EXPERIMENTS ON PAIN REFERRED FROM DEEP SOMATIC TISSUES

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EXPERIMENTS ON PAIN REFERRED FROM DEEP SOMATIC TISSUES *

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Pain provoked by the irritation of tissues deep to the skin has a characteristic quality and tends to be diffusely "referred". Unlike acute pain from the skin, it persists for a considerable period of time, is rather slowly transmitted to the consciousness, and is often associated with autonomic or other "reflex" concomitants, such as bradycardia, a fall in the blood pressure, nausea, and skeletal muscle spasm.

Although the radiating nature of deep pain has always been of theoretical and clinical interest, it has been experimentally investigated in muscle only since Lewis [6] and Kellgren [4] used the method of injecting hypertonic saline. Kellgren [5] mapped the segmental areas of deep pain and tenderness below the fourth cervical vertebra by systematically stimulating the "interspinous ligaments" of three subjects. His technique was used by Campbell and Parsons to produce referred pain from the upper cervical "somites". Inman and Saunders studied the relation of experimentally induced pain to clinical problems of deep pain and introduced the concept of "sclerotomes".

These studies have received only scanty critical consideration. It also still seems to be frequently taken for granted that the segmental distribution of deep pain follows the familiar dermatomes. Little attention, moreover, has been paid to the autonomic and affective concomitants which are characteristic of pain in deep tissue.

A systematic study of the patterns of pain which follow the stimulation of paravertebral ** and limb muscles was, therefore, carried out [8]. The number of subjects used was larger than that investigated in Kellgren's work, and the upper cervical segments were included. In addition, observations were made on such concomitant phenomena as the autonomic repercussions and the cutaneous sensory changes in the skin overlying areas of deep pain, and on the influence of somatic and sympathetic-nerve block.

METHOD

Subjects

The paravertebral muscles of the neck and back were systematically injected with a 6 per cent. saline solution at each intervertebral level from the atlanto-occipital area to the lower portion of the sacrum. Five subjects were used in the testing of each injection site. A total of 140 individual observations was made. The subjects were the authors approximately seventy-five medical students, and three laboratory assistants.

Procedure

The desired level for a particular injection site was first obtained by reference to adjacent bony landmarks and by palpation of the vertebral spinous processes. An intradermal wheal was raised, by the use of 1 per cent. procaine solution. This point was situated in the mid-line, midway between two adjacent spinous processes. The test injection of 0.5 to 1.0 milliliter of 6 per cent. saline solution was then made by means of a 2-inch 24-gauge needle. After the skin had been punctured, the needle was directed about 15 degrees toward either the right or the left. The depth of the insertion depended upon the adiposity of the subject, the essential requirement being the placement of the needle tip

* A contribution from the Biomechanics Group, sponsored by the Department of Orthopaedic Surgery and aided by a grant from the Advisory Committee on Artificial Limbs, National Research Council.

** By the term *paravertebral muscle* is meant the musculotendinous tissue immediately on either side of the mid-line of the spine.

Figs. 1-A through 1-D: Drawings show the patterns of referred pain after intervertebral injections of 6 per cent. saline solution. At each level, the areas of deep pain found in five subjects are superimposed. The levels included in this series are from the first through the eighth cervical.

