Monographs in Anaesthesiology

Relief of Intractable Pain

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edited by Mark Swerdlow

second edition, completely revised

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Relief of
Intractable Pain

To my wife Elizabeth Swerdlow

"But Pain
is perfect miserie
the
Worst of Evils . . ."

John Milton (1608–1674), Paradise Lost Bk. VI

Monographs in Anaesthesiology

VOLUME 1

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Foreword

The relief of pain is a prime duty of a doctor. Fortunately most pains that afflict us are transient, and those that are not, warn of disease which is curable. It is when the cause cannot be removed or cannot be found that the pain becomes intractable. The alleviation of such pain is all too frequently neglected, partly because of lack of the necessary experience and skill, partly because busy practitioners cannot or will not devote the time and sympathy to it, but mostly because doctors as a whole are largely unaware of what can be done for the unfortunate patients who are so afflicted. Fortunately a growing number of doctors, mostly anaesthetists, but also others from nearly every specialist group are taking an interest in intractable pain. A group of them have combined under an able editor to produce this splendid book. The ability to perform skilfully and effectively the various technical procedures they discuss is important, but they are not difficult for anyone to acquire with practice; but if there is one outstanding lesson to be learnt herein, it is that no one doctor is likely to have experience of all the varieties of intractable pain, or to be so wise as to be able to make the right choice of treatment in all cases. A correct diagnosis is essential to the treatment of intractable pain, and this needs a group team of interested specialists from a number of appropriate branches of medicine.

The comprehensive nature and the intellectual approach of the contents of this

book will make it an important source of knowledge on intractable pain for a long time. It is certain to stimulate interest as well as good practice; both will be to the benefit of the sufferers, who for so long have been a neglected section of the sick community.

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Preface to the first edition

Ideally, severe pain would be relieved by the removal or treatment of the cause and would never be allowed to become intractable. In reality there are many conditions which are not at present amenable to such management and intractable pain is an all too common challenge in medical practice. Happily, there have been advances in the methods of treatment of the causative diseases, especially cancer, and progress has also been made in the development of pain-killing procedures and in the formulation of analgesic drugs. Recent advances in neurophysiology are producing a less purely anatomical approach to the interruption of the sensory pathway for relief of pain. Furthermore, the existence of an increasing number of Pain Clinics shows that there is a growing awareness of the problem of intractable pain and a willingness to try to tackle it.

The object of treatment is to provide the maximum relief of pain with the minimum of complications and disadvantages. The form of treatment which will offer the best prospects will differ from case to case and will depend, among other things, upon the aetiological condition, the age and fitness of the patient and his life expectancy. The management of patients with pain calls for a multi-disciplinary approach, not only in arriving at a decision as to the cause and prognosis, but also in deciding on what is likely to be the most effective line of treatment and in carrying it out. However, there is nothing more harmful to the psychological welfare of the patient than diverging or

conflicting statements by several physicians with different philosophical approaches to this problem.

This book is intended to give a concise but comprehensive picture of the methods and agents which are now of use in the relief of intractable pain. It should be of value not only to those who work in Pain Clinics, but also to family doctors and specialists of many kinds who have to deal with patients suffering chronic pain. It is hoped that the reader will gain a more profound knowledge of the part which his speciality can play, and also an increased awareness of the range of usefulness of the other disciplines in this field. The relief of pain is, however, only one contribution to the improvement of the patient's comfort and quality of life, just as the pain itself is only one of his many problems. The latter fact often becomes apparent after the pain has been removed, when many other therapeutic and rehabilitative services will still be required.

No attempt is made to give a detailed description of all the nerve blocks; these have been very adequately described and illustrated in the several text books expressly written on this subject and the reader is referred to these:

Bonica, J. J. – The Management of Pain. Lea & Febiger, Philadelphia, 1953.

Erikssen, E. – Illustrated handbook in local anaesthesia. Lloyd-Luke, London, 1969.

Moore, D. C. – Regional Block. C. C. Thomas, Springfield, Illinois. 4th Edition, 1965.

Preface to the second edition

The reception accorded to the first edition of this book was very gratifying and confirmed a widespread interest in the subject of relief of pain. The few years since the first edition was written have seen a massive proliferation in the number of pain relief clinics and in the number of countries providing this service, an expansion so great that it has been referred to as 'Medicine's new growth industry'.

There has also been an increasing involvement of basic scientists studying the mechanisms of chronic pain syndromes in collaboration with clinicians. The gradual revelation of the role and influence of certain central brain areas is giving us a new understanding of pain mechanisms and the import of encephalins, endorphins etc. is rapidly becoming clearer. The importance of these advances in knowledge is clearly reflected in Chapters 1, 4 and 10.

