A.2 Opiate Narcotics

INTRODUCTION
The term narcotic has had wide and inconsistent usage in lay, legal and scientific circles. Some use the word to characterize any drug which produces stupor, insensibility or sleep; many apply it only to derivatives of the opium plant (`opiates'); others consider the term equivalent to 'addiction-producing'; and in legal matters, 'narcotics' may refer to almost any allegedly dangerous drugs, (for example, marijuana and cocaine are often included with opiate compounds in narcotics regulations in spite of the dissimilarity of their effects). To reduce some of this ambiguity, the specific phrase opiate narcotic is used in this report and is restricted to opium, morphine and related alkaloids obtained from the opium poppy plant (Papaver somniferum), and the semi-synthetic derivatives of these alkaloids and wholly synthetic substances with similar pharmacological properties. Opium is prepared from the dried juice of the unripe seed pod (capsule) of the poppy plant, obtained soon after the flower petals begin to fall; the alkaloids are obtained from opium by various extraction processes.

In 1803, the major active constituent in opium was isolated—an alkaloid given the name morphine after the Greek god of dreams, Morpheus. Raw opium is about ten per cent morphine by weight. In the next half century, various other active alkaloids, such as codeine (methylmorphine), were discovered. Since then, hundreds of semi-synthetic and wholly synthetic morphine-like drugs have been developed. Heroin (diacetylmorphine) and hydromorphone (Dilaudid®) are semi-synthetic compounds derived from morphine. Fully synthetic drugs in this class include methadone (Dolophine® in the U.S.), piminozidine (Alvodine®) and pethidine (also called meperidine or Demerol®). These various natural and synthetic compounds have the potential of producing qualitatively similar actions (at different doses), although there is considerable variability among them in the potency of their various effects. With a few exceptions they will be dealt with as a group, with morphine as the prototype.

Heroin is several times more potent on a weight basis than morphine, but is otherwise not significantly different in action from it. Heroin was originally considered 'non-addictive' when first introduced at the end of the 19th century, and was even suggested as a cure for opium and morphine dependence. Heroin is usually the choice of the chronic opiate narcotic user in North America today, although members of the medical and related professions who use these drugs non-medically, as well as others who have become dependent as a result of medical use, usually take morphine or the synthetics. Methadone, first used for its analgesic properties, has become important in the management of opiate narcotic dependence, and has recently gained some popularity among illicit users. Although methadone will be mentioned from time to time in this general opiate narcotic discussion, a separate overview of methadone and its long-acting derivatives is presented later in this section. Heroin is often
referred to as 'H', 'junk', 'smack', `scag', `horse' or 'jazz'. Methadone may be called 'don' or 'dollies'.

Thebaine is an opium alkaloid, present in a number of poppy varieties, which has little morphine-like activity itself. A series of hundreds of semi-synthetic derivatives of thebaine have been developed which are referred to as the Bentley Compounds. Many of these compounds have morphine-like effects, and range in activity up to more than 1,000 times the potency of morphine and heroin. Some are equally effective opiate narcotic antagonists. One highly active drug, M-99 (Etorphine®) and a corresponding antagonist, M-5050 (Diprenorphine®) have received considerable attention and are available for veterinary use in the United States.4, 94, 137, 221 As yet, there are no indications of thebaine derivatives entering the illicit market.

Propoxyphene is a synthetic compound, chemically related to methadone, which is primarily used medically to relieve light or moderate pain, typically in combination with acetylsalicylic acid (A.S.A.) as in some Darvon® preparations. Although originally introduced as a "non-narcotic analgesic", there is growing evidence that propoxyphene is more like the narcotic analgesics than was formerly realized. Its psychological effects are similar to those of codeine in many respects. The appropriate pharmacological classification of propoxyphene is still a matter of some controversy, but it is considered with the opiate narcotics in this report. Similarly, pentazocine (Talwin®) was once heralded as an effective non-narcotic analgesic, but it is now recognized that this drug has significant morphine-like properties and can produce dependence. Dextromethorphan is often referred to as a non-narcotic antitussive and is present in some cough medicines such as Romilar®. The drug lacks significant analgesic properties and has little dependence liability, although it is sometimes used non-medically for its mild euphoric effects.

