diagnosis because of confusion with the psychological effects of cocaine, different emphases on the importance of diagnosis, and different settings. The divergence may also represent differences in sampling procedures and the composition of samples. It is important that treatment programmes routinely collect information on the presence of psychiatric illness, using standard techniques, not only because this may have important

¹ GRIBENOW, W. ET AL. *Psicoterapia de grupo en farmacodependencia*. Presented at the Fourth National Psychiatric Congress, Lima, Peru, 1980.

² SMITH, D. E. *Treatment and aftercare for cocaine dependency*. Presented at the Institute of Alcoholism and Drug Abuse Studies Conference on Cocaine: problems and solutions. Baltimore, USA, 25 January 1984.

implications for treatment, but also to permit intercountry comparison of data. Structured interviews by trained, non-medical, personnel, have been shown to provide reliable data at low cost. The two most common diagnoses made are depression and bipolar disorder, with a small percentage of cases of attention deficit disorders.¹

Treatment of the acute post-cocaine phase

In the treatment of cocaine-dependent persons, there is no need for gradual withdrawal of the drug, as in treatment of narcotic or sedative dependence. Indeed, attempts by users to decrease gradually their dosage have almost always ended in failure (31). Cocaine use should therefore be stopped abruptly. There are three major psychiatric complications that occur at this stage of treatment: dysphoric agitation, severe depression, and psychotic symptoms. Dysphoric agitation is best treated with oral or intravenous diazepam; propranolol may also be given to more persistent cases (14). Suicidal ideation and other depressive symptoms often occur during the post-cocaine “crash”, but they are usually transient, require no acute treatment other than close observation, and resolve following normalization of sleep patterns. The effects of chronic cocaine use on neuroendocrine hormone levels in the brain have prompted the use of agents such as pyridoxine, tryptophan L-tyrosine, phenothiazine derivatives, and tricyclic antidepressants. Controlled studies to confirm the efficacy of these agents have not yet been carried out. Psychotic symptoms are also usually transient (lasting less than 4 days) and usually remit following normalization of sleep patterns. Neuroleptics such as chlorpromazine, haloperidol, and promazine have all apparently been used successfully to manage patients with these symptoms. Oral or intravenous solutions have been used in malnourished patients who cannot take solid food, and may be needed in individual cases, but have not been systematically studied.

Inpatient versus outpatient treatment

Inpatient stays ranging from a few days up to a year or more have been variously advocated. However, relapse rates are significant, even after long hospital stays. Outpatient treatment, if it is possible, is preferable to inpatient treatment because of its lower cost, and the fact that it causes less disruption to the patient and his/her family.

¹ WEISS, R. D. ET AL. *Psychopathology in chronic cocaine abusers*. Presented at the 13th annual meeting of the American Psychiatric Association, New York, USA, 4 May 1983.

Inpatient treatment is, however, strongly recommended for patients with severe depression accompanied by suicidal ideation or psychotic symptoms, if either lasts beyond the third day of the post-cocaine period, or homicidal ideation, and for those who have had several relapses following outpatient treatment. Other conditions that may require hospitalization include: heavy free-base, coca-paste or intravenous use; concurrent dependence on alcohol and other drugs; serious psychiatric or medical problems; lack of motivation; lack of family or social support.

Maintenance of abstinence—psychological approaches

The psychological approaches to maintenance of abstinence fall into three categories: behavioural, supportive, and psychodynamic. All three can be useful in the treatment of cocaine abusers and it is important to establish a flexible individualized approach. Severity of dependence, degree of psychological problems, and presence of psychosocial support are only three factors among a number that influence which approach should be used and when.

The *behavioural methods* used include contingency contracting, desensitization, and relaxation training.

For the vast majority of people who come to treatment, cocaine use has become a central part of their life. Some seek treatment with a strong conviction that they have lost control of their drug use, and pay too heavy a price for it, both financially and personally, but a substantial number have much more ambivalent feelings. While they may realize that cocaine harms them, they often feel they can control their drug use and do not want to give up the drug-induced feelings. Often pressure from family members or from the law has led them to seek treatment. If these clients are to remain in the programme, psychotherapy must address this ambivalence. Contingency contracting emphasizes this area by focusing and magnifying the particular harmful effects of cocaine use (3).