In the present volume there has been a great deal of 'updating' in all the chapters. In particular the chapters on peripheral and on sympathetic nerve blocking have been enlarged to provide a more comprehensive coverage of their subjects as well as a fuller neurophysiological explanation of the conditions involved. A chapter is now devoted to the value of large fibre nerve stimulation methods, both central and peripheral, in the relief of pain and a new section has been introduced on pituitary ablation by neurolytic injection.

An unhappy recent trend has been the increasingly frequent occurrence of

litigation and publicity in cases of accidents following invasive pain-relieving measures. Where posisble, relevant complications are detailed throughout the text in order to make the reader more aware of the dangers.

The editor would like to thank the expert contributors, both old and new, for the time and trouble they have taken to make this work up-to-date, comprehensive and authoritative. Every effort has been made to keep the work relevant to clinical practice. It is hoped that the more widely international spread of authorship in this edition will reflect a wider concensus of present ideas.

It is a pleasure once again to acknowledge the invaluable secretarial assistance of Mrs. Kathleen Hayes in the preparation of this volume and the expert help of Miss Patricia Cummings, A.L.A., Manchester University Medical Library, who carried out the indexing. My thanks are also due to Dr. P. S. Jackson of Elsevier/North Holland Biomedical Press for his courteous and efficient cooperation.

Manchester, Oct. 1977

M. Swerdlow (ed.) Relief of Intractable Pain

1

The Neurophysiological Basis of Pain Perception

AMIRAM CARMON

Introduction

Pain has been considered either as one of the specialized sensations or as an interpretive percept of other sensations, but this distinction is merely semantic. Operatively, it can be stated unequivocally that pain, like other sensations and percepts, is essentially a physiological event taking place in the nervous system. The neurophysiological study of pain is an attempt to understand the nature of this event, and to outline the neural mechanisms which subserve it. Furthermore, and from a clinical point of view even more important, neurophysiology investigates the neural circuits which presumably control or inhibit the processing of the pain signals. The major part of this chapter will be devoted to discussion of those issues.

Inasmuch as neural activity is the precursor of the painful sensation, certain pathological states afflicting neural tissues can arouse pain, even in the absence of external noxious stimuli, or alternatively, abolish pain perception even without the introduction of analgesics. Reference will be made to several neurological syndromes of hyper- and hypo-algesia which give clinical evidence in support of the neurophysiological mechanisms. Since, in this book, other chapters are dealing with neurosurgical procedures and with the pharmacology of analgesics, only brief reference to these aspects will be made here.

Prior to a discussion of the neurophysiological aspects of pain, it is important to bear in mind that pain is manifested primarily in behaviour and therefore reference to the behavioural aspects of pain should be made in conjunction with the physiological examinations. Lack of such approach can make theories of pain untenable, since the reference in this case is to a state of stimulation that is not necessarily representative of pain.

A fundamental problem in the neurophysiological study of pain is the proper definition of the stimulus which inflicts pain. In a controlled experimental situation, as well as in clinical observations, it is necessary to define a stimulus as 'painful' before labelling the neural structure activated by it as a neural system involved in transmission or in perception of a painful event.

The Problem of Receptor Specificity

The scientific study of pain has been confounded from the beginning by this problem. Johannes Müller's doctrine of specific nerve energies (1844) assigned to a class of receptors the exclusive role of reacting to pain-producing stimuli. It further designated their communicative pathways as the specific channels through which the external noxious signals are transmitted to the central nervous system, thus generating an awareness of the painful state. This deterministic approach regarded pain as a property of the stimulus, and considered that once information about it is brought to the conscious mind, pain is felt and the organism activates the bodily defence mechanisms to spare it from possible harm. Sherrington referred to the specific receptors which react to the potentially harmful stimuli as 'nociceptors'. Much later, however, it was found that a subjective sensation of pain is not necessarily the result of tissue damage, since high frequency air-jet pulses can arouse painful sensation without an apparent damage to the skin (Adrian *et al.* 1931). Adrian's observation concurred with another theory which disclaimed a sensory specificity of pain and proposed the concept that a given pattern of neural impulses is interpreted by the brain as 'pain' (Goldscheider 1916). Protagonists of both theories spent a large amount of effort in attempts to either discover the peripheral specific receptors, which supposedly are concerned solely with nociception, or in attempts to disclaim their existence. Von Frey's (1894) psychophysical experiments, attempting to localize pain-sensitive spots on the skin, were based on the rationale that since the receptors are specific and since they are not present at every point, sensitivity to pain will not be uniform on the skin. By localizing a sensitive spot it was hoped that the specific receptor underlying it would be available for isolation and identification. The theory derived

