OBSTETRIC ANALGESIA AND ANESTHESIA

SNYDER

OBSTETRIC ANALGESIA AND ANESTHESIA

Their Effects upon Labor and the Child

By

FRANKLIN F. SNYDER, M. D.

ASSOCIATE PROFESSOR OF OBSTETRICS AND ASSOCIATE PROFESSOR OF ANATOMY, HARVARD MEDICAL SCHOOL

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To My Father

ELWOOD S. SNYDER, M.D.

PREFACE

The present status of the use of pain-relieving drugs in obstetrics is set forth in this volume with due regard to the recent advances in this field. The experimental investigations and clinical reports of obstetricians throughout the world have been studied and taken into full account. Hazards to the safety of the mother and child, which are inherent in the practice of obstetric analgesia and which cannot be circumvented or uprooted, have been pointed out specifically and thus in part brought under control. The present undertaking is the result of the author's observations and experiences concurrently in the hospital and in the laboratory. The results of clinical experience have been supplemented at crucial points by evidence obtained in animal experiments. In numerous instances, problems long puzzling and unsolved in patients in the clinic were transferred to the laboratory, where under controlled conditions in animals decisive results were obtained.

It is now a century since Sir James Simpson introduced ether and chloroform into obstetrics and thereby added a new factor in the conduct of labor—the action of anesthetic drugs. Only since 1900, however, with the advent of scopolamine have pain-relieving drugs been administered throughout the entire period of labor instead of merely at the time of delivery. Today, after forty-five years of experience with obstetric analgesia, it can be said that "the most widely discussed and the most controversial problem in obstetrics is pain relief in labor."

The significance of the introduction of a new factor influencing the outcome of labor—anesthetic drugs—extends far beyond the range of the usual problems of anesthesia. It is evident that much is to be gained from advances in the general field of anesthesiology. However, the role of analgesic agents in the conduct of labor involves much more than the conquest of pain. From the standpoint of mortality, escape from the uterine environment is the most dangerous experience of life. The consequences of impairment of the labor mechanism are measurable in terms of life or death. Thus, the heart of the problem of obstetric analgesia lies in knowledge of the labor mechanism and of the fetal environment—long among the major objectives of obstetric investigation. Progress in obstetric analgesia is indeed linked with innovations in pharmacology and with new technics of anesthesia, but it depends primarily upon the growth of knowledge of labor and of its effect upon the child.

Analysis of labor from the standpoint of the child reveals the preeminence of fetal respiratory injury as a cause of death associated with birth. Since all drugs commonly given for the relief of pain tend

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to alter the functioning of respiration, thus striking the fetus at the point of maximum susceptibility to injury during labor, it is obvious that measurement of the pharmacologic factor in labor is closely linked with the detection and measurement of fetal respiratory changes. It is considerations such as these that prompt the detailed inquiry in the following pages concerning the history of the respiratory organs before birth and the principal types of pathologic alteration which involve them—asphyxia, atelectasis and pneumonia.

Of outstanding significance is the introduction of new methods of experimental analysis by which one drug can be compared with another in terms of the amount of respiratory depression caused in the fetus and the amount of impairment produced in the labor mechanism. Safety in the employment of drugs now in every-day use is increased by taking into account the results of such quantitative comparisons. When applied under controlled conditions in experimental animals, these methods greatly facilitate prediction of the results of clinical trial of any new drug proposed for obstetric use.

Every physician is aware of the long list of drugs which have been employed for relief of distress during labor, and less experienced students of medicine find orientation in this subject proportionately difficult. In order to profit from the vast experience accumulated in the numerous clinical case reports on obstetric analgesia, the usefulness of the data in answering two chief questions must be determined: (1) the amount of pain relief for the mother, and (2) the margin of safety, especially for the child. When such analysis is carried out, a basis is obtained for comparison of one drug or one dosage level with another. In brief, three chief factors have been taken into account in the evaluation of the role of an analgesic agent in the conduct of labor: (1) potency in the relief of pain, (2) effect upon the fetus and (3) effect upon the mother, especially the labor mechanism.