The earliest unambiguous description of opium to which we have access was written in the third century B.C., although some scholars have cited references to the medical and non-medical use of opium or opiate-like drugs dated more than 5,000 years ago.24, 145, 218 Many believe that Homer's 'Nepenthe' was opium. More modern authors, such as De Quincy in 1821, have written extensively of the perils and pleasures of opium.53, 157

Although opium eating has been known in Asia for thousands of years, common use of the drug did not occur until the development of the British East India Company's wholesale opium empire in the 18th century. The practice of smoking opium developed later in China after American tobacco was introduced to the Orient. Chinese attempts at prohibition of the British-Indian opium precipitated the Opium Wars in the 1840s and 1850s, which forced China to open its doors to British (opium) trade.24, 48, 145, 189, 218, 218 The majority of the illegal opiates on
the North American market today come originally from Southeast Asia in areas of Burma, Thailand and Laos, and from parts of the Middle East. However, India remains the major legal producer of opium. (See Appendix B.2 Sources and Distribution of Opiate Narcotics.)

Prior to the 19th century, opium was taken orally in various forms or smoked, and both practices have continued in some areas. There is a decidedly lower dependence liability with these modes of use than with practices which followed, and it was not until the isolation of morphine and the invention of the hypodermic needle that opiate narcotic use became a serious problem in the Western World. Morphine was widely acclaimed among medical practitioners, and injections were used freely to treat pain during the American Civil War, sometimes producing a dependence called, in those days, the 'army disease'. Tincture of opium was employed in many patent medicines and household remedies (such as Laudanum and Paregoric), and the quasi-medical oral use of such opiate preparations was a common practice in North America during the last century. While some degree of dependence is reported to have often developed as a result of this symptomatic treatment, the associated abstinence syndrome was typically mild and often not recognized as a product of drug use. The actual extent of opiate narcotic use and associated problems at that time is difficult to ascertain, since little systematic reporting was done; however, it would appear that the use of these drugs was not a major moral or legal issue. On the West Coast, the influx of Chinese labourers, some of whom smoked opium, apparently stimulated non-medical use to some degree. In the latter part of the 19th century and early part of the 20th century, restrictions on manufacture and trade of opiate products were instituted in North America. In many cases, non-medical possession was prohibited by criminal law.24. 26, 146, 218

The first special notice of opium use in Canada was the indirect result of the anti-Asiatic riots which took place in Vancouver in 1907.49 Mr. Mackenzie King, then Deputy Minister of Labour, was sent to British Columbia to process claims from the Chinese community for financial compensation. Two claims appeared from opium merchants for losses sustained in the riots. This prompted Mr. King to inquire into the opium trade as well as the causes of the labour unrest. In his opium report, he noted that the drug was making headway, "not only among white men and boys but also among women and girls", and recommended immediate and strict legal action.

Still little public notice was given to the opiate narcotics in Canada until the 1920s. At that time, Emily Murphy, a Winnipeg police magistrate and judge, wrote a series of articles on "the drug menace" (for Macleans Magazine) which were later expanded and published in a book entitled The Black Candle. Opium smokers were described as "ashy faced, half-witted droolers" with no more blood in their bodies "than a shrimp".166
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Historically, the popular conception of the 'narcotics addict dope fiend' has established an image of the non-medical drug user which persists and intrudes into almost every examination or investigation of drug use today. Furthermore, the opiate narcotics have played an important role as a model in much of the past and present drug legislation and in the general criminolegal approach to the control of socially disapproved drug use. Although many important questions about the opiate narcotics are still unanswered, it is clear that much of what has commonly passed for fact is fiction.

Until recently, many observers did not consider the opiate narcotics to be the cause of a major public health problem in Canada. In the last few years, however, increasing attention has been given to reports of growing use of these drugs by young people both here and in the United States. (See Appendix C Extent and Patterns of Drug Use.)