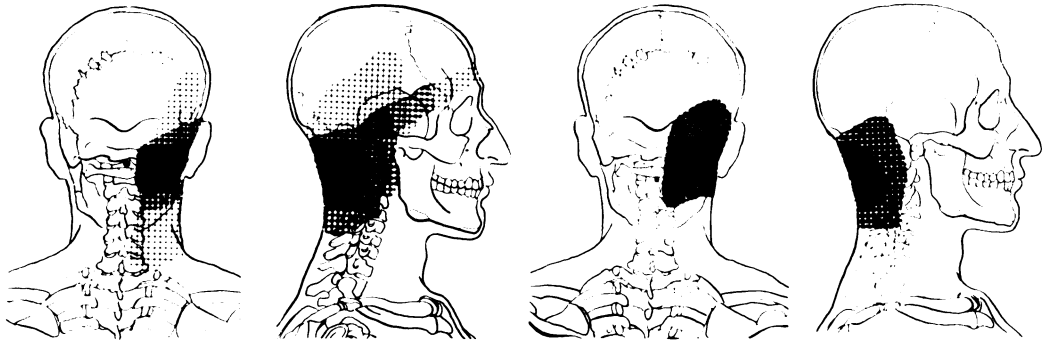

FIG. 1-A

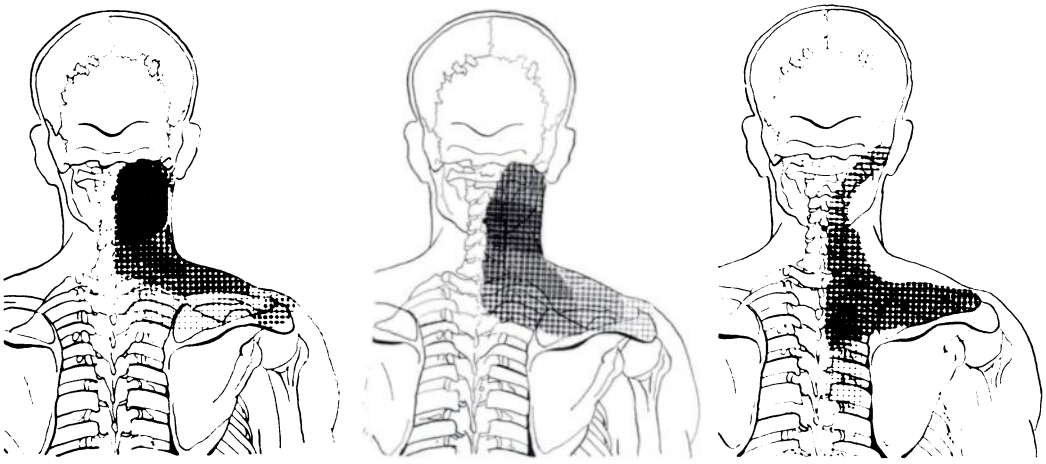

FIG. 1-B

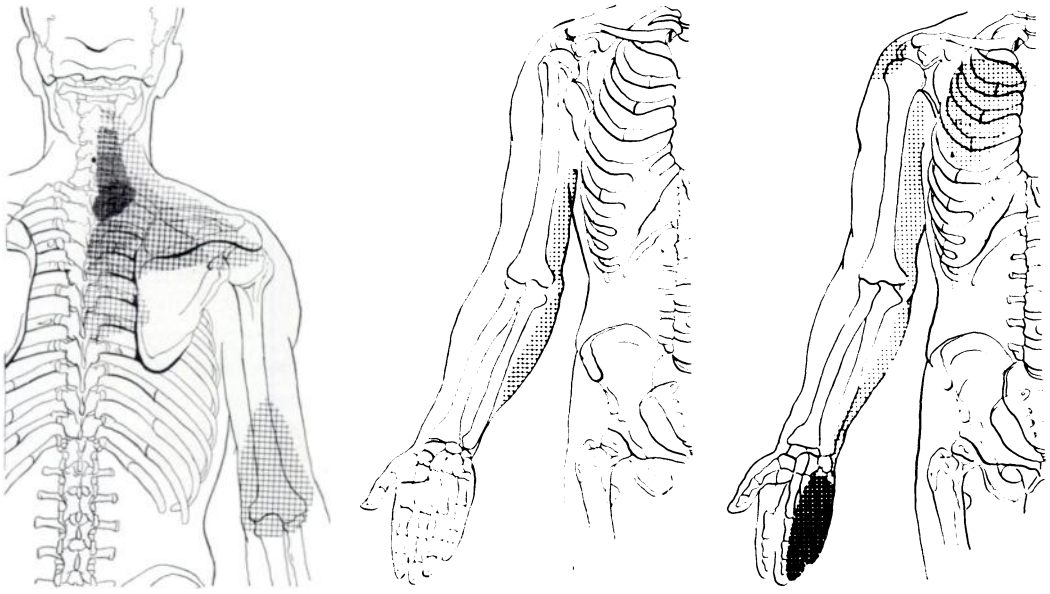

FIG. 1-C

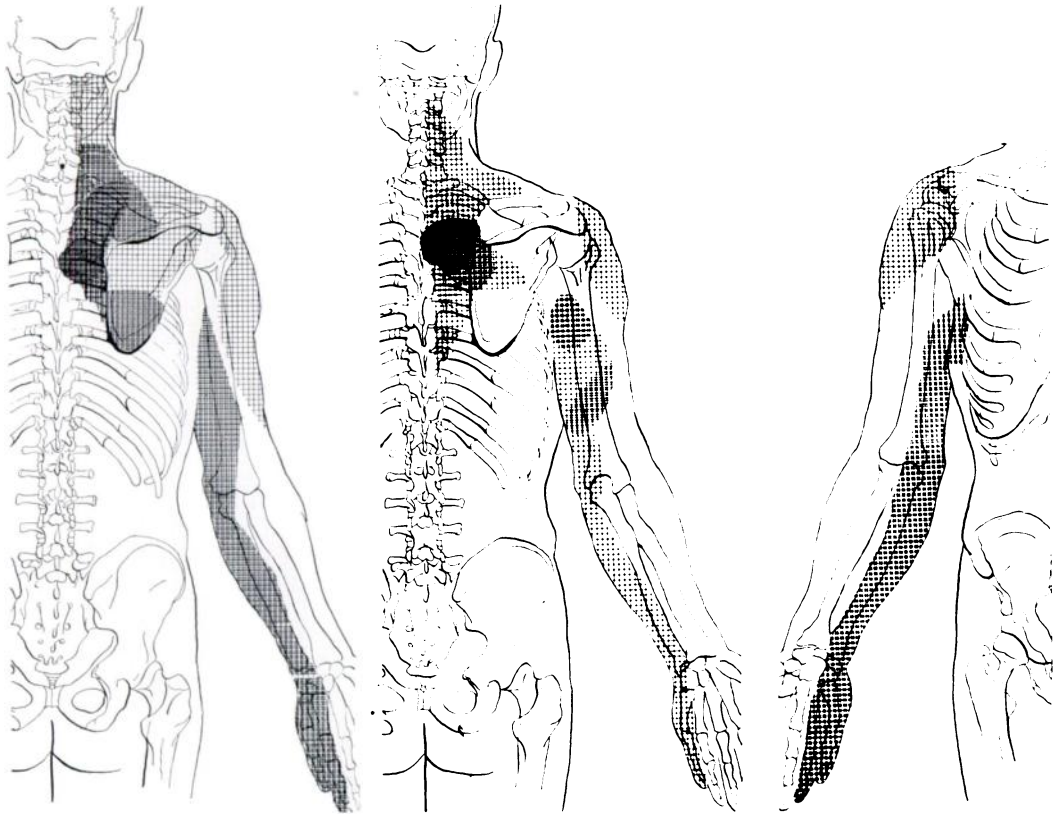

FIG. 1-D

in the musculotendinous interspinous tissues. A small lead pellet was taped to the overlying skin as a marker for roentgenographic confirmation of the precise level.

The subjects were briefed on the entire procedure and during the testing were given notice of each step in order to reduce apprehension. They were told that the pain, while likely to become quite severe, would fade rapidly and would disappear entirely in eight to

Figs. 2-A through 2-H: Drawings show the patterns of referred pain after intervertebral injections of 6 per cent. saline solution. At each level the areas of deep pain found in five subjects are superimposed. The levels included in this series are from the first through the twelfth thoracic.