Contingency contracting has two basic elements: the subject agrees to participate in a urine monitoring programme; and an aversive contingency is attached to either a cocaine-positive sample or a failure to produce a scheduled sample. The aversive contingencies are derived from the patient's statements of the adverse consequences expected to result from continued cocaine use. Such an adverse effect is then scheduled to occur at the very next use of cocaine. For instance, the patient may be requested to write a letter of irrevocable personal consequences, such as a letter admitting to cocaine abuse addressed to his/her employer or professional licensing board. This letter is then held by the therapist and sent to the addressee in the event of a lapse by the patient. Such contracts, coupled with supportive psychotherapy, appear to be effective as long as the patient is willing to take part.

The clear emphasis that this method gives to the deleterious effects of cocaine abuse can also be repeatedly reinforced in psychotherapy using individual, group, and family techniques in a less potentially harmful manner than contingency contracts. Contingencies could also be used in a graduated fashion. In addition, it might be useful to try positive contingencies—for example, obtaining a sum of money from the patient initially and giving part back for each clean urine sample. Some cases might benefit from a combination of positive and negative reinforcement.

Desensitization is a form of therapy in which anxiety-evoking stimuli are presented to the patient while he or she is in a state of deep muscle relaxation, in an attempt to weaken the bond between the stimuli and the anxiety. In relaxation training, the patient is taught various relaxation techniques for controlling physical stress and tension. Desensitization and relaxation training have not been systematically studied for cocaine abusers but they have been used for other substance abusers with mixed results. They appear to be useful as one part of a total package, but not when they are the sole or main technique employed.

Urine monitoring on a frequent, random basis can be an important tool in treatment programmes. Such monitoring may both detect slips before they become full relapses and reveal the use of other mood-altering chemicals. It should be remembered, however, that cocaine metabolites can only be detected in the urine with any certainty up to approximately 27 hours after the last use. Occasional use may, therefore, pass undetected for a period of time.

Supportive methods emphasize the need to dissociate the abuser from situations where cocaine is used and from cocaine sources, and to help him/her to manage impulsive behaviour in general, and cocaine use in particular (30). The following supportive methods have been tried with varying degrees of success: supportive psychotherapy sessions; education concerning behaviour consistent with stopping cocaine use such as the destruction of all accessories and drug stashes; encouraging of increased contact with friends who do not use cocaine, and avoidance of social contact with cocaine users and dealers; and training to deal with high-risk situations. During therapy, patients should review potential problem situations and how they might manage them, e.g., by calling a supportive friend, taking vigorous exercise, or postponing use for one hour at a time.

Self-help groups, such as Narcotics Anonymous and more recently Cocaine Anonymous in the USA, can provide structure and limits as well as group support and a helping network. They employ supportive and behavioural techniques. Although some users and clinicians have described these groups as effective, there have as yet been no controlled studies of their usefulness.

The role of the family is of crucial importance. Wherever possible, family members should be involved in the treatment process. They need education on both the dangers and consequences of drug use and how to deal with the manipulations of the abuser. Limit setting, consistency of behaviour towards the drug user, and avoidance of double-bind communications can all be profitably discussed with the family. Some programmes refuse to treat a patient unless the family is involved since their support and pressure are so important. On a cautionary note, however, the family may be so disorganized or disturbed in some cases that their involvement will do more harm than good, so again the importance of individualizing the treatment approach needs to be stressed. The specific approach to be used, e.g., individual treatment or involvement of the family, will depend also on cultural attitudes and therapist training.