MEDICAL USE

Most of the current medical uses for the opiate narcotics were fairly well understood and established in Europe by the middle of the 16th century and were probably well known in certain areas long before that time. These drugs are primarily used in the relief of suffering from pain, in the treatment of diarrhea and dysentery, and to reduce cough. They were also once commonly used as tranquilizers and antidepressants. Hundreds of related compounds have been synthesized in attempts to retain the clinical benefits but reduce the dependence liability of the opiate narcotics. These efforts to develop substitute drugs which do not produce dependence have not been very successful, and morphine and related compounds are still considered by physicians to be among the most valuable drugs available to the practitioner today. Heroin is rarely used medically in Canada, and no new stocks can be produced or imported.

A recent report from a World Health Organization scientific group concluded that the natural and semi-synthetic opiate narcotics are not indispensable in the practice of modern medicine, since wholly synthetic drugs are now available which are in many respects equivalent or superior to the natural compounds. However, none of the synthetic alternates are free from adverse effects, and the report did not suggest that the natural and semi-synthetic opiate narcotics be replaced at this time.

CHEMICAL ANALYSIS OF ILLICIT SAMPLES IN CANADA
Opium is uncommon in Canada, and only 42 samples were identified by police analysts during a 12-month period ending in March 1973. Methadone, morphine, codeine and pethidine are occasionally noted in seizure reports. These latter drugs are generally of high purity and are presumed to result from the diversion of legally produced materials.

A study of police seizures of heroin in 1959-60 indicated that the illicit heroin available in Canada was of surprisingly high quality. Ninety-five per cent of the 229 seizures examined contained between 24 and 68 mg of heroin per capsule, with a mean of 46 mg. The mean purity of these samples was 53%. Lactose (milk sugar) had been used to dilute the heroin in almost all cases. Nine samples (4%) also contained quinine. There were no other indications of deliberate adulteration or any unidentifiable substances.

The Commission has investigated the chemical properties of illicit heroin available in Canada in recent years. In one study, 90 samples from 20 different police exhibits of heroin (seized between February 1968 and May 1970) were selected from the vaults of the Bureau of Dangerous Drugs and were analysed in the Health Protection Branch laboratories. Material packaged in unit doses (capsules or envelopes) ranged in total weight from 9 mg to 143 mg with a median of 77 mg. The actual quantities of pure heroin in these units ranged from 0.6 mg to 94 mg with a median of 25.6 mg. The purity of these samples covered a range of 0.5% to 96% heroin, with a median of 35%. Although a few large seizures showed exceptional uniformity among capsules, considerable variation in heroin content within single bulk seizures was typical. For example, the content of 10 capsules selected randomly from a total of 60 seized in a single package varied between 21 mg and 62 mg of pure heroin. In another case, the content of five seemingly identical capsules from the same source ranged from 0.6 mg to 30 mg of heroin. In this study, in only one case was another drug (procaine) identified in the heroin samples. No quinine was reported. Non-drug materials (diluents) used to dilute or cut the heroin were not positively identified.

The Health Protection Branch of the Department of National Health and Welfare provided the Commission with data on 168 police seizures of heroin quantitatively analysed during the period of June 1971—October 1972. The results of these analyses are generally similar to those just presented. The actual heroin content per packaged unit dose ranged from 5.4 mg to 92.5 mg with a median of 33 mg, and the purity of bulk powder samples ranged from 1.4% to 100% heroin with a median of 25.6%. Many of these samples were selected for special analysis because of previously detected impurities and consequently cannot be considered representative. The purity of randomly selected samples might be significantly higher. Products of faulty or incomplete synthesis (such as monoacetylmorphine) were often found. A few mixtures of heroin with other non-opiate drugs, such as caffeine, methaqualone and MDA were
identifying, but such cases did not make up a significant proportion of the total number of police seizures. Quinine was found in only three instances. Non-drug diluents were not positively identified.

In the Commission’s collection of illicit drug samples and survey of ‘street drug’ analysis facilities in Canada (1971-72), 18 samples had been presented as heroin.[159] [e] Of these, only nine contained any opiate narcotics. In addition, out of almost a thousand drug analyses reported, opiates were identified in only eleven cases where the substance had been unspecified or alleged to be another drug. No case of ‘opiated’ hashish or marijuana, alleged to be pure, has ever been chemically documented in Canada in spite of the popular impression that this is an established combination. Samples presented as ‘opiated hash’ or ‘smack grass’ have invariably been found to be relatively pure cannabis.