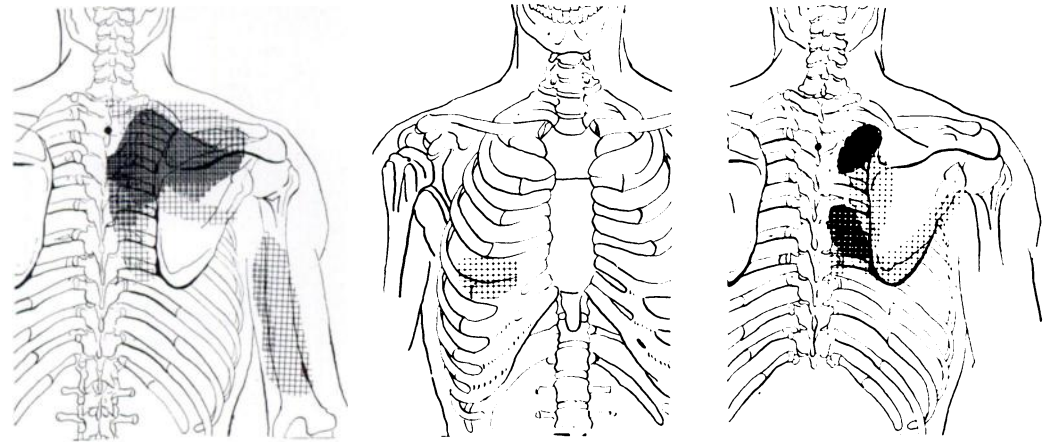

FIG. 2-A

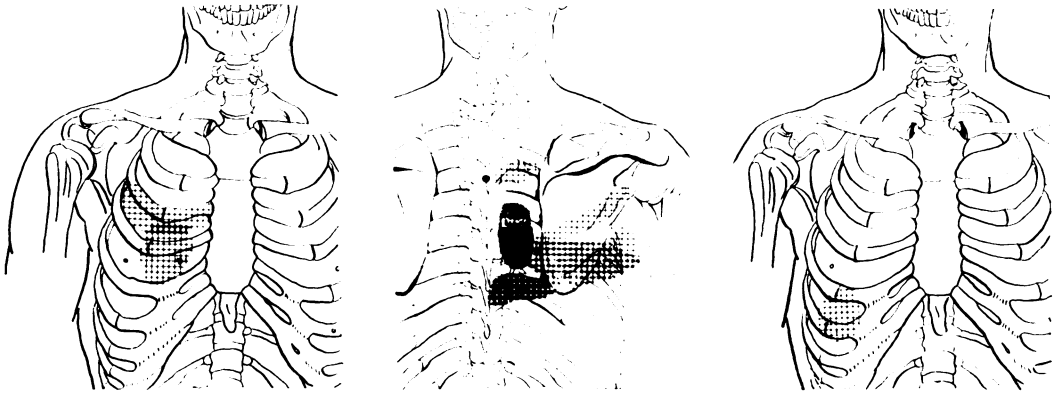

FIG. 2-B

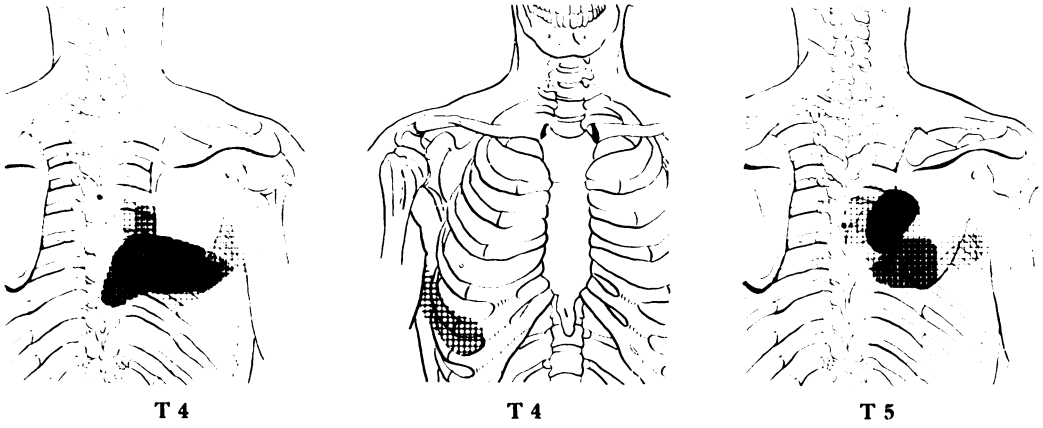

FIG. 2-C

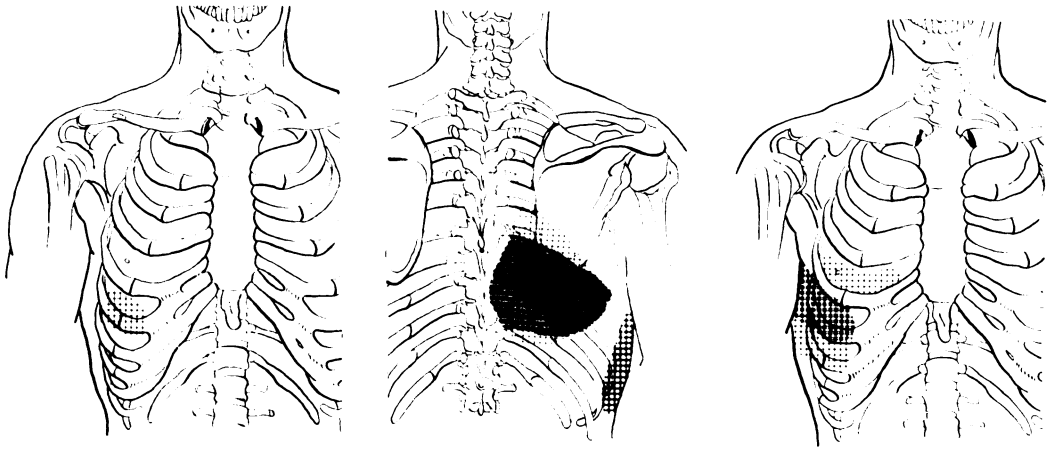

FIG. 2-D

ten minutes. Care was taken, however, to avoid suggestion of either the possible referral pattern or the character of the pain.

The pain resulting from injections of hypertonic saline solution is of sufficient severity and duration for the subject to describe its character and spread. The subject's running comments were recorded by one observer, while another sketched the location of the reported pain on a printed outline of the body and skeleton. The medical training of the subjects added to the reliability of recording.

The pattern obtained in each individual experiment was transferred to transparent paper with fine square rulings and was then cut out. With the individual patterns from each of the five subjects superimposed, gradations in density of shading resulted which

