

Reports of Scientific Meetings

Ellis N. Cohen, M.D., Editor

International Symposium on Pain

Heightened public interest in new methods of treating pain made spring 1973 a propitious time for the International Symposium on Pain, sponsored jointly by the University of Washington School of Medicine and the National Institutes of Health. More than a hundred authorities on pain research, therapy and diagnosis attended. The meeting was held in a secluded conference center in the rural town of Issaquah, Washington. The "science retreat" atmosphere stimulated more individual involvement than possible in the usual big-city whirlwind. The pace of the meeting was unrelenting, from early in the morning till late in the evening, with regular after-dinner sessions and discussion groups.

The scientific program was divided into two parts, basic sciences occupying the first two days, and diagnosis and therapy of pain the final two and one-half days, with pathology bridging the two sections.

The high scientific standards and judicious selection of speakers at the meeting were evident from the start with the papers by Drs. Perl (University of North Carolina) and Iggo (University of Edinburgh). The former introduced the topic of nociceptors and their conduction pathways. The old debate of specific versus nonspecific receptors is slowly swinging towards specificity again. Cutaneous receptors that respond only to extreme mechanical stimulation can be isolated. Other receptors are activated by a spectrum of inputs, ranging from mild to severe, with corresponding gradation of firing rates. Evident from the morning's presentations was the absence of any notion of what a "pain receptor" is, does, or looks like. This should be a promising research area.

The afternoon session dealt with acupuncture research. Presentations included a potpourri of approaches, indicating—if nothing else—the difficulty of studying "pain" experimentally. A device to sound a buzzer when near the "concentrated potentials" of an acupuncture point worked admirably when searching along the speaker's face. Not mentioned in the national press coverage, how-

ever, was that the gadget also beeped when returned to the investigator's pocket. Differences of opinion, some quite strong, about the quality and value of current acupuncture research were voiced in the subsequent discussion led by Professor Patrick Wall (University College, London). But, as one commentator said, "If we aren't prepared to listen, we shouldn't have bothered to come."

As brought out in subsequent comments, pain research is still shackled by continuing difficulties in defining pain in other than human terms. Further, in anatomy (and undoubtedly physiology too), man differs again from both cat and monkey. Add to that our inability to express pain in physicochemical terms, and one can perhaps better appreciate the frustrations of pain-related research. To compound the problem, pain studied in young healthy volunteers is not the same as that suffered by patients in chronic pain. Subtle and not-so-subtle psychological differences may make data obtained from healthy subjects as difficult to extrapolate as those obtained from non-human species. Too, animal research must be placed in proper perspective relative to pain in man. One problem in interpretation is anesthesia which affects neural cells, those of the pain system in particular. Experiments on deeply anesthetized animals thus may have little direct bearing on understanding pain in awake man. Clearly there is room for high quality pain research, but most observers shared this reporter's view—we still don't know how best to go about it.

Emerging from the neurophysiology sessions, where pain was traced from periphery to brain, was a wealth of available information about spinal cord systems. The last decade has seen a considerable spurt of work on this CNS region that is all too often still regarded as a bundle of inert telephone cables. Far from it! Evidently the spinal cord plays an important role in modulating the upward flow of "pain impulses," and one still cannot be sure how much impulse modulation at the spinal level contributes to the overall perception and interpretation of pain in man.

Of interest to anesthesiologists are the

striking effects of anesthetic agents on signal transmission through the spinal afferent system. Each general anesthetic studied thus far depresses by 50 to 100 per cent cutaneous impulses generated by natural stimuli. The effect is dose-related and occurs in the clinical anesthetic dose range. How this ties in with the analgesic action of anesthetics remains a moot question, but it raises the potential for a greater research effort into cord mechanisms of anesthesia.

From evidence presented at the meeting it was possible to synthesize a reasonably comprehensive view of afferent throughput. Three, and possibly four, cord areas appear to be candidates for receiving and relaying pain-related impulse traffic. One is the marginal area of lamina I cells that cap the substantia gelatinosa. These cells can be fired from the periphery as well as backfired from the thalamus. The bogey of species differences in neural research, however, again arises, in that lamina I cells, so prominent in the monkey, form only a thin veil in the cat, and some of the neural effects can be demonstrated only in deeply anesthetized monkeys. It is conceivable that normally a heavy inhibitory shield prevents lamina I cells from responding, perhaps explaining why many investigators have been unable to detect much activity in this cell layer.

Currently the most promising and productive cord areas are laminae IV and V. These anatomic sites in the central portion of the dorsal horn have attracted investigators since the Melzack and Wall gate theory of pain focused on this region. It can be shown that cells of laminae IV and V respond to a wide variety and modality of input, ranging from tiny hair displacement to tissue-destructive manipulations. Neurons here show many characteristics of central pain receptors; marked convergence, inhibitory as well as excitatory qualities, and recruitment by other sensory modalities. Anesthetics profoundly affect these properties, both by reducing impulse throughput, and by progressive shrinking of the cutaneous receptive field—the latter disappearing when transmission has been blocked.

Another prominent array of cord cells related to the pain-transmitting paths is found in laminae VII and VIII, located in the cord's ventral horn. Units here respond vigorously to backfiring from thalamic and cortical re-

gions. Madame Fessard (University of Paris), among others, demonstrated not only thalamic but also reticular projections through this region. In monkeys, unlike cats, projection from the VP thalamic nuclei was mainly confined to lamina V cells.