The data now available in Canada do not provide an adequate basis for clear statements regarding regional differences in illicit heroin or changes in the quality of the drug available in the past few years. It is clear that the purity of illicit heroin and the quantity of the drug packaged for consumption in the form of single capsules or bags varies over a considerable range. Adulteration of heroin with other drugs is apparently rare. The substance most often mentioned in reports of diluted or cut heroin is lactose. Quinine, a drug which was a common diluent in the U.S.[66] [76] [97] is rarely found in Canadian samples. It would appear that opiate narcotics are very rarely disguised or misrepresented as other drugs in Canada, although some of the materials sold as opiate narcotics on the illicit market may not contain any heroin or morphine.

ADMINISTRATION, ABSORPTION, DISTRIBUTION AND PHYSIOLOGICAL FATE

Opiate narcotics are produced in a variety of tablets and capsules, elixirs, cough syrups, ampules for injection, rectal suppositories and, on the illegal market, some are also available in a gummy, solid or powdered form. Codeine and some of the synthetics are often marketed in mixtures with non-opiate analgesics (e.g., APC&C, ‘222®’, Darvon®). While opiate narcotics may be readily absorbed from the gastrointestinal tract, in most instances this route is less effective and often erratic and unpredictable compared to injections. Among non-medical users, subcutaneous (‘skin popping’) and intravenous (‘mainlining’) injections are commonly used with heroin and morphine, and heroin powder is sometimes sniffed (‘snorted’). Raw opium is generally ingested or smoked. Methadone is commonly given orally in medical use, although it is also available in injectable form. Smoking heroin in a cigarette or pipe is very inefficient since the high temperature of combustion (approximately 750°C) causes extensive decomposition of the drug. However, with sufficient quantities of heroin, it is possible for physical dependence to develop from smoking. Less intense (sub-combustion) heating may release a fair amount of active material in fumes (e.g., 50-75%) which is well absorbed by inhalation, and such use of heroin has been reported in the Far East.[89] [188] Intravenous injection of opiate narcotics
produces the most rapid and intense effects. Oral administration generally results in a slower, milder, but longer lasting effect.

Only a minute fraction of the drug absorbed actually enters the central nervous system, its most important site of action. The actual mechanisms by which these drugs exert their effects are largely unknown. There is recent evidence that the primary "opiate receptor" in the central nervous system (CNS) is associated with acetylcholine.182

The duration and intensity of the effects are dose-related and vary considerably with the different drugs in this class; the duration of major action of the natural alkaloids may vary from two to six hours or more. The effects of methadone and some of the other synthetics may last many times longer. The opiate narcotics are usually inactivated or modified in the liver and excreted in the urine. Detectable amounts may also be present in saliva and sweat.

Heroin is rapidly metabolized in the body to 6-monoacetylmorphine and morphine, and likely exerts its effects indirectly, primarily as the morphine metabolites.228 Unchanged heroin apparently has little direct effect. Codeine is chiefly metabolized and excreted in the urine in the form of inactive metabolites, but at least a small fraction is transformed into morphine."3

DETECTION OF OPIATE NARCOTICS IN BODY FLUID AND TISSUE

A wide variety of standard techniques are available for the detection of opiate narcotics and their metabolites in body tissues and fluids.15, 45, 215

There has been considerable related research activity over the past few years, and significant progress has occurred in several areas.125, 162 Much attention has focussed on developing techniques for large-scale urine monitoring programs. Important advances in the detection of opiate narcotics in blood and saliva have also been reported. There is a clear need for convenient techniques for screening for a broad spectrum of drugs in methadone maintenance programs. Several automatic and semi-automatic systems are now commercially available which facilitate the rapid analysis of large numbers of urine samples.125

The general analytic methods most commonly used for the detection of opiate narcotics include: thin-layer chromatography (TLC), gas-liquid chromatography (GLC), spectrophotometry,
immunoassay, and a variety of simple chemical and colour reaction tests. Some of these methods are useful for general qualitative identification only, while others can provide precise quantitative information as well. The relative value or appropriateness of these various techniques depends on the practical applications intended. Among the factors to be considered in evaluating such methods are: cost, convenience, speed, sensitivity, and specificity. Many of the available methods, if used alone, can be expected to produce a significant number of false positive or false negative indications. The importance of such errors depends, of course, on the application involved. By a combination of methods, under optimal conditions false reports in detecting recent opiate narcotic use can virtually be eliminated.9, 56, 209

Gas-liquid chromatography (GLC) is very sensitive and precise, but is relatively slow and requires a high degree of specialized technical training. In addition, the equipment is expensive and delicate.