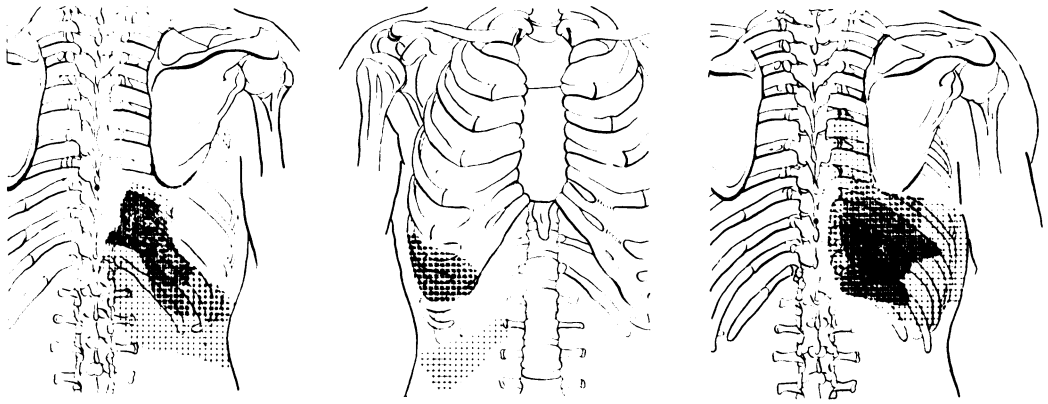

FIG. 2-E

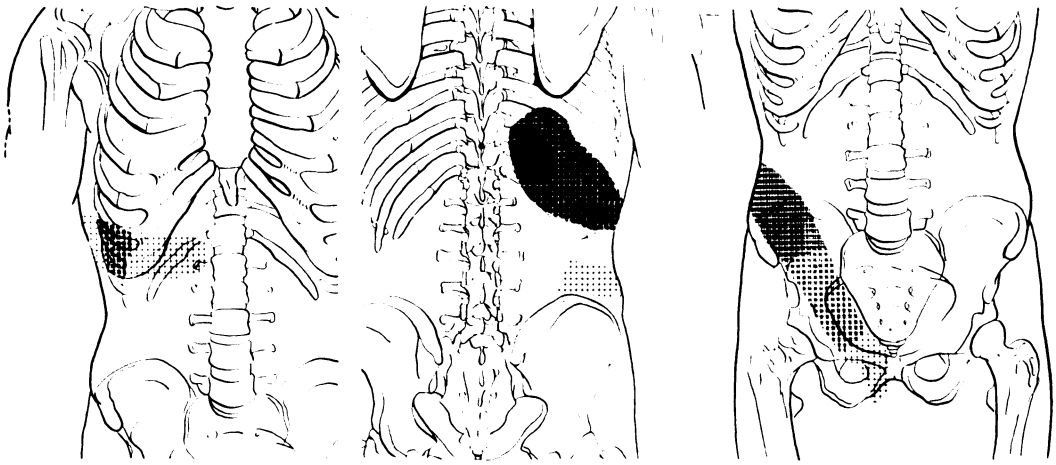

FIG. 2-F

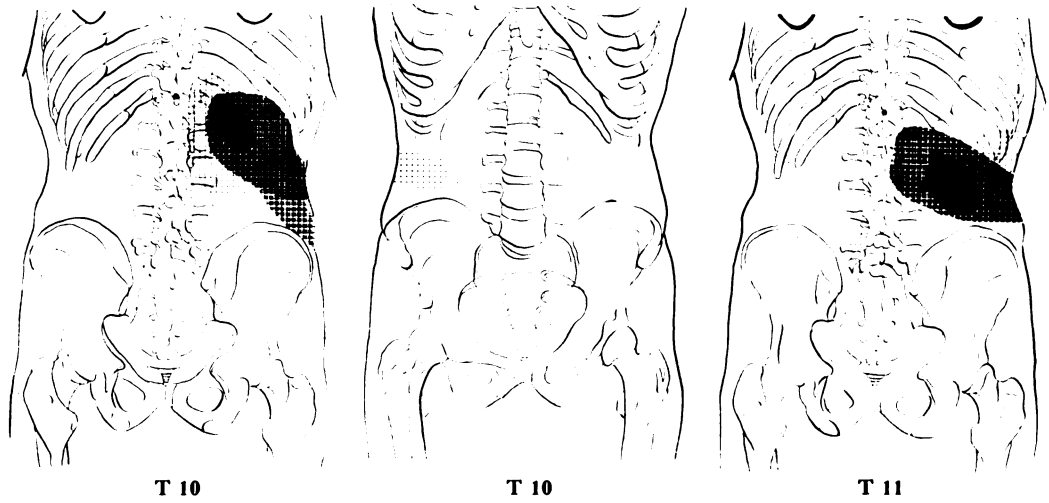

FIG. 2-G

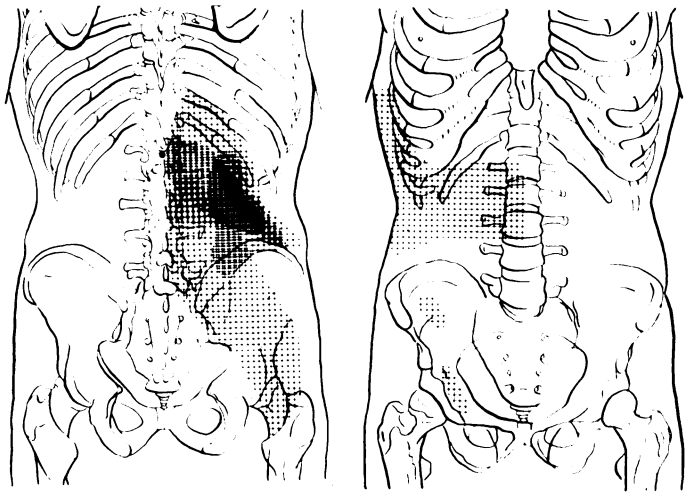

FIG. 2-H

gave the average distribution of deep pain for each segmental level (Figs. 1-A through 4-B). Although the injections were made to either side of the mid-line, on the final outlines the distributions of pain have been transposed to the same side of the body.

In order to study the patterns of deep pain activated by peripheral stimuli, as opposed to axial stimuli, injections of 6 per cent. saline solution were made into limb muscles, and the spread of pain was recorded in the manner described (Figs. 5-A–5-F).

OBSERVATIONS

1. *Character of the Pain*

Although different individuals varied in their reactions, there was considerable agreement concerning the quality of the pain. While it was variously described as "gripping", "boring", "heavy", "crampy", or "lumpy", all subjects agreed that the pain was

Figs. 3-A through 3-C: Patterns of referred pain after intervertebral injections of 6 per cent. saline solution are shown for the levels of the first through the fifth lumbar. At each level, the areas of referred pain in five subjects are superimposed.

