
Contents

Foreword by <i>Albert D. Fraser</i>	v
Preface	vii
Contributors	xv

CHAPTER 1

Pharmacology of High-Dose Buprenorphine

<i>Pierre Marquet</i>	1
1. Introduction	1
2. Pharmacokinetic Properties	1
2.1. Absorption and Bioavailability	1
2.2. Distribution	3
2.3. Metabolism	5
2.4. Excretion	5
3. Pharmacodynamic Properties	5
4. Administration Schedules	8
5. Clinical Effects of Buprenorphine	8
6. Conclusion	9
References	9

CHAPTER 2

Controlled Drug Administration Studies of High-Dose Buprenorphine in Humans

<i>Marilyn A. Huestis</i>	13
1. Introduction	13
2. Bioavailability	14
3. Dose-Effect Profiles	16
4. Abuse Liability	16
5. Toxicity	19
6. Safety and Abuse Liability of High-Dose Intravenous Buprenorphine	21
7. Conclusion	23
References	24

CHAPTER 3

High-Dose Buprenorphine for Treatment of Opioid Dependence

Eric C. Strain	29
1. Introduction	29
2. Buprenorphine Solution vs Tablets	30
3. Efficacy of Buprenorphine vs Placebo: <i>Clinical Trials</i>	31
3.1. Summary of Placebo-Controlled Studies	34
4. Efficacy of Buprenorphine vs Other Medications: <i>Clinical Trials</i>	34
4.1. Summary of Studies Comparing Buprenorphine to Other Medications	44
5. Safety and Side Effects of Buprenorphine	44
6. Summary and Conclusions	45
Acknowledgment	47
References	47

CHAPTER 4

Foreseeable Advantages and Limits
of Buprenorphine-Naloxone Association

Michel Mallaret, Maurice Dematteis, Celine Villier, Claude Elisabeth Barjhoux, and Chantal Gatignol	51
1. Introduction	51
2. Advantages of Buprenorphine-Naloxone Association	52
2.1. Advantages of Opiate-Naloxone Association: <i>Lessons of the Past</i>	52
2.1.1. Epidemic of Pentazocine and Tripeleminamine Abuse in the United States	52
2.1.2. Epidemic of Analgesic Buprenorphine Abuse in New Zealand ...	53
2.2. Buprenorphine and Naloxone: <i>A Complex and Controversial Pharmacology</i>	53
2.3. Clinical Aspects	54
2.3.1. Pharmacokinetic/Pharmacodynamic Advantages of Associated Naloxone in BupNx Combination	54
2.3.2. Sublingual Naloxone in BupNx Tablets Does Not Decrease Buprenorphine Effects	55
2.3.3. Sublingual Naloxone in BupNx Tablets Does Not Decrease Blockade Effects of Buprenorphine in Opioid-Dependent Patients	55
2.3.4. Sublingual Naloxone in BupNx Tablets Does Not Precipitate Withdrawal Symptoms in Opioid-Dependent Patients	56
2.3.5. Is the BupNx Combination Effective for Detoxification or Treatment of Depressive Symptoms in Opioid-Dependent Patients?	56

2.3.6. What Is the Abuse Liability of Intravenous BupNx Combination in Nonopioid-Dependent and Opioid-Dependent Patients?	56
2.3.7. Intravenous Naloxone May Decrease Respiratory Depression by Buprenorphine	58
2.3.8. What Will Be the Epidemiological Consequences and Potential Economic Impact of the Use of BupNx Combination?	59
3. Limits of Buprenorphine-Naloxone Association	59
3.1. Potential Risk of Inefficacy of Naloxone in BupNx Combination	59
3.2. Abuse Liability of Intravenous BupNx Combination: <i>Low But Still Possible</i>	60
3.3. Adverse Buprenorphine Reactions and Sublingual BupNx Combination	60
3.3.1. Respiratory Depression	61
3.3.2. Involuntary Overdoses	62
3.3.3. Experimental Buprenorphine Hepatotoxicity	62
3.4. Specific Risks in Office-Based Treatment (BupNx Combination) of Opiate Dependence	63
4. Conclusion	63
References	64