I welcome this opportunity to express my appreciation of the interest and help of many colleagues at the Johns Hopkins Hospital, the University of Chicago Lying-In Hospital, the Boston Lying-In Hospital and Harvard Medical School. I wish to thank Dr. Morris Rosenfeld, Department of Pharmacology, Johns Hopkins Medical School, who was associated with this work in the beginning. I am especially grateful to Dr. E. M. K. Geiling, Professor of Pharmacology, University of Chicago, for invaluable aid.

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FRANKLIN F. SNYDER

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CONTENTS

SECTION I

RESPIRATORY INJURIES OF THE CHILD

Chapter 1

THE PHARMACOLOGIC FACTOR IN LABOR 3

Chapter 2

THE INCIDENCE OF RESPIRATORY INJURY BEFORE BIRTH . . . 14

Chapter 3

RESPIRATION BEFORE BIRTH 29

Chapter 4

INTRAUTERINE PNEUMONIA 63

Chapter 5

ATELECTASIS 100

Chapter 6

ASPHYXIA 133

Chapter 7

A LABORATORY METHOD OF ASSAY OF THE EFFECTS OF VARIOUS ANESTHETIC AGENTS UPON THE MOTHER AND FETUS . . 188

SECTION II

THE TREATMENT OF PAIN DURING LABOR

Chapter 8

ANALGESIC AGENTS AND LABOR PAIN 213

Chapter 9

MORPHINE 221

Chapter 10

SCOPOLAMINE 254

Chapter 11

SCOPOLAMINE-MORPHINE ANALGESIA 266

Chapter 12

BARBITURATE 277

Chapter 13

RECTAL ETHER, MAGNESIUM SULFATE AND AVERTIN 299

Chapter 14

PARALDEHYDE 311

Chapter 15

CHLOROFORM 324

Chapter 16

NARCOTIC GASES—NITROUS OXIDE, ETHYLENE, CYCLOPROPANE . 337

Chapter 17

LOCAL ANESTHETICS 356

INDEX 389

Section I

RESPIRATORY INJURIES OF THE CHILD

Chapter 1

THE PHARMACOLOGIC FACTOR IN LABOR

Drugs for the relief of pain during labor are used today more commonly than during any previous period in obstetric history. The employment of a variety of agents to induce anesthesia, analgesia and amnesia has become established as a part of the routine of the conduct of labor in obstetric clinics throughout the country. This is true in the case of normal as well as of pathologic labor. From the practical standpoint, therefore, the termination of pregnancy has come to involve a pharmacologic factor.

In the past, considerable limitation was placed upon the use of obstetric analgesia by conditions prevailing when labor was conducted in the home rather than in the hospital. The striking increase in hospital deliveries in recent years has opened the way to a more extensive use of drugs during the entire period of labor. In the hospital, nursing and medical personnel are in attendance throughout labor and a wider choice of methods of analgesia is available than is possible in the home. It is hardly surprising, therefore, that coincident with the increase in hospital care during labor, there has been more extensive use of obstetric analgesia than ever before. Some indication may be obtained as to how widespread is the use of analgesic agents during labor by noting the increase in number of hospital deliveries. Seventy-nine per cent of all live births in the United States in 1945 occurred in hospitals, according to the U.S. Census Bureau. In cities with a population of 100,000 or more, 94 per cent of the babies were born in hospitals, while in rural areas only 61 per cent were delivered in hospitals.

DESCRIPTION OF LABOR AMPLIFIED

The pharmacologic approach to the study of labor is of great practical importance. Any discoveries in this field find immediate application in obstetric practice. Furthermore, this approach embraces a considerable part of current obstetric investigation, and after four decades of intensive study, continues to hold front rank in importance.

With the rise of interest at the beginning of this century in the use of drugs for pain relief at all stages of labor and not merely during delivery, a strong impetus was given to carrying the analysis of labor beyond the stage of anatomic description or mechanical aspects to that of a consideration of the functional factors responsible for the

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normal outcome of birth. The fetus likewise has become an object of interest from the physiologic rather than from merely the morphologic standpoint. Thus topics which formerly were the center of interest, such as the conformation of the pelvis and the anatomic adjustments of the fetus in the process of extrusion through the birth canal, no longer dominate the writings and investigations in this field.