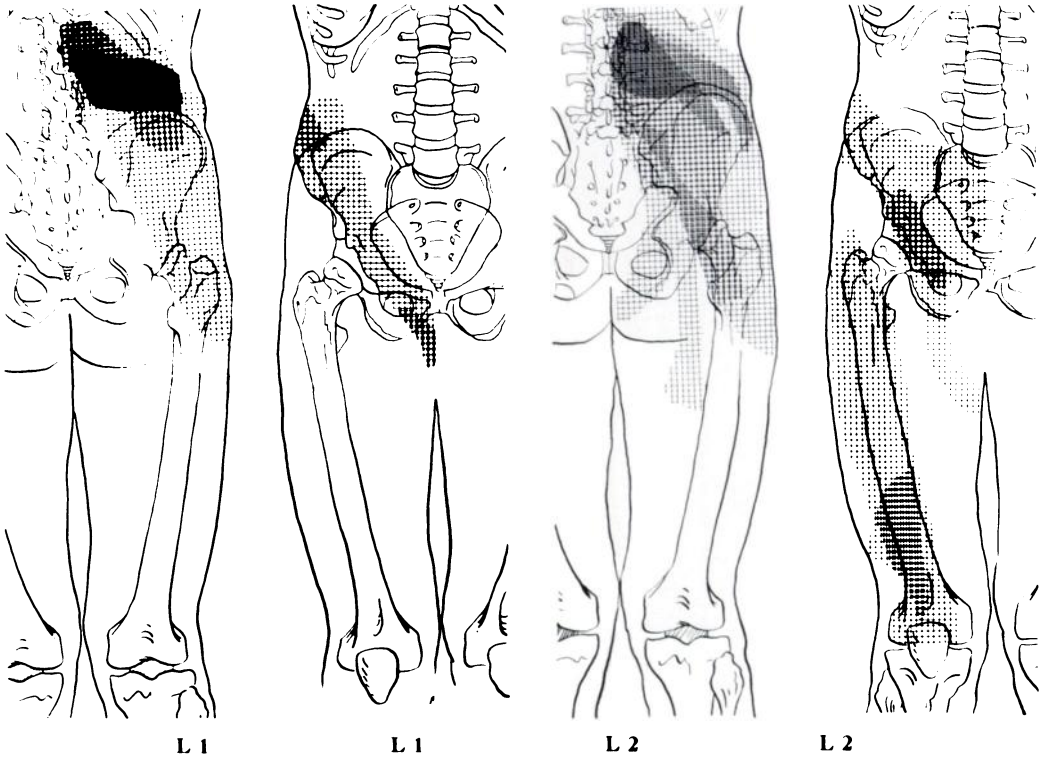

FIG. 3-A

"deep", and most of them used the word "aching". The word "area" did not seem appropriate for expressing the essentially three-dimensional character of the pain.

The intensity of the pain ranged from the absence of discomfort in two subjects to extreme pain, frequently accompanied by acutely unpleasant autonomic reactions. The amount of pain depended upon the amount of saline injected, but the autonomic concomitants did not seem to be proportional. There was usually a gradual increase of pain

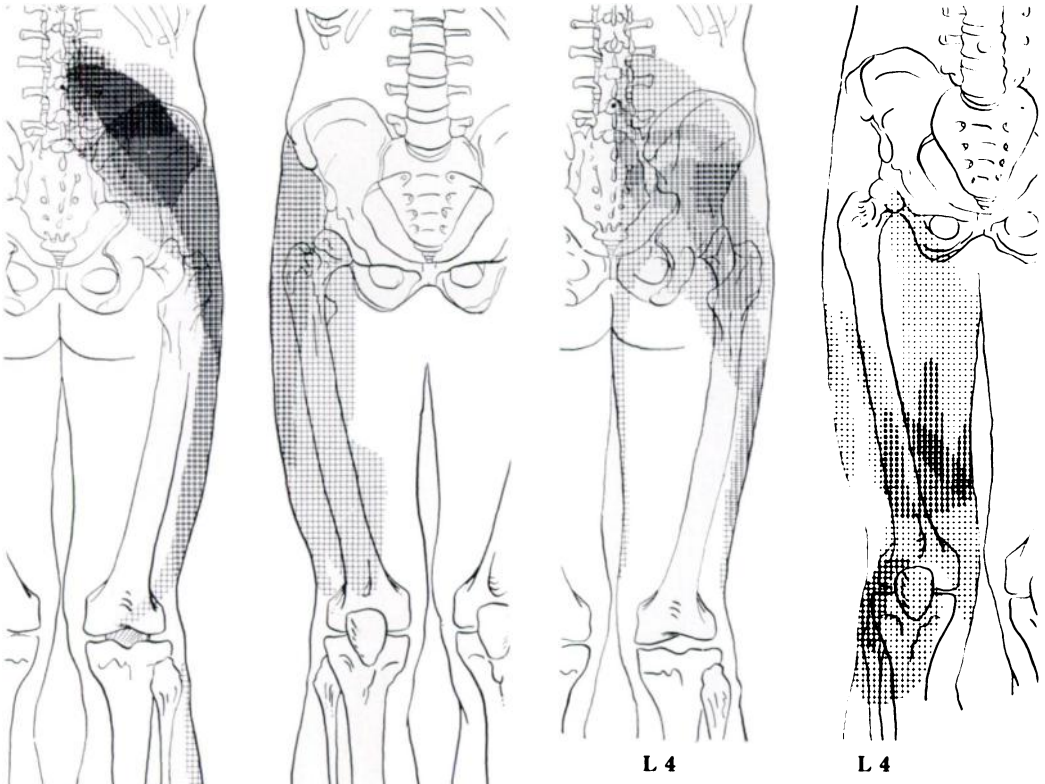

FIG. 3-B

to a peak intensity within one minute. First, a diffuse, poorly localized pain was felt in the vicinity of the injection. Even before attaining peak intensity, the pain spread from this area, occasionally in a continuous manner. More often, however, there was a discontinuous referral of pain to a distant area. The distant or referred pain frequently gained in intensity as the local pain continued to increase, and quite often the referred component persisted fully as long as the local pain.

2. *Distribution of Pain following Stimulation of the Paravertebral Muscles*

Figures 1-A through 4-B represent the distribution of pain following the stimulation of interspinous tissue innervated by the posterior rami of the spinal nerves from the first cervical level to the third sacral level. On the skeletal outlines a dot marks the site of the injection. The densest part of the overlay pattern represents the distribution of referred pain common to five subjects.

The factors influencing the extent of the area of referral were (1) individual variations and (2) the amount of irritant used. Greater amounts of saline tended to produce larger painful areas.