Psychodynamic treatment approaches are aimed at understanding the function that cocaine has played in the abuser's life and at helping him or her fulfil these functions without drugs. Sexual problems, feelings of inadequacy in interpersonal relationships, boredom, narcissistic needs, and a sense of inner emptiness are all areas that can be usefully explored for some cocaine abusers. Understanding these needs may provide an increased sense of control in the abuser which may reduce the need to turn to cocaine.

A combination of all three approaches—behavioural, supportive, and psychodynamic—is probably the most common form of both inpatient and outpatient treatment. The optimal mixture is best determined by assessing the needs of the cocaine abuser at the time he/she seeks treatment. Behavioural methods seem particularly useful for mild and moderate abusers, while supportive measures are most appropriate for moderate and severe users. Moderate users respond to dynamic treatment better than to other forms of therapy. Severe abusers may also benefit from dynamic treatment at a later stage. It is also important to recognize the assets and liabilities that patients bring to the treatment process, since this will be important in determining the outcome. Some patients may need rehabilitation to return to previously satisfactory levels of function while others, who have never functioned adequately, will need habilitation.

The role of abstinence

There is general agreement that the goal of treatment should be total abstinence from cocaine use. It is highly unlikely that the compulsive abuser can ever return to occasional controlled use, and relapse often results from an attempt to do so. There is less agreement as to whether individuals need to abstain from all mood-altering drugs, e.g., alcohol

and cannabis, if they have not previously had a problem with these agents. Abstinence is probably desirable because relapse often occurs when the abuser is under the influence of other drugs, and because of the danger of developing a new addiction. However, many patients resist such total abstinence until they learn from their own experience that it is necessary.

Pharmacological treatments

At present all pharmacological treatments should be considered experimental since large, random assignment, double-blind studies have not yet been done. However, there has been an accumulation of clinical experience and open trials suggesting that certain agents may be useful in particular cases.

Lithium appears to be useful in patients who have been diagnosed as having bipolar disorder or cyclothymic personality. Although lithium was originally studied as a potential blocking agent for cocaine euphoria, it does not appear to act in this way, and has been found useful only in patients with the above diagnoses (13).

Tricyclic antidepressants, especially desipramine, seem to be potentially useful for all patients. This may result from the effect of desipramine on dopamine levels; the depletion of dopamine levels by chronic cocaine use may be the cause of the post-cocaine depression often associated with cocaine craving and relapse.

Stimulants such as methylphenidate may be helpful for patients diagnosed as having attention deficit disorders (20). Their potential for abuse means that they should be used cautiously and selectively.

Phenothiazine derivatives have been used to control impulsive behaviour and decrease cocaine craving. While some clinical experience suggests that they are useful, the unpleasant side-effects and frequent dysphoria associated with their use greatly limit patient acceptance.

Other approaches

Psychosurgery, e.g., bilateral anterior cingulectomy, has been tried, mainly in South American countries, for some severe intractable cases. Results have been mixed and, in general, such an approach appears unwarranted at this time.

There are a variety of other unproven techniques that have been, or are being, tried by street users and clinicians in various countries, to deal with the dysphoric post-cocaine symptoms as well as to maintain abstinence. They are not discussed in this book since there are no published reports available for study.

Relapse prevention

To prevent relapse a special effort should be made to educate the patient and to help him/her anticipate potential problems (34). The following areas are especially crucial: re-education of patients who forget the deleterious effects of cocaine and only remember the pleasant effects; the role of conditioning factors and triggering stimuli in precipitating cocaine use; high-risk situations; early warning signals; and the “abstinence violation” effect, whereby one slip is seen as nullifying months of abstinence. Relapse often occurs, not when the patient is feeling bad, but when he feels overconfident and believes he can return to occasional use because he has overcome the problem.

As with abuse of any other substance, relapse is not uncommon and both patients and families need to avoid unrealistic expectations.

Conclusion

A number of treatment approaches are currently in use, but further controlled studies are required. No single treatment is likely to become the definitive treatment for all cocaine abusers. Instead, the integration of various approaches based on the needs of patients seems to be the best method of treatment.