"The relief of pain during labor is today the most widely discussed subject in obstetrics, and at the same time the most controversial" (Harris and Waters). This wide interest makes evident the great practical importance of reviewing the conduct of labor in the light of certain recent physiologic and pharmacologic studies. Indeed, a consideration of the action of anesthetic agents administered during labor brings one to a focal point of much of the current research in obstetrics.

PRACTICAL AND EXPERIMENTAL ADVANTAGES

The use of anesthetic agents in the conduct of labor presents two main aspects: (1) primarily it is an end in itself, the relief of pain; (2) secondarily it has afforded a means of experimental analysis of a wide range of factors concerned in the injuries of both mother and child which occur during labor. Outstanding is the fact that the pharmacologic factor in labor represents a definite entity which can be introduced at any stage of the process, or withdrawn, as desired. This has opened the way to experiment. Furthermore, it is especially significant that this type of study may be carried out in the clinic as well as in the laboratory. Thus, the description of labor and birth injury along traditional lines may be amplified by fresh exploration. Indeed, the investigation of various factors in labor, including the pharmacologic, may often be carried out under more favorable conditions in the clinic than in the laboratory. The anatomic and physiologic description of labor both normal and abnormal has given rise to a much greater literature in the human than in the case of all other species together, and no doubt reflects the fact that a fuller understanding of various aspects of parturition has been gained in the clinic than in animal studies. On the other hand, it will be easy to illustrate in the following pages that progress would be slow indeed, were it not possible to find the answer to many puzzling questions by the expedient of a clear-cut animal experiment.

Drugs Old and New. Much of the current clinical investigation of obstetric analgesia has centered upon the trial of new substances for the control of pain, a long list of which is now familiar to all obstetricians; recently also interest in extending the use of various types of regional anesthesia to the control of pain throughout labor has greatly increased. As a result of extensive clinical experience, the group of

anesthetic agents which has proved of value in the conduct of labor has been well defined. The drugs which are commonly employed for relief of pain during labor, namely, morphine, barbiturates, scopolamine and certain volatile anesthetics, are certainly among the most widely used and best known of all therapeutic agents. From the standpoint of general knowledge of their action in all varieties of clinical conditions, it might be reasonable to anticipate that a comparable degree of safety would attend their use in obstetrics. However, this is not the case. What one finds, in fact, is the steady growth of a considerable literature bearing upon the technic and hazards of the use of these substances during labor. Danger of injury to the child has proved to be the outstanding hazard. Unlike the mother, the child cannot report the results of medication from moment to moment; nor can the magnitude of the effect of an anesthetic upon the fetus be readily inferred by merely noting the effect upon the mother. It is indeed paradoxical that, while the relief of pain primarily concerns the mother alone, in reality, in the practice of obstetric analgesia, injury of the child commonly becomes the chief concern.

ANESTHESIOLOGY IN OBSTETRICS

The volume and character of the literature on obstetric analgesia are evidence of the puzzling nature of the factors which are involved. For example: (1) How can the action of drugs be isolated from the numerous other factors concerned in the outcome of labor, all of which are operative simultaneously? (2) If anesthetic agents administered to the mother during labor also pass to the fetal circulation, how can the direct effect of such powerful substances upon the fetus be dissociated from indirect effects upon the child which may result from changes in the mother such as deficient oxygenation of the placental blood or alteration of the uterine expulsive mechanism? (3) To what extent are the usual pharmacologic methods adequate for analysis of the influence of narcotics upon the mother and child, and what additional types of evidence must be added?

When one attempts to evaluate the methods and results of the current search for better analgesic agents it is evident that with respect to the treatment of pain in labor the advances in obstetrics fall far short of the revolutionary achievements of recent years in the use of new drugs for the control of infectious diseases. It is of importance to note, however, that the obstetric problem is fundamentally different from that of infection. In this latter instance, the object is protection of the body against death-dealing invasion by micro-organisms from without. In the obstetric use of pharmacologic agents, however, the object of therapeutic attack is not an invader from outside. The problem arises from within the body. Pain attends the parturient

woman from the beginning, with tightening grip as the hours of labor approach a climax. No doubt pain may be considered as protective as long as it assists in warning the individual of the imminence of danger. Unfortunately, pain does not often stop when it has accomplished its protective function. From a beneficent mechanism it becomes a destructive force distorting normal functioning of mind and body. The control of pain becomes a dominant objective of therapeutic effort continuing through the hours of labor. In order to obtain relief from pain anesthetic agents are required.