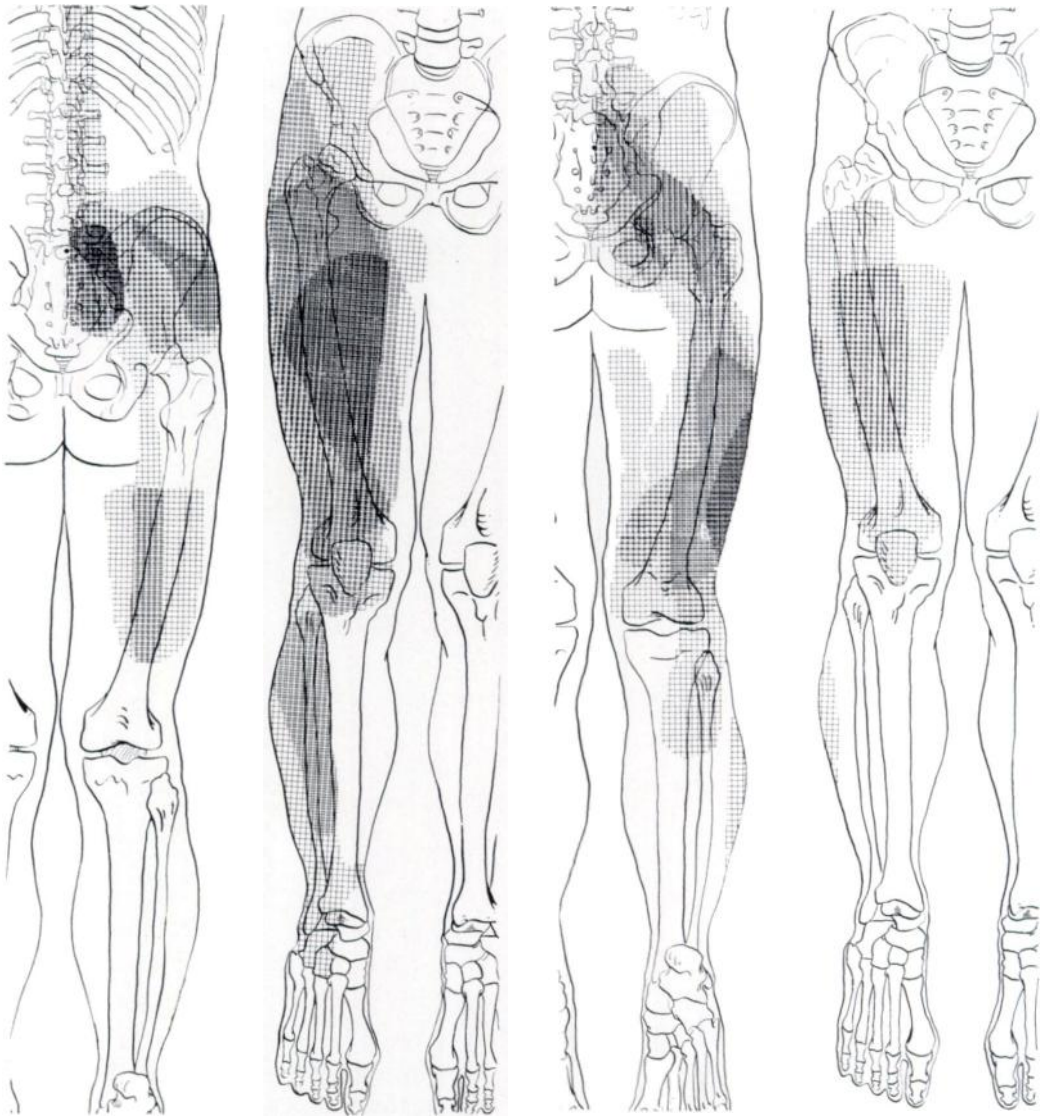

FIG. 3-C FIG. 4-A

Figs. 4-A and 4-B: Patterns of referred pain after intervertebral injections of 6 per cent. saline solution are shown for the levels of the first through the third sacral. At each level the areas of referred pain in five subjects are superimposed.

Stimulation of the first cervical level provoked pain in the occipital region. In one instance, pain was referred to the forehead (Fig. 1-A, *C1*). The posterior aspects of the neck and occipital region were affected by stimulation of the second, third, and fourth cervical levels. Referral into the shoulder was observed following stimulation as high as the third cervical level. There was a particularly marked overlap in the upper cervical region. This may possibly be accounted for by the fusion of the cervical and occipital segments which takes place during development. Thus, stimulation of the tissues derived from the third, fourth, and fifth cervical segments may give no separable distributions of pain.

Following stimulation of the sixth cervical segment, pain was referred into the arm and forearm in two of the five subjects. Stimulation of the seventh cervical segment provoked pain in the ulnar side of the arm and forearm. The same distribution was produced

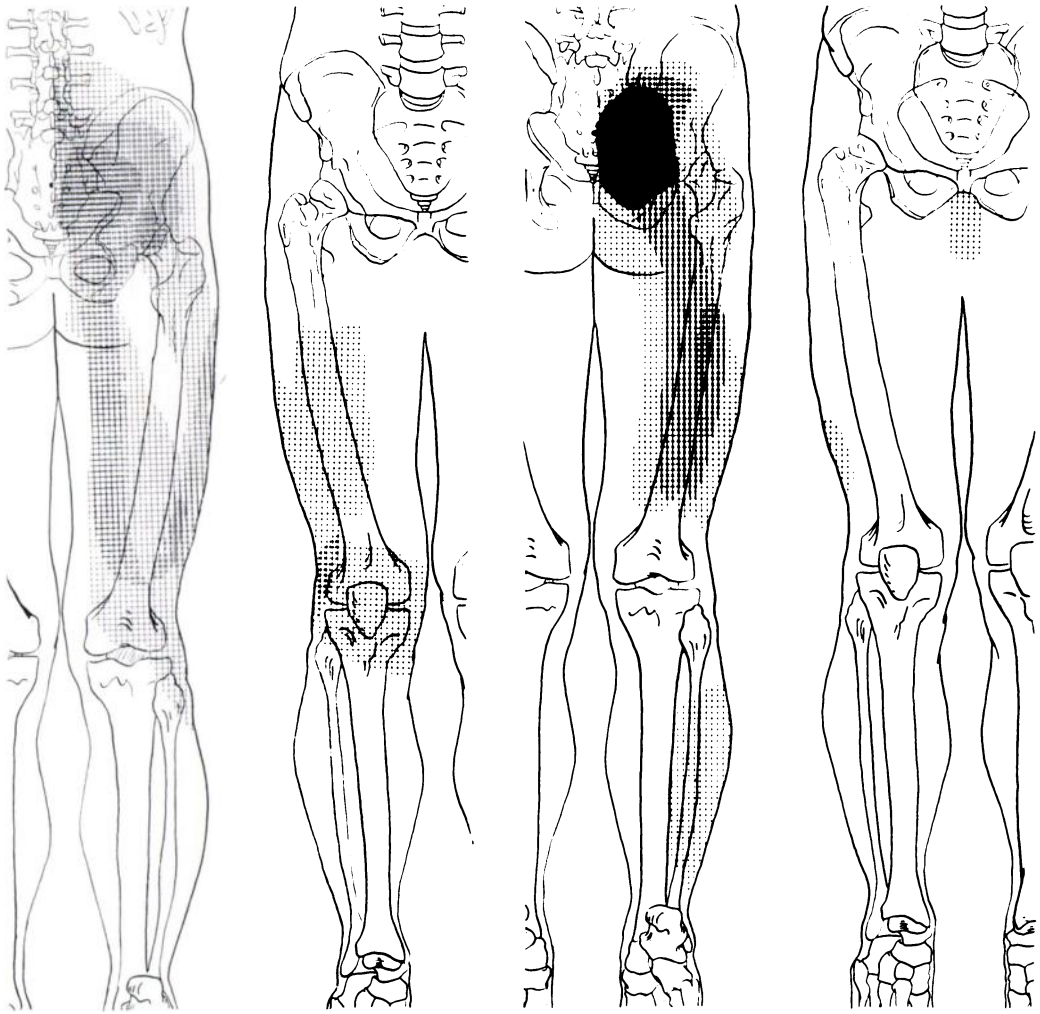

FIG. 4-B

at the eighth cervical segment. Referral to the radial side of the forearm and the hand occurred in none of the subjects. With stimulation of muscle supplied by the thoracic roots, pain was confined to the chest and abdomen, with the exception that stimulation at the twelfth thoracic segment gave referral into the hip region. Stimulation of muscles supplied by the lumbar and sacral nerves produced pain extending fairly uniformly into the buttock and thigh region. Pain from the third lumbar, fifth lumbar, and first sacral levels was referred into the calf of only three subjects. The foot was not a site of referred pain in any of the experiments. The areas of deep pain referral, especially in the extremities, are thus located differently from the conventional dermatomes and are far more overlapping.