strength from morphological observations of a large variety of cutaneous receptors, each supposedly geared to perceive a different somatic sensation. Beside free nerve endings, myelinated or nonmyelinated, with diameters ranging from less than 1 μ to several μ, nearly 100 different types of receptors with more complex structures were identified. Certain 'specificities' were assigned to several of these receptors and some were considered to be involved in responding to painful stimuli. However, in a recent report on the morphology of the cutaneous receptors, Andres and Von During (1973) commented that the exact morphological ultrastructure of cutaneous nociceptors has not been unequivocally determined as yet. The assumptions of nerve endings which are geared to react to specific stimuli were met with opposition by various investigators who could not ascertain a clear correlation between structure and function of receptors (Weddel 1961). Once peripheral neural specificity was denied, the alternative was to accept that pain is felt when the central nervous system perceives a certain increase, temporally or spatially, in the neural activity in any of the somatic neural channels (Sinclair 1955).

This controversy should be judged also in the light of the technical complexity of stimulating a single cutaneous receptor and recording from the nerve fibre supplying it, or in following the pathway through which the activity is transmitted to the brain. In addition, most neurophysiological studies have been conducted in preparations which are not well suited for pain studies, since, in animals, the painful nature of the stimulus can be inferred only from an aversive behavioural response of the animal. The behavioural definition of pain is, however, closely tied to the verbal report of pain, a response which can be expressed only by humans. Studies of the peripheral and central events in the nervous tissue can be more advantageous if they are carried out in man, since in this case the stimulus–response connection is clearer. However, humans cannot be subjected to the full gamut of neurophysiological procedures. Albe Fessard and Fessard (1975), discussing this issue within the framework of the neurophysiology of pain, suggested therefore that the term 'noxious' be used to qualify nerve impulses and messages engendered in animals by stimuli which induce pain in man.

Peripheral Nerve Fibres Associated with Pain

There have been few attempts to study the characteristics of peripheral nerve fibres responding to noxious stimulation in man. Technical problems of recording from single fibres in conscious humans make such studies difficult.

The few human studies (Torebjörk & Halin 1973; Halin & Torebjörk 1973;

Van Hees 1976), as well as numerous studies in animals, however, have shed some light on the relation between peripheral nerve fibres and noxious stimulation (Perl 1971; Burgess & Perl 1973; Iggo 1974). Fibres feeding on the peripheral somatosensory receptors can be divided morphologically into three main categories: (1) thick myelinated fibres (A-alpha, beta and gamma fibres), (2) thin myelinated fibres (A-delta fibres), and (3) thin unmyelinated fibres (C-fibres). In human experiments, C-fibres and A-delta fibres were found to be activated when a strong stimulus, inducing also a subjective feeling of pain, was delivered to the subject. In parallel, animal work showed that when stimuli that are usually painful to man were administered, A-delta and C-fibres were those which were activated.

Experimentally, it is more efficient as well as more precise to classify the activity of peripheral fibres according to the magnitude of their sensitivity rather than the nature of the external stimulus to which they respond. This classification eliminates the confounding factor imposed by the perceptual quality of the stimulus. The thick myelinated fibres have low thresholds and respond with similar frequency to a weak and to a strong stimulus. On the other hand, the two other groups of fibres, the A-delta and the C-fibres, have a relatively high threshold and their rate of activity increases parallel to the strength of the stimulus. As a general rule, the threshold is inverse to the conduction velocity, and thus to the thickness of the nerve fibres. It seems, therefore, that the thinner the fibres, the more they are involved in reacting to potentially noxious stimuli and in responding quantitatively to the strength of the stimulus.

The two groups of fibres which respond to strong stimuli behave differently with respect to stimulus modality and have a different topography of sensitivity. A-delta fibres respond mainly to strong mechanical stimuli; their receptive fields are numerous and small, i.e. a single fibre reacts to 20–30 minute points within a relatively large area (8–10cm^2). The C-fibres, on the other hand, have polymodal sensitivity, reacting to both strong thermal and strong mechanical stimuli, and have only one minute receptive field. The two groups are also differentiated on the basis of the time course of their activity. A-delta fibres adapt rather rapidly, and repetitive stimulation will result in reduction of their sensitivity. C-fibres, on the other hand, show an increased sensitivity following repetitive stimulation: their threshold becomes lower and they continue to respond long after the stimulus has been withdrawn, indicating that they are sensitized by noxious stimulation (Perl 1976).

In summary, it can be stated that there are at least two categories of peripheral nerve fibres which respond selectively to noxious stimuli. It seems as if the more important category is that of the polymodal nociceptors which respond both to mechanical and thermal painful stimuli. These fibres comprise about 80% of all