

OPIOID DEPENDENCE

Mechanisms and Treatment

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To my wife

Preface

A major problem in the treatment of opioid dependence has been the persistence of relapse despite detoxification and enforced prolonged abstinence from drug use, with or without conventional psychotherapy and other efforts at rehabilitation. Both initial addiction and subsequent relapses are usually ascribed to the quest for opioid-produced *euphoria* in persons with character disorders. This formulation is in accord with one-half of the common sense "pleasure-pain" principle, but it ignores the other half, namely, the long-lasting *dysphoric* consequences of repeated opioid use (distressing abstinence phenomena, sexual disturbances, disruption of marital status, unemployment, enmeshment in criminal activities, arrests, and imprisonment). In any case, the pleasure-pain principle is an empty tautology since it is incapable of refutation by any conceivable objective data that might seem contradictory, inasmuch as it can be "saved" by invocation of untestable unconscious intervening variables.

Less tied to the pleasure-pain principle is the view that relapse is due to long-lasting sequelae of previous opioid addiction, resulting from complex conditioning processes, both operant and classical, involving pharmacological, environmental, social and personal variables. In this view, relapse is not simply a re-enactment of initial opioid use, but is a "disease, *sui generis*" a disease of its own kind. The factors contributing to this disease, *sui generis* are reviewed in this book. Among them are the far-reaching alterations of homeostasis produced by single doses of opioids ("antiprotective" actions, of which relief of pain is one facet), the counteradaptive responses of the central nervous system to such effects (which have been shown by use of narcotic antagonists to begin after

one or a few repeated doses of morphine), the consequent development of tolerance and physical dependence (characterized not only by the easily recognized "early" abstinence syndrome but also by the more subtle, long-lasting "protracted" abstinence syndrome), the possible role of endogenous opioid peptides in all of these processes, and the operant conditioning of opioid-acquisitive behavior as well as the classical conditioning of the opioid agonist-abstinence cycle. While the persistence of such classically conditioned responses in detoxified "street addicts" can be detected by sophisticated techniques under experimental conditions (O'Brien, Greenstein, Ternes, McLellan, & Grabowski, 1979), extinction of the conditioned autonomic responses that are part of the disease, *sui generis* is more difficult to carry out. In the opinion of the author of this book, the elimination of the disease, *sui generis* is essential for the optimal prevention of relapse, in addition to therapies directed at the presumed causes of initial opioid use. How far this central theme applies to non-opioid drug dependencies (which are described very briefly in the opening chapter) is unknown at present; new techniques will have to be developed for detection of long-lasting consequences of such drug use and the conditioning processes that inevitably accompany them in man (Wikler, 1971; Ludwig, Wikler, & Stark, 1974).

The author is solely responsible for the interpretations of the data reviewed in this book. The names of the persons who have contributed importantly to elucidation of the long-term sequelae of drug dependence are too numerous to list here, but because of close association with them for many years in Lexington, Kentucky, the author's former colleagues at the NIDA Addiction Research Center (including Drs. Harris Isbell, Havelock F. Fraser, Harris E. Hill, Donald R. Jasinski and Charles W. Gorodetzky) and his present colleagues at the University of Kentucky Medical Center (Drs. William R. Martin, Arnold M. Ludwig, John A. Dougherty and Dianne B. Miller) should be mentioned. To them the author expresses his indebtedness, not only for important research findings but also for stimulating discussions. Thanks are also due to the National Institute on Drug Abuse for its highly informative Research Monographs and to the editors of Plenum Publishing Corporation for their helpful cooperation.

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