3. *Distribution of Pain following Stimulation of Limb Muscles* *

To compare the segmental referral patterns following paravertebral (axial) irritation with those following peripheral irritation, a series of single peripheral muscles, which had given rise to referred pain in the paravertebral series, were injected with 6 per cent. saline solution (Figs. 5-A through 5-F). The muscles were: brachialis (fifth and sixth cervical

* Part of this work was submitted by Marion Cleeves (now Dr. Marion Cleeves Diamond) in partial fulfillment of the requirements for the Master of Arts degree, University of California.

Figs. 5-A through 5-F: After injections of the limb muscles with 6 per cent. saline solution (three or four subjects), deep pain was distributed as shown in the drawings. Cross-hatch areas indicate deep pain, while parallel lines indicate cutaneous hypo-algesia.

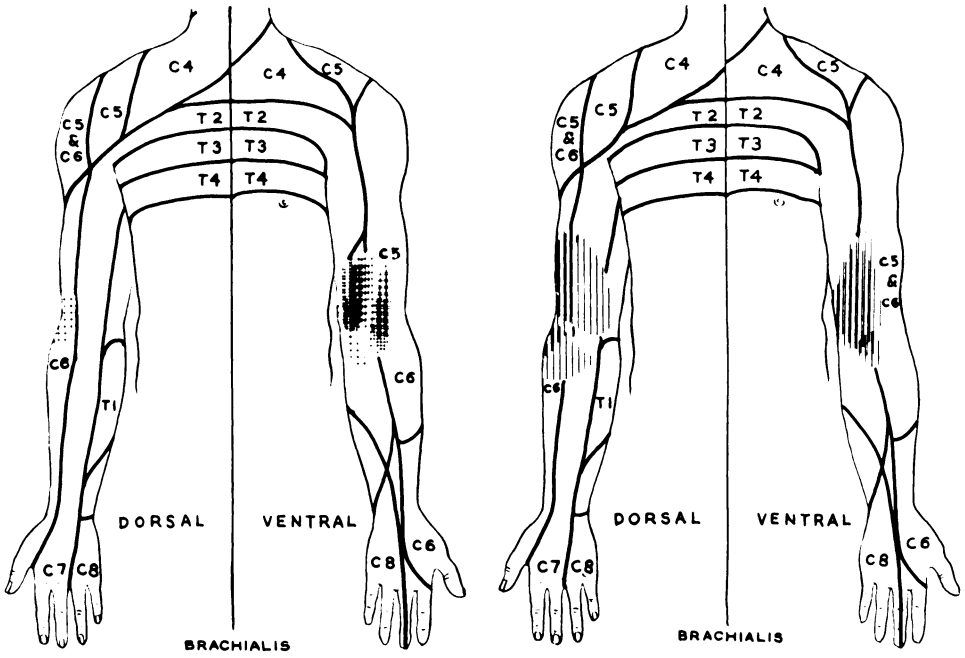

FIG. 5-A

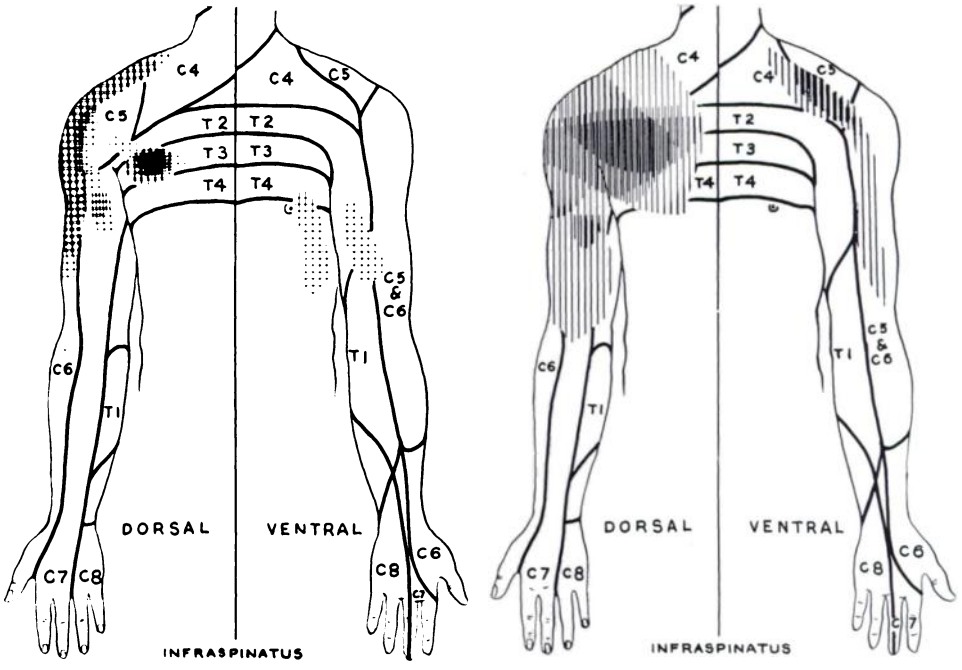

FIG. 5-B

levels), infraspinatus (fifth and sixth cervical levels), extensor digitorum communis (sixth, seventh, and eighth cervical levels), serratus anterior (fifth, sixth, and seventh cervical levels), flexor carpi ulnaris (eighth cervical and first thoracic levels), and pectoralis major (fifth, sixth, seventh, and eighth cervical levels)*. Three or four subjects were used for each muscle.

* Innervations after *Morris' Human Anatomy*. Ed. 11, p. 1152, 1953.

As it was in the series with injections of paravertebral muscle, the deep pain was felt immediately in the vicinity of the injection; and, within a minute, it spread along the muscle fibers. The area of pain, however, was neither confined to the whole muscle nor did it always occupy the whole muscle. Referred pain arose at variable distances from the injection site, and the affected areas were sometimes larger and sometimes smaller than the anatomical outline of the individual injected muscle.