At the present time thin-layer chromatography (TLC) apparently provides the most practical general method for detecting a wide variety of drugs in urine.125, 126 Many TLC methods are available, all requiring the prior extraction of drugs from biological specimens before analysis. The sensitivity of TLC systems to opiate narcotics depends in part on the volume of the sample tested, and can be enhanced by pre-treatment (hydrolysis) of the material. Methods have been developed which employ preliminary extraction of drugs from the urine onto ion-exchange paper.125' 127 This simple step can be easily performed with a minimum of equipment and technical skill. Identification information can be written or typed directly onto the treated paper, which may be sent to a central laboratory for subsequent chemical analysis. Storage or transportation of urine is not necessary with these techniques. Furthermore, unanalysed papers can be conveniently stored for years, if desired, for possible later analysis. Papers can also be collected over a period of time and pooled for a single general analysis, thereby providing considerable savings in time and expense. Kaistha and Jaffe have recently presented a detailed analysis of the costs involved in a large-scale urine screening system employing ion-exchange paper and TLC.128

Radioimmunoassay, spin immunoassay and other related antibody and enzyme techniques have recently been developed which allow the rapid detection and quantification of extremely low concentrations of various opiate narcotics in very small quantities of untreated urine, blood, saliva and perhaps sweat.1, 86, 136, 197, 210, 211, 225 The spin-label method (also called the free radical assay technique or FRAT) requires only a tiny drop (e.g., 20 microliters) of sample fluid, and can provide analysis within seconds. Such techniques have obvious application in assisting emergency diagnosis of drug overdose cases, for example. The FRAT system has received wide usage by the United States military to determine heroin use in Vietnam.111 EMIT (enzyme multiplied immunoassay technique) is comparable to FRAT in most respects but requires less expensive equipment.135, 197 Radioimmunoassay can provide greater sensitivity than the
other immunoassay techniques, but is slightly slower. With the radio-label method, false positives in the general identification of opiate narcotics are minimal. With immunoassay techniques, the administration of a single dose of heroin or morphine may be detected in body fluids for several days after use.86, 212

Methadone does not interfere significantly with the immunoassay of natural opiate alkaloids, but codeine cannot presently be efficiently distinguished from morphine or heroin using these techniques. It may be possible to specifically identify codeine by a combination of other methods, however. It is generally not practical with available urinalysis methods to determine whether morphine or heroin were used. Immunoassay techniques are much simpler, faster and more sensitive on a sample-volume basis than TLC, but are less versatile. The range of different drugs which can be identified with immunoassay methods is presently limited compared to TLC, although antibody techniques for the detection of many other drugs are anticipated in the near future.

PSYCHOLOGICAL EFFECTS

The subjective psychological effects of opiate narcotics may vary considerably among different individuals and situations. The once popular notion that morphine-like effects are intrinsically so pleasurable that most persons who experience them are promptly addicted has not been scientifically documented. In one experiment, in which injections of morphine were given to 150 healthy male volunteers, only three were willing to allow repeated administration and none indicated that he would have actively sought more." Other researchers have also reported that the majority of normal pain-free individuals found the effects of opiates quite unpleasant.130, 2" In addition, many dependent users report that their initial experiences with opiate narcotics were not very enjoyable. On the other hand, numerous individuals report that they became infatuated with heroin on their first exposure to it and immediately decided to use it in the future as often as possible.