What makes the introduction of anesthetic agents in the course of labor an obstetric problem of first magnitude is that the influence of these substances upon the outcome of labor is so great that the risk involved for mother and child may be out of all proportion to the gain in pain relief.

It is worthy of emphasis that substances of this group which are capable of inducing narcosis are among the most powerful agents known in pharmacology. To obtain amnesia and analgesia early in labor, a different group of drugs comes into use in contrast to those commonly employed for anesthesia at the time of delivery. All drugs used for relief of pain, however, have the common property of acting upon the nerve elements. All readily escape from the maternal blood across the placental boundary and reach the fetal circulation. The destruction or elimination of these agents by the body imposes an added burden not only upon the mother but—what is of greater danger—upon the child. In fact, so complicated have the pharmacologic and clinical aspects of this group of drugs become that a new branch of medical science, Anesthesiology, has developed in the course of endeavor to establish rational principles and practice in this field.

THE HAZARD OF BIRTH

In view of the hazards which are obviously inherent in any use of anesthetic agents it can hardly be surprising to find that when these effects are superimposed in the parturient woman upon numerous complications of labor there may be added danger for both mother and child. The relief of pain becomes inseparably linked with factors concerned in labor where life or death may be in the balance, especially survival of the child. The chief point is that an already vulnerable mechanism, which often falls short of a functional level adequate for the birth of uninjured offspring, is the site of action of powerful drugs.

It is considerations such as these which prompt inquiry as to how dangerous the transition is from the intrauterine environment to that of external existence. (1) What is the magnitude of fetal mortality during the period of birth; and (2) what types of fetal injury occur

during parturition? Such a summary of the quantitative and qualitative effects of labor upon the child is presented in Chapter 2. The aim is first of all to obtain a baseline by this method from which to evaluate the magnitude and especially the type of fetal injury which may be attributed to the pharmacologic factor introduced therapeutically during labor.

Before going further let us consider briefly certain conclusions to be drawn from such inquiry.

1. Birth is closely associated with death. The highest peak of mortality of any time during the entire life span coincides with the day of birth. In this sense, the escape from the uterine environment to the external world is the most hazardous experience of life. The nature of birth injury obviously ranks among the foremost medical problems of the time.

2. The mere statement of the magnitude of the problem of birth injury prompts inquiry as to what types of injury are commonest and especially to what extent they are preventable. In the cases which prove fatal the autopsy findings regarding the cause of death may be classified under two chief types of injury: (1) structural and (2) functional, i.e., absence of demonstrable lesions. From the standpoint of preventability of the two types of injury, it is obvious that structural changes such as subdural hemorrhage cannot be undone once they have occurred; functional alterations like asphyxia, on the other hand, lie much nearer to the margin of reversibility to a normal equilibrium; and in this sense form an objective for measures of prevention. It is all the more significant to find, therefore, that of the principal causes of death associated with birth, a majority of the injuries are of the functional type.

3. From the thousands of autopsies and case records there is evidence not only that intranatal injuries are to a considerable degree functional disorders but also that the respiratory system of the child bears the brunt of the attack. Fetuses die during labor or soon afterwards chiefly from respiratory impairment. Four principal types of abnormality of the respiratory system are found: (1) asphyxia, or the functional failure of the nervous mechanism of respiration; (2) atelectasis, or the incomplete dilatation of the pulmonary alveoli; (3) congenital pneumonia, a consequence of the breathing of contaminated amniotic fluid; and (4) prematurity, in which respiratory involvement is conspicuous. In fact, there is evidence that the ability to survive in the external environment, i.e., the onset of viability, is determined not so much by the weight or size of the fetus as by the development of a regulatory mechanism of respiration that responds to changes in oxygen and carbon dioxide.

Further discussion of these injuries will be taken up later.