One possible treatment scheme is as follows:

- Mild abusers might be treated using behavioural methods without adjunctive pharmacotherapy or intensive psychotherapy.
- Moderate abusers might be treated using primarily supportive methods and psychodynamic psychotherapy with additional diagnosis-related pharmacological treatment.
- Severe abusers or those resistant to the above treatment might be treated within a primarily supportive therapeutic framework with the addition of pharmacotherapy designed to combat cocaine craving and restoring disturbed neuroendocrine hormone levels.

A final cautionary note needs to be added. The treatments described in this chapter require highly trained staff and considerable time to individualize care. In a number of countries the problem of cocaine abuse has become so large that there may not be sufficient resources available. Therefore, a major priority of treatment research is the development of simple, inexpensive approaches that can be implemented by less highly trained personnel.

The need for prevention

There is clearly a need for both primary and secondary prevention in order to control the use of cocaine and coca paste and the resulting problems. The enormity of the problem will not be reduced merely by successfully treating the few users who seek help. Certainly treatment is needed, and treatment resources, at some level, exist in all countries. However, prevention programmes in many countries do not focus on cocaine or even include it as an important topic of concern. Other countries have fragmentary, uncoordinated programmes whose impact is uncertain. Whatever is done should be evaluated scientifically at both a trial or pre-implementation stage, and again when the programme is fully functional.

Primary prevention refers to the prevention of new cases of drug use. Secondary prevention refers to efforts to identify drug-related problems at an early stage and to prevent them from escalating into major concerns. It includes studies to identify high-risk populations.

Prevention programmes will necessarily involve a wide variety of activities including legal controls on cultivation, manufacture and distribution of cocaine-containing substances, and crop substitution. Programmes aimed at reducing demand would include mass media and school-based programmes to educate the public, special efforts to reach experimental users and high risk subpopulations, special educational involvement with parents and families of users, and a concerted effort to develop anti-cocaine attitudes in the public at large. Not all of these efforts can be carried out at the same time in many communities, and some efforts may be more appropriate than others at any given time. To be successful a prevention programme must have both political and public acceptance. Consequently, cocaine prevention programmes must reflect the needs, values, and priorities of the society in which they are being carried out. Countries can learn from prevention efforts that are undertaken elsewhere, but each must carefully adapt their strategies to meet the realities of the local culture, customs, and resources available.

It is important to decide during the planning of a prevention strategy exactly what is to be prevented. There is considerable evidence to show that where there is extensive use of cocaine products many problems exist. In addition, cocaine use at a recreational or social level can quickly develop into heavy compulsive use with all the many accompanying social and health problems. Few users ever expect to have problems with cocaine, but many do. It is doubtful that a safe level of cocaine use exists; "use" and "problem use" are so closely interrelated that prevention strategies must focus on the prevention of all cocaine and

coca-paste use. References to social or recreational use of cocaine are therefore inappropriate and should not be used to specify a level of safety for either the user or society.

Primary prevention

Primary prevention involves a variety of strategies ranging from legal controls to education and persuasion of all types. Societies adopting primary prevention programmes seek to limit both the availability of cocaine-bearing substances and the motivation of people to try them for the first time. Experience shows that cocaine use can be reduced as a result of vigorous prevention efforts. For example, the use of cocaine early in this century in North America and Europe was virtually eliminated as a result of strict laws limiting its availability in pharmaceuticals and patent medicines, and because of mass media reports on the associated dangers. Cocaine-containing substances are reported to have disappeared from some countries in South America and in south-west Asia because of strenuous interdiction. What is required is both a change in the public attitude regarding cocaine and strict legal controls on its use.

A crucial aspect in prevention is to have strict laws that reduce supplies and curtail possession and trafficking. No country can successfully control cocaine use when supplies are plentiful and available at low cost. Some countries have introduced mandatory jail terms for possession of certain amounts of cocaine. Others have mandatory sentences without parole for trafficking or for the possession of amounts thought to be too large for personal use. Some jurisdictions confiscate the assets of dealers and traffickers. The manufacture and sale of cocaine paraphernalia, e.g., pipes and cocaine-like substances, are also illegal in some countries. Strict laws concerning possession and trafficking, consistently enforced, give a message to both potential users and the public at large that governments are serious about the dangers of cocaine.