Even after some adaptation or tolerance develops, nausea and even vomiting frequently occur early in the 'high', especially after injections. This does not necessarily indicate dysphoria, however. Regular users report feelings of warmth, euphoria or well-being, peacefulness and contentment as a result of the drug. Drowsiness, dizziness, inability to concentrate, 'mental clouding', apathy and lethargy are also commonly noted. Certain individuals, especially when fatigued, may be stimulated into feelings of energy and strength. Higher doses produce a subjective turning inward and sleep. Often a pleasant dream-like state occurs. Some users describe their drug experiences in near ecstatic, and often sexual terms—especially the 'rush' of intravenous injection. Persons with a high degree of tolerance to opiate narcotics may experience relatively little euphoric response to the drugs; some heroin-dependent individuals claim that the drug merely helps them feel 'normal', rather than 'high'. 
The most prominent aspect of opiate narcotics, from a medical point of view, is their considerable analgesic or pain-relieving property. The potential of these drugs to relieve suffering from pain depends upon several mechanisms. The major effect is not on the sensation directly, but on the psychological reaction to it. Often individuals can still perceive the pain sensation and rate its intensity reliably, in spite of the fact that much or all of the negative or unpleasant aspects are absent. In other words, after the drug, a person may still feel the pain, but it does not bother him to the same extent. Morphine has little effect on the other senses and, unlike non-narcotic analgesics and sedatives, it can often control severe pain at doses which do not necessarily produce marked sedation, gross intoxication or major impairment of motor coordination, intellectual functions, emotional control or judgment.\textsuperscript{113} In addition to reducing the anxiety of pain and, therefore the motivation to avoid it, the opiate narcotics also tend to decrease other primary motivation associated with sex, food, and aggression.

The psychological effects of chronic opiate narcotic use are often rather straightforward extensions of the short-term response. In regular users, much of the variability and unpredictability of the immediate response is lessened, partly because individuals who find the experience unpleasant tend to avoid additional exposure, and also because many who were initially upset by the drug's unusual physiological and psychological effects learn to tolerate and even seek some of these sensations. The commonly experienced decrease in sex drive with chronic use is often a complicating factor in marital problems. While some individuals who become dependent on the opiate narcotics withdraw from regular social activities and live what appears to be an immoral, criminal and slovenly existence, others are able to lead an otherwise normal life with little change in work habits or ability to meet responsibilities. Possible factors underlying these differences will be discussed later.

Opiate narcotics typically do not disrupt psychomotor performance to any significant degree, although with higher doses there may be some impairment, possibly related to general sedation or motivational factors.\textsuperscript{13, 73, 85, 208}

Performance is likely to be significantly impaired during the early stage of withdrawal after regular use. It has been reported that persons dependent on heroin have poorer driving records than would be expected in the general population.\textsuperscript{*} However, other evidence indicates that heroin users may drive more extensively, and, if driving exposure is taken into account, they may actually have fewer accidents per unit distance driven.\textsuperscript{22}

There is no evidence of permanent changes in cognitive or intellectual functioning due to chronic opiate narcotic use. Nor is there any indication of psychosis or other major psychiatric complications caused by these drugs.\textsuperscript{28, 107, 129, 174, 183, 213} In spite of the lack of serious psychiatric complications (other than dependence) caused by opiate narcotics, users of these drugs may be hospitalized in psychiatric institutions from time to time for treatment of their dependence.
In the Commission's national survey of psychiatric hospital diagnostic records in the spring of
1971, opiate narcotics were noted as factors in the primary or secondary diagnosis of 24 (0.1%
) of the 22,885 patients in the hospitals surveyed.98. [d] In British Columbia, psychiatric wards
in general hospitals were surveyed as well, and in this population opiate narcotics were
mentioned in the diagnostic records of 5 (1.7%) of 293 resident patients. According to the
mental health data provided to the Commission by Statistics Canada, 139 (0.25%) of the first
admissions and 100 (0.20%) of the readmissions to psychiatric institutions or wards in Canada
in 1971 were attributed to dependence on natural or synthetic opiate narcotics.122• [e] In these
data, males outnumbered females by approximately two to one. (See also Tables A.5, A.6 and
A.7 in the Annex to this appendix.)