Vulnerability of Fetal Respiratory System

How labor affects the fetus or what organs are most vulnerable to injury during birth are, of course, considerations of the first importance in any endeavor to combat the lethal factors operative in parturition. For our present purpose of tracing the effects of anesthetic agents introduced during labor, the foregoing findings afford clues of the greatest significance. Pharmacologists have shown that all drugs commonly given for the relief of pain tend to alter the functioning of respiration. Since these substances have been demonstrated to pass rapidly from the mother into the fetus it is clear that one may seek evidence of their effect upon the child in the same types of injuries as those just noted to be most frequently associated with birth. Anesthetic agents thus strike the fetus at a point which has been found to be of maximum susceptibility to injury during labor—the respiratory system.

Origin of Prenatal Injuries Traced. Whether one asks how intranatal injuries most frequently occur or whether the question is restricted to that of how one particular factor during labor, such as anesthetics, can cause fetal injury, it is evident that the picture presented at autopsy seldom is adequate to reveal the full etiology as it often does, for instance, in disease of bacterial origin. Likewise, the identification of the particular abnormality of labor which is involved often is unrevealed by postmortem examination. The evidence of pathologic anatomy must be supplemented by taking into account various functional abnormalities which leave little or no imprint after death. This involves, of course, going back into intrauterine life in order to trace the sequence of alterations in the fetal environment that resulted in the damage first revealed at the time of birth. For it is clear that such injuries as asphyxia, atelectasis and pneumonia must originate during intrauterine life inasmuch as they are already present at the moment of birth. The detection of the origin of changes of a pathologic nature long before the anatomic structures bear evidence of any abnormality involves, therefore, observation of the living fetus in its normal environment.

FETAL RESPIRATION UNMASKED

When one turns to the investigations upon the functional state of the respiratory system before birth, of first importance is the demonstration that intrauterine respiratory movements normally occur throughout a large part of fetal life. Instead of a state of prolonged apnea, as was previously thought to be the case, fetal respiratory activity increases as term is approached.

It was long held that before birth the respiratory system of the fetus

was characterized by a state of prolonged apnea. The origin of the first breath after birth was a matter of considerable uncertainty. Accordingly, asphyxia or respiratory failure of the newborn was approached by the clinician and the physiologist from a standpoint which regarded the problem to be a matter of the sudden initiation of activity in a previously dormant system. Even in recent years the solution of the problem was sought in terms of possible causes of the first breath of the newborn; search was directed toward discovery of some mechanism which suddenly came into operation at the time of birth. What escaped recognition was that this viewpoint is based upon inadequate experimental technic. A more detailed knowledge of the labor mechanism is required than had been generally appreciated, and the special physiology of the fetus, particularly with respect to the action of anesthetics, must be reckoned with. In order to gain access to the fetus lying within the protection of the uterine wall and membranes, and still maintain the essential features of the physiologic environment, more preparation is required than merely to open the abdominal wall, or to perform hysterotomy in a saline bath. Snyder and Rosenfeld showed that the striking changes in irritability of the uterus as term is approached must be taken into account and the influence of such changes upon the placental circulation and aeration of the fetus must be recognized and controlled. Likewise, the discovery of the exquisite sensitivity of the fetal respiratory system to depression by anesthetic agents made clear the need for revision of the bulk of previous work, since general anesthetics had been routinely used.

Direct observation of the fetus breathing in the intrauterine environment brings into view the prenatal history and development of respiratory responses. At the same time it opens the way for the first time to a direct determination in terms of respiratory movements of the influence of changes in oxygen and carbon dioxide tension and to a comparison of the effects upon the fetus of various anesthetics before birth. Factors which have long been suspected of possessing lethal potentialities for the fetus can be brought within range of direct observation and quantitative measurement.

Intrauterine Injuries Linked with Environment

As fresh data and new theories are introduced in the attempt to describe the state of activity of the respiratory system before birth, one rigid test of their validity is always at hand. Do they fit in or clarify the picture of the pathologic changes in the respiratory organs noted in fetal life? Frequently, the transition from normal to abnormal structures or functions is revealed by either an exaggeration or by a deficiency beyond the standard range. In either case, the

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