The fourth and final group of candidates includes an ill-defined cluster of periaqueductal neurons brought into action by prolonged stimulation. Little is known about their physiologic and pharmacologic properties, and even less about their significance.

Of interest to many dealing with human pain, the existence of the classic crossed spinothalamic tract is being questioned. Kerr (Mayo Clinic) and Mehler (University of California) independently reported degeneration studies that cast doubt on the existence of an identifiable spinothalamic tract. In particular, the crossing-over of the tract is less certain now than had been assumed in the past. This surgically important consideration followed from studies with longitudinal transection of the cord which showed largely intact impulse passage following extensive midline myelotomy. Either uncrossed pathways or Noordenbos-type short-chain multisynaptic projections (or both) may provide the major upward road for pain-related neural traffic.

Adding to the general uncertainty about the spinothalamic tract are differences in the courses of other fiber tracts between cats and monkeys; with man himself yet again different. For instance, man lacks a spino-olivary tract altogether (Dr. Mehler). Further, the cat's spinocervical tract assumes some of the functions associated with the spinothalamic projections of primates. Finally, many non-pain-related tracts course through the anterolateral columns, which evidently contain no C-fibers. In fact, Lissauer's tract may be the only nonmyelinated CNS tract.

Careful planning was evident in the lively discussion groups scheduled for the evenings. People with common interests were able to get together and exchange views in more detail. For instance, the rather dull title, "Ascending Pathways of Spinal Cord," camouflaged vigorous discussions ranging from fundamental physiology to clinical anesthesiology. Because of prevailing uncertainty, one participant suggested a "black box" approach to the spinal cord. However, the group agreed after some discussion that there was

little need for so gloomy a view, and that they merely had to deal with a "grey box."

Part of the spinal cord discussion group's time was spent with clinical considerations. It was reassuring to note that clinicians *can* contribute to guiding the future course of research. The physiologists were eager to learn more about causalgia, phantom limb and tourniquet pain during spinal anesthesia. No satisfactory physiologic explanation based on current anatomic models could be brought forward. Thus it became apparent that the spinal cord might not be man's sole pain-transmitting system. Afferent sympathetic fibers, or other pain-related axons, may travel upward for variable distances along the paravertebral sympathetic trunks before entering the cord.

Reinforcing the mood of frontiers of knowledge was Tuesday evening's address by Professor Wall. His topic—Pain Research—ranged from fundamental cellular investigation to clinical studies. Characteristics that brand a cell as part of a pain-related transmission system are its ability to respond to a wide variety and modality of input; marked convergence, responding to stimulation of an identifiable circumspect receptive field; inhibitory as well as excitatory qualities; and recruitment by other sensory modalities. These characteristics probably are common to central pain systems, though they are by no means exclusive. Impulse patterning in the time and frequency domains probably serves a major coding function. How major this function will be depends on methods of signal detection now being developed.

Dr. Wall gingerly touched on the topic of acupuncture. He leaned towards viewing it along the lines of hypnosis, though admittedly this cannot explain all facets of the phenomenon. Whether it will work on western man in a western society remains to be seen. Unfortunately, not much help was given to prospective investigators as to where to look and how to go about it.

Dr. Wall's address further bound the clinician and basic scientist. He pointed out that each serves as a stimulus and impetus for the other. Thus, while new approaches to the treatment of pain developed from the spinal gate concept, it in turn grew out of clinical observations that were unexplainable by then-current anatomic and physiologic information.

By remaining in touch with clinicians, the investigator gains a broader picture of where his research leads and can be of potential assistance to the clinician.

Stimulated by the above considerations, informal get-togethers attempted to identify other problems facing pain researchers. One question not easily resolved is how electrical volleys relate to actual pain. If one faults the use of electrical volleys, then "natural" stimulation may be the answer. However, this mode of stimulation is not easily controlled, except with rather complicated machinery. Further, repeated application of tissue-damaging stimuli may cause prolonged alterations in the receptor-nerve system which sharpen its ability to respond excessively (perhaps due to local pH changes?). The rapidly-controlled temperature probe may be one of the better means of applying a known and graded noxious stimulus.

The latter days of the meeting dealt with territory more familiar to anesthesiologists. Various methods of diagnosis and therapy were discussed and their role in the overall management of pain stressed. This clinical portion of the program was broadly structured following the organizational pattern of the University of Washington Pain Clinic. Radiology, physical therapy, pharmacology, psychiatry, anesthesiology, and neurosurgery all were given forums for their views and respective roles. Emphasized repeatedly was the need for careful patient evaluation prior to performing a nerve block, so as not to pave the way for irreversible destructive procedures. A comment seemed pertinent: could we be placing too much stress on destructive approaches to pain at the expense of simpler physical therapy?

An important outgrowth of the International Symposium was the formation of an International Association for the Study of Pain, headed by Dr. Bonica. Finally, to cap off an unusually successful meeting, indications are that the Symposium Proceedings will be available in record time, towards the end of 1973 (Raven Press).

RUDOLPH H. DE JONG, M.D.
*Professor of Anesthesiology and
Pharmacology
University of Washington
Seattle, Washington 98195*