PHYSIOLOGICAL EFFECTS

Pure opiate narcotics may produce few significant physiological effects in low therapeutic
doses, although they affect, to a minor degree, practically all systems of the body. The
immediate or short-term physiological response usually includes a general reduction in
breathing and cardiovascular activity, a depression of the cough reflex, a constriction of the
pupil of the eye and a minor reduction in visual acuity, a small change in some hormone levels,
increased biliary pressure, itching of the skin, dilation of superficial blood vessels and warming
of the skin, increased perspiration, a decrease in gastrointestinal activity (which typically causes
constipation), nausea and sometimes vomiting. Sleep disturbances may occur in some
individuals. In higher doses, insensibility and unconsciousness result. The primary toxic
overdose symptoms are coma, shock and, ultimately, respiratory arrest and death.

There appears to be little direct permanent physiological damage from chronic use of pure
opiate narcotics.7, 10, 26, 112, 213 Major complaints centre around persistent constipation and
reduced sexual performance during chronic use. Numerous complications are observed,
however, if the overall drug use pattern involves adulterated or diluted street samples, unsterile
and shared needles, unhygienic living standards, poor eating habits and inadequate general
medical care—all of which are commonly part of the behaviour syndrome of criminalized users.
Commonly reported disorders in illicit users are hepatitis, tetanus, numerous cardiovascular and
lung abnormalities, scarred veins (`track marks'), local skin infections, ulcers and abscesses,
changes in muscle tissue, and obstetrical problems in pregnant females. Serious lung damage,
possibly resulting in death, may be caused by intravenous injection of colloidal or partly soluble
contaminants—often substances used to dilute or 'cut' illicit heroin, or the chalk or talc
commonly found in licitly manufactured drugs (such as methadone) designed for oral use rather
than injection. Although users often heat, or "cook" their drugs to increase solubility, and
subsequently filter the drug through a wad of cotton to remove major particles prior to injection,
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this procedure is only partially effective, and may, in fact, introduce other contaminating materials, such as cotton fibres. There is some evidence of opiate narcotic alteration in gonadal tissue and function, although gross changes in 'sex hormone' levels apparently do not occur. Tuberculosis, pneumonia and venereal disease are more common among dependent users than in the general population. Since similar problems have been reported in England where pure drugs are available for intravenous self-injection, contamination or adulteration of street drugs must be considered only part of the overall problem."

In the 1930s and 40s malaria, transmitted by unsterile needles, was a frequent correlate of opiate narcotic dependence in North America. For several decades later, no such drug-related malaria deaths were reported. In the past few years, however, malaria has again appeared on the scene in California. Quinine, which was once commonly used to cut or dilute illicit heroin in the United States (especially on the East Coast), has some therapeutic effects in connection with this parasitic disease and may have been, at least in part, responsible for the decline in malaria cases. On the other hand, quinine may increase the likelihood of tetanus after subcutaneous injection.""

ACUTE TOXIC REACTIONS AND DEATH

The mortality rate among persons dependent on opiate narcotics is considerably higher than that of individuals of similar age in the general population. Although considerable variability exists among reports, it has frequently been estimated that in the United States, over 1% of the heroin-dependent population dies each year. Generally similar estimates can be derived from available Canadian data. In addition to deaths resulting directly from the use of various drugs (representing the majority of the fatalities), a disproportionately high number of heroin users die from violent causes (including murder, suicide and various accidents) and, as discussed above, from numerous infections and diseases. Henderson's report of heroin-related fatalities in British Columbia presents a remarkably similar picture to that described in New York by Helpern and Rho.

There is likely significant underreporting of opiate narcotic- and other drug-related deaths for a variety of reasons. To begin with, autopsy, with full toxicological analysis, is not conducted in a large proportion of deaths, and other relevant information as to drug use habits of the deceased is frequently unavailable or not actively sought., Furthermore, there is often considerable reluctance on the part of examining physicians to attribute fatalities to drug use, especially in ambiguous cases. Variations in the numbers of drug death reports from location to location, or from year to year, may represent differences in the examiners'
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sophistication, and in the interest in and attention paid to possible drug-related cases, as well as differences in extent and patterns of drug use. As effort and sophistication increases, we can expect a corresponding increase in the accuracy (and often the frequency) of drug-related death reports.

The Commission has investigated reports of opiate narcotic-related toxic reactions and fatalities in Canada in considerable detail. Some of the findings are presented below.