CHAPTER 5

Buprenorphine Maintenance Treatment in Primary Care: *An Overview of the French Experience and Insight Into the Prison Setting*

Marc Deveaux and Jean Vignau 69

1. Introduction	69
2. Implementation of BMT Through French Primary Care System	70
2.1. A Late But Considerable Concession to Harm Reduction Paradigm	70
2.2. Legal Framework of Therapeutic Use of Buprenorphine	70
2.2.1. Essential Landmarks of French Health Services	70
2.2.2. Opioid Maintenance Treatments	71
3. Observable Effects of French Policy	72
3.1. Is BMT Accessible and Acceptable?	72
3.2. Is BMT Safe?	72
3.2.1. Data from Preregistration Studies	73
3.2.2. Data from French Experience	74
3.3. Is BMT Effective in Controlling Opiate Addiction and Preventing Subsequent Relapses?	75
4. Prison	76
4.1. Drug Addicts in French Prisons	76
4.2. Legal Framework of BMT in Prison	76
4.3. Procedures in Loos-lez-Lille Prison	77
5. Conclusion	78
Acknowledgments	79
References	79

CHAPTER 6

Buprenorphine as a Viable Pharmacotherapy in Australia

John H. Lewis 83

1. Introduction	83
2. Buprenorphine	84
3. National Evaluation of Pharmacotherapies for Opioid Dependence	86
4. Conclusion	86
Acknowledgments	87
References	87

CHAPTER 7

Separative Techniques for Determination of Buprenorphine

Vincent Cirimele 89

1. Introduction	89
2. Determination of Buprenorphine in Blood	90
3. Determination of Buprenorphine in Urine	96
4. Determination of Buprenorphine in Biological Tissues	99
5. Determination of Buprenorphine in Hair	99
6. Conclusion	106
References	106

CHAPTER 8

Buprenorphine-Related Deaths

Pascal Kintz 109

1. Introduction	109
2. Forensic Aspects	110
3. Buprenorphine Fatalities	110
4. Conclusion	115
References	116

CHAPTER 9

Pharmacology of Opiates During Pregnancy and in Neonates

Pierre Marquet..... 119

1. Introduction	119
2. Perinatal Pharmacokinetics of Opiates	119
2.1. <i>In Utero</i>	119
2.1.1. Transfer Through Placenta and Distribution in Fetus	119
2.1.2. Transfer Through Blood-Brain Barrier	120
2.2. Postnatal	120

3. Perinatal Pharmacodynamics of Opiates	120
3.1. Opioid Receptors and Development of Embryos	120
3.2. Perinatal Effects of Exogenous Opiates	121
3.2.1. On Development	121
3.2.2. On Opioid System	122
4. Maintenance Treatments During Pregnancy	122
References	123

CHAPTER 10

Case Study of Neonates Born to Mothers

Undergoing Buprenorphine Maintenance Treatment

***Pierre Marquet, Pierre Lavignasse, Jean-Michel Gaulier,
and Gérard Lachâtre*** 125

1. Introduction	125
2. Clinical Findings	126
2.1. Neonates Included	126
2.2. Questionnaire and Toxicological Survey of Mothers	126
2.3. Neonates' Outcomes	130
3. Toxicological Investigations	130
3.1. Materials and Methods	130
3.2. Results	131
4. Discussion	133
5. Conclusion	134
Results	135

CHAPTER 11

Buprenorphine and Pregnancy:

A Comparative, Multicenter Clinical Study of High-Dose Buprenorphine vs Methadone Maintenance

***Claude Lejeune, Sandrine Aubisson, Laurence Simmat-Durand,
Fabrice Cneude, and Martine Piquet*** 137

1. Introduction	137
2. Materials and Methods	138
3. Results	139
4. Discussion	143
5. Conclusion	145
Acknowledgments	145
References	145

Index	147
-------------	-----

Buprenorphine Therapy of Opiate Addiction

Kintz, P.; Marquet, P. (Eds.)

2002, 168 p. 22 illus., Hardcover

ISBN: 978-1-58829-031-1

A product of Humana Press