At present, there is considerable debate about the eradication of the coca crops. Some crops are legal and are used to produce coca for pharmaceutical products. Such crops should be carefully monitored to minimize the amount of coca that is diverted to the illicit market.

Most illicit coca comes from crops grown specifically for the illicit market. These crops could be eradicated with airborne herbicides and some countries are attempting to do this. Some illicit crops are burned, but the amounts actually destroyed are small in comparison to the total growth. Eventually, crop replacement may be a practical solution. However, when demand for coca is high, farmers are unlikely to find other crops that are as lucrative. Coca bushes can be harvested three or four times a year, whereas substitute crops such as coffee, fruits or

vegetables, give only one or two crops per year and a lower financial return.

The mass media can be of great value in programmes aimed at preventing cocaine use because they provide a way to reach all levels of society. In the majority of countries the most powerful and influential media are television and radio, followed by films and newspapers. The media should be used to inform the public about the effects of cocaine, the symptoms of its use, and especially the risks involved. Unfortunately, in several countries at present, the mass media seem to be glamorizing cocaine use, rather than providing cautions and anti-cocaine messages. Cocaine is often portrayed in television programmes, for instance, as an exciting drug, possessed of a certain “chic” and without danger. Efforts will be needed to remove such pro-cocaine messages from programmes.

Mass media messages about the dangers of cocaine and other drugs are being developed in several countries. In some cases the messages focus on cocaine itself; in others the emphasis is on education about drug dependence in general. An effort is being made to discourage all types of illicit drug use. Some countries accentuate healthy life-styles with an emphasis on nutrition, exercise, and the avoidance of both excessive alcohol use and illicit drug use. The type of programme selected depends on the particular needs and priorities of the country. Simple scare-tactics are unlikely to be effective.

Evidence suggests that mass media programmes about drugs are unlikely to affect drug-using behaviour or dissuade users. However, the effect of many such programmes, together with legal controls, is to promote an anti-drug (or anti-cocaine) climate. Mass media efforts should create an awareness of the cocaine problem and educate the public about its hazards. They can give information such as where to obtain help for drug users and also provide advice for families.

Mass media anti-cocaine programmes should be persuasive, informative, and aimed at a particular audience. For general information the audience may be all listeners or readers. For specific anti-use programmes, the emphasis will be on high-risk groups, chiefly young males, often those not attending school. The messages and those who present them must be credible. Mass media messages can be sensational, but they should always be accurate, honest, and believable. Unfortunately, many mass media programmes are not pre-tested on their target audience before being used. They should be pre-tested and evaluated for their impact on a real audience.

Special pamphlets and educational material can be created for cocaine users, to try to dissuade them from further use, and to provide information about adverse effects and treatment. Such pamphlets may also be of interest to the families of cocaine users.

Many countries have school-based programmes on drug education. Many of the available programmes have not been evaluated, hence their

effectiveness is unknown. There is some concern in a few countries that a focus on cocaine is inappropriate, especially in younger age groups. If cocaine is rarely used, education about it may stimulate interest and experimentation. Probably only those countries that have immediate crises related to cocaine should provide specific education on the drug.

Sophisticated drug education programmes require sophisticated teachers. In many countries the training of teachers in the field of drug education, including cocaine use, is inadequate. Teachers must be well prepared to help students. Some use has been made of ex-drug users as drug education experts, but these people must be carefully selected. They may portray a wealthy, successful role model who dabbled in drugs and came through with no lasting problems; this type of ex-user is not recommended as a teacher. Instead, someone who has suffered through a drug experience is a more credible source for young people. Special education programmes are required for those who teach young people about drugs, whether they be professional teachers or ex-users.