The Federal Poison Control Program has records of over one thousand "narcotics" poisonings or adverse reactions (non-fatal and fatal) for 1971. More than three-quarters of these involved pharmaceutical preparations of codeine and acetylsalicylic acid (A.S.A.), such as `222'. The relative importance of A.S.A. and codeine in these later cases is unclear. (A.S.A. preparations [e.g., Aspirin®] alone account for more poisonings annually than any other drugs.) The A.S.A.-codeine poisoning rate in the population was highest for children under 5 years of age. More than one-third of the cases involved persons 10-25 years of age. There were reports of 179 Darvon® (propoxyphene, typically with A.S.A. and other drugs), 162 heroin, 21 methadone and 19 Demerol® (meperidine or pethidine) toxic reactions. Almost three-quarters of the heroin and methadone cases were males; for all other drug categories, women substantially outnumbered men. A little over one-half of the heroin and methadone cases were 10-24 years of age. Thirty-two deaths were reported which involved natural or synthetic opiate narcotics; 11 of these reports noted Darvon® or propoxyphene, 8 heroin or morphine, 5 methadone, and 4 codeine with A.S.A. and/or other drugs. The persons who died ranged in age from 17-64 years with a median of 28; none of the fatalities involved children.
Cyclazocine has been used clinically in regular, daily doses in opiate narcotic-dependent persons. However, antagonists do not block the craving or hunger associated with heroin dependence only if equivalent doses which produce comparable effects. Antagonists are refined. In addition, subcutaneous injections of a lightly granular partly biodegradable plastic containing cyclazocine, levo-BC-2605 and EN 1639A can be effective for 24 hours; typical doses of these antagonists developed for immunoassay of opiate narcotics in body tissue and fluid. There are a large number of drugs available which block or counteract the effects of opiate narcotics. It is difficult to distinguish from other per-

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<th>TABLE A.2</th>
<th>OPIATE NARCOTIC-RELATED DEATHS IN CANADA (1969–1971)*</th>
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<td>1. Heroin or morphine</td>
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<td>3</td>
</tr>
<tr>
<td>3. Propoxyphene‖</td>
<td>2</td>
</tr>
<tr>
<td>4. Other or Unspecified Narcotic</td>
<td>3</td>
</tr>
<tr>
<td>TOTAL CASES:</td>
<td>17</td>
</tr>
</tbody>
</table>

† In combination with other drugs.
‡ Includes 2 heroin-methadone combinations also included in row 1.
§ Includes 1 heroin-methadone combination also included in row 1.
‖ When Darvonal® alone was reported, it was tabulated as a single drug case. In some of these instances, however, the presence of heroin and possibly other drugs.

While some users refuse to become involved in criminal activities and consequently stop using heroin, others may continue to use the drug. Those who refuse to become involved in criminal activities are usually able to obtain the funds needed to support their habit through legitimate channels and have adequate funds. While it is difficult to determine the areas of primary CNS action of opiate narcotics, experimentally induced changes in opiate narcotic-associated deaths occurred in that city in 1971 and 65 occurred in 1972. In the official Causes of death reports provided by the Federal Government, opiate narcotic-associated deaths occurred in that city in 1971 and 65 occurred in 1972. There is some suggestion that an allergic or general hypersensitivity reaction to heroin or some other opiate narcotic is necessary for these individuals, and that such a condition is, in some way, associated with the craving or indifference to pain, and so forth. The long-acting methadone derivatives also result in relief of or indifference to pain, and so forth. The long-acting methadone derivatives also result in the suppression of abstinence syndrome. However, high doses of cocaine appear to increase the toxicity of heroin in this species. It was found that the effects of cocaine and heroin were additive in some effects but show no interaction on others, and may have additive effects on certain subjective measures. It has been reported that amphetamines may enhance the drug's pain-relieving and anti-depressant properties when the two are administered together. Cocaine or amphetamines are sometimes mixed with heroin as a 'speedball' to produce a more intense high. While some users refuse to become involved in criminal activities and consequently stop using heroin, others may continue to use the drug. Those who refuse to become involved in criminal activities are usually able to obtain the funds needed to support their habit through legitimate channels and have adequate funds.