Secondary prevention

A variety of secondary prevention strategies have been tested in different countries. Those at especially high risk for cocaine use are young males, particularly those who have already tried cannabis. In most countries, coca-paste users tend to be young urban males from the lower social classes, and are often those with some delinquent background. In some countries, these groups can be reached through school programmes, but many do not attend school. Specific programmes for high-risk groups should be developed in areas where they are needed. They may be centred on special youth centres, social clubs, sports activities or other events that attract young males.

Another approach is to focus on the families of cocaine users who are undergoing treatment. The whole family should be involved since there is a high risk that family members will start to use cocaine. This risk seems to be especially high if an older sibling in a large family is the cocaine user. Treatment personnel can inform family members about the dangers of cocaine use and support their efforts to avoid these dangers by discussing with them peer pressures and family dynamics.

The early identification of some cocaine users has been made possible by urine testing. Some schools, industries, and armed forces have experimented with mandatory urine-testing programmes for suspected users, or random urine testing. If cocaine is found in urine, the individuals may be suspended, given a strong warning or required to undergo treatment.

The role of parents and family

Parents and family are greatly affected if one member of the family uses cocaine. The family may tolerate any economic hardship to conceal the user's habit or they may deny that any problem exists. These families must be helped to see that such denial is counterproductive. Many countries have found it necessary to develop special seminars and programmes to educate parents about cocaine. Parents can be the first to recognize cocaine use and should be taught about its effects, how to recognize symptoms, and where to get help.

In several countries, special parent groups interested in controlling drug abuse have been formed. Such groups are often very large and influential. They tend to be strongly opposed to drug use and to press for stronger anti-drug laws and harsh enforcement. Other groups may act primarily as self-help bodies for parents in order to avoid the onset of drug-use, emotional crises, and other dysfunctional states, among family members. These groups should be encouraged and special efforts should be made by professionals to help and educate them.

Education for professionals

Physicians, nurses, psychologists, and other health care personnel are frequently confronted by users of coca paste and cocaine during their daily work. They often do not recognize the patients as cocaine users since the symptoms are unknown to them. Many qualified before cocaine and coca-paste use became popular and hence they learned little about these drugs during their professional training. Special seminars about cocaine and coca-paste use are needed to update many professional groups.

Chapter 8

Overview of research

In view of the fact that cocaine was first used for medical purposes over one hundred years ago, it might be assumed that the scientific knowledge available concerning cocaine is relatively complete. However, this is not the case. Much of what is known about cocaine, its local anaesthetic properties, central nervous system stimulatory actions, and general subjective and cardiovascular effects when ingested by a variety of routes, was described 50–100 years ago. Most of the “new” facts regarding the pharmacology of cocaine have been collected and reported since 1975, when the United States National Institute on Drug Abuse funded a series of research contracts to study the pharmacology of cocaine in man. These and subsequent studies provided detailed descriptions of the relationship between dose, route of administration, blood levels of cocaine, and limited physiological or psychological effects. However, there are still many large gaps in our knowledge concerning the biological and behavioural basis of cocaine abuse. In this chapter the gaps and the specific areas of research needed to fill them are discussed.

Cocaine and brain function

The neurochemical basis of cocaine’s action and its locus of action are still not known with certainty. Experiments by Wise and his colleagues (36), studying the reinforcing properties of intracranial self-administration of cocaine in animals, have thrown considerable light on the subject, but many questions remain to be answered. There is evidence to suggest that dopamine mediates the major brain effects observed with cocaine use (37). It must, however, be kept in mind that the neurobiology of reinforcement may not be the same as the neurobiology of euphoria, i.e., the brain mechanisms responsible for the compulsive self-administration of a drug may be different from the brain mechanisms underlying the perception of joy.

Clearly, further research is needed on the chronic effects of cocaine and coca-paste smoking on brain function and structure. Of particular interest is the phenomenon known as kindling; this is the increased sensitivity and responsiveness of various neural systems. Studies are needed to clarify whether the progressive increases in irritability, restlessness, hypervigilance, and paranoid behaviour observed following prolonged high-dose cocaine abuse, as well as some cases of adult onset epilepsy, are manifestations of kindling.

Although there is little to suggest that irreparable brain damage results from cocaine abuse, further research is needed in this area. Of particular interest would be the use of imaging techniques such as nuclear magnetic resonance and positron emission tomography.

The toxicity and pharmacological activity of psychomotor stimulants such as cocaine and amphetamine appear to be subject to modification by sensory stimulation. Furthermore, it has been shown experimentally that the psychopharmacological and neurophysiological effects of cocaine depend on the context in which the drug is given. The extent to which general environmental factors influence the psychoactive properties of cocaine should be investigated as well as the mechanism underlying this interaction. Other possible factors that might play a role in the predisposition towards cocaine use are genetic factors, the nutritional state, and possibly certain other conditioning factors. Research into the biological basis for cocaine-seeking behaviour would contribute to an understanding not only of stimulant abuse but of drug-seeking behaviour in general.

Cocaine is a potent psychomotor stimulant and this is the basis of its abuse. In addition to ongoing studies of the neurochemical basis of cocaine action, particularly with respect to various central neurotransmitters (e.g., dopamine, norepinephrine, and serotonin), more attention needs to be paid to the interaction of cocaine with other drugs of abuse, such as opiates (e.g., pethidine), alcohol, and other substances that might be used in conjunction with cocaine. Investigators should be encouraged to examine, at the preclinical level, the interaction of cocaine with other abused drugs. These studies might include investigation of the influence on brain neurophysiology of either the acute or chronic administration of cocaine in combination with other abused drugs. Researchers might also correlate the neurochemical or neuroanatomical consequences of cocaine administration with various behavioural patterns to define the existence, duration, and reversibility of functional disruption resulting from the drug interactions or reactions.

Pharmacology of cocaine

It is becoming increasingly common for cocaine to be used for an extended period of time; the effects of this practice on various bodily functions are virtually unknown. One of the best known established effects of cocaine is the suppression of appetite. Very little is known about the nutritional consequences of chronic administration of cocaine, nor is it known whether tolerance to appetite suppression develops. Cardiovascular toxicity has been reported in some individuals, especially when cocaine is given with epinephrine, but the long-term effect on the cardiovascular system is unknown.

It would also be of interest to determine to what degree cocaine-induced tolerance, dependence, and withdrawal exist. The nature and extent of the neuropharmacological, chemical, and physiological changes that result from long-term cocaine administration need to be defined. In addition, the development of models that can be used in studying

tolerance, dependence, and withdrawal is of interest, as are investigations to define the psychological versus the physical nature of dependence and withdrawal.

Cocaine metabolism and kinetics

Biochemical assays to measure tissue levels of cocaine and its metabolites in man are now available. A basic understanding has developed of the relationship between cocaine dose, route of administration, and its effects, but some uncertainty remains and new questions have arisen.

Major questions regarding cocaine use are why, and under what conditions, do use patterns change from recreational to compulsive? For example, there may be individual differences in metabolism. Can this be related to disease prognosis? Is metabolism significantly altered by the route of administration, i.e., smoking or injection? Further research is required to answer these questions. The effect of route of administration on the kinetics of cocaine action also needs further research.

Behavioural pharmacology

Various species of animal will self-administer cocaine, using different routes of administration, and under different environmental circumstances.

It would be useful to compare cocaine's reinforcing effects with those of other reinforcers. In experimental studies, cocaine and amphetamine show similar patterns of self-administration. However, when the breaking point of a progressive fixed-ratio schedule is used to compare the reinforcing magnitude of various psychomotor stimulants, cocaine is by far the strongest reinforcer. It is not clear how much of the "desirability" of the narcotics is partitioned between the alleviation or prevention of withdrawal and the production of euphoria. In 1977, Woods (38) wrote that "the comparison of cocaine's reinforcing effects with other drugs and non-drug reinforcers is both an important theoretical and empirical issue which has received little experimental attention." A comparison between drug classes is still needed.

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