Although it was never referred to the paravertebral muscles, the pain radiation on the whole coincided with the patterns which had been obtained from stimulation of the interspinous tissues of the same levels of innervation. With injections into the serratus

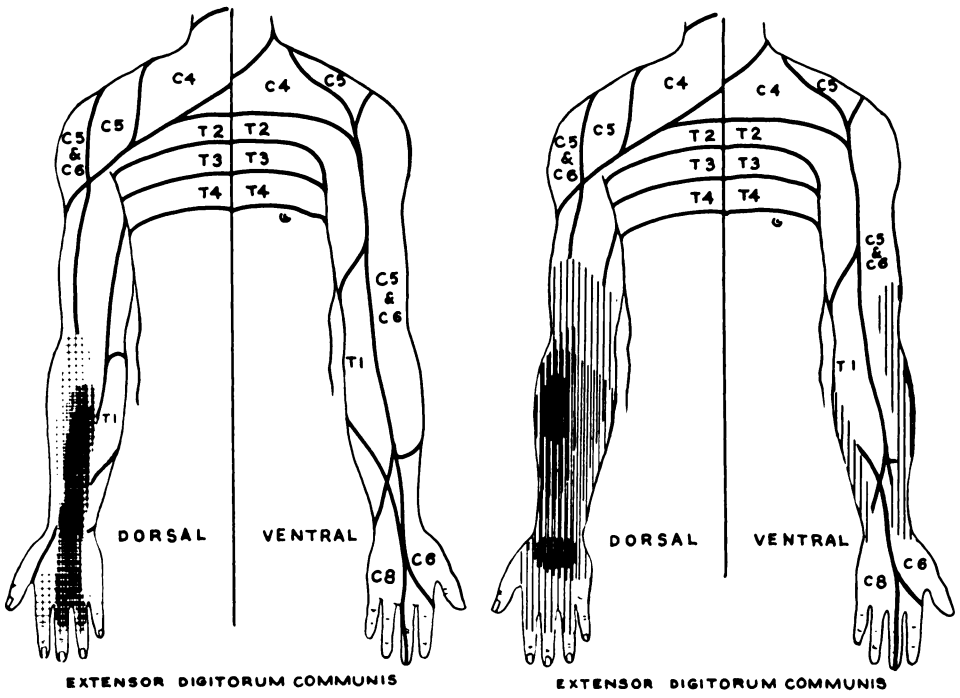

FIG. 5-C

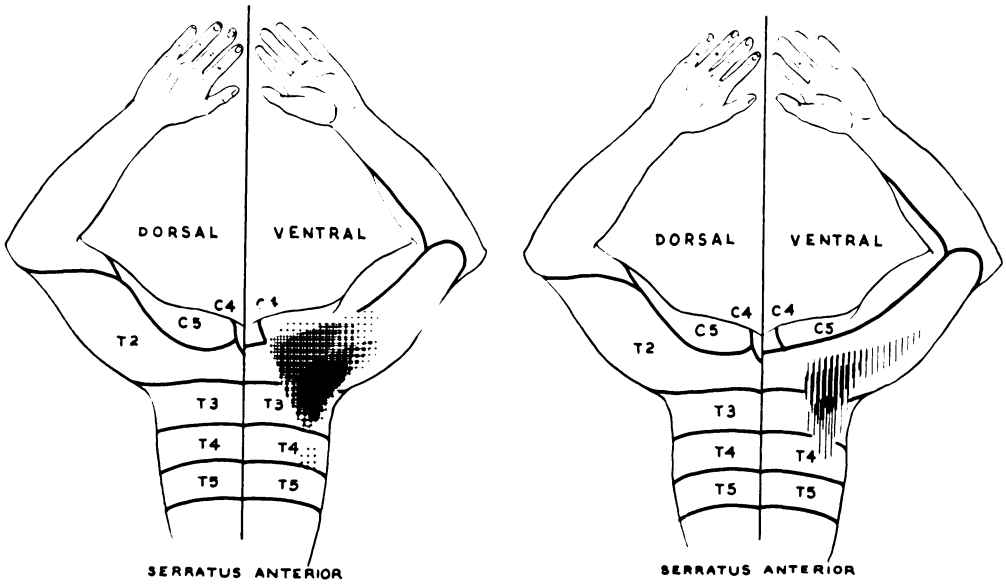

FIG. 5-D

anterior (fifth, sixth, and seventh cervical levels), the pain spread to the contiguous area underlying the second and third thoracic dermatomes, that is, the axilla and its surroundings (Fig. 5-D). On the other hand, there was also evidence that muscles innervated by the same roots of the brachial plexus referred pain to the same area. Thus, when saline solution was injected into the latissimus dorsi (sixth, seventh, and eighth cervical levels), the pain involved the sum of those areas which could be obtained individually from separate injections into the flexor carpi radialis longus (sixth cervical level), abductor pollicis longus (seventh cervical level), and first dorsal interosseus (eighth cervical level).

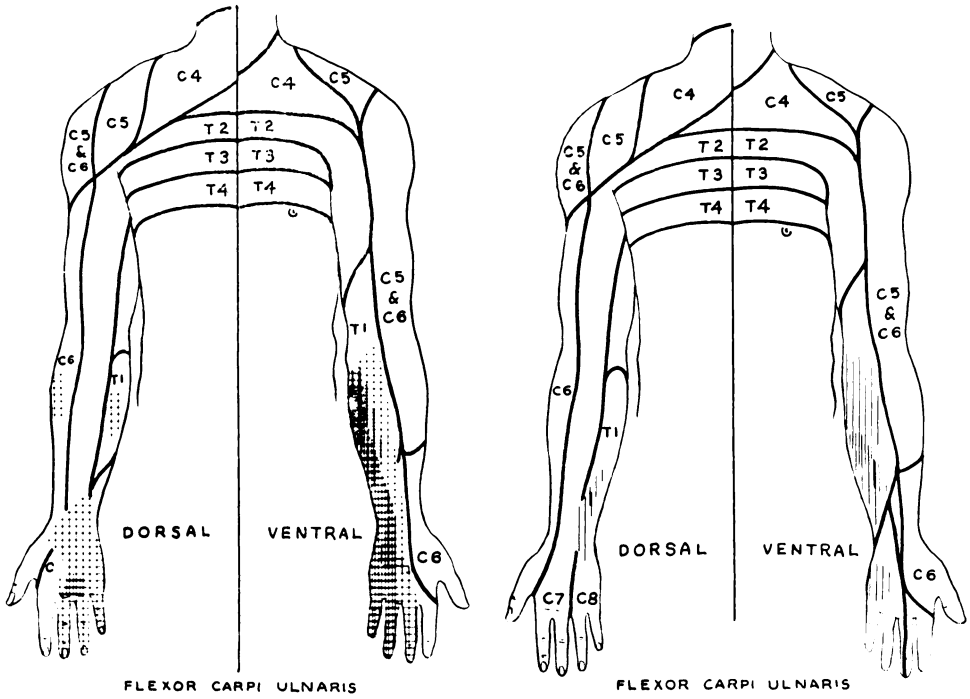

FIG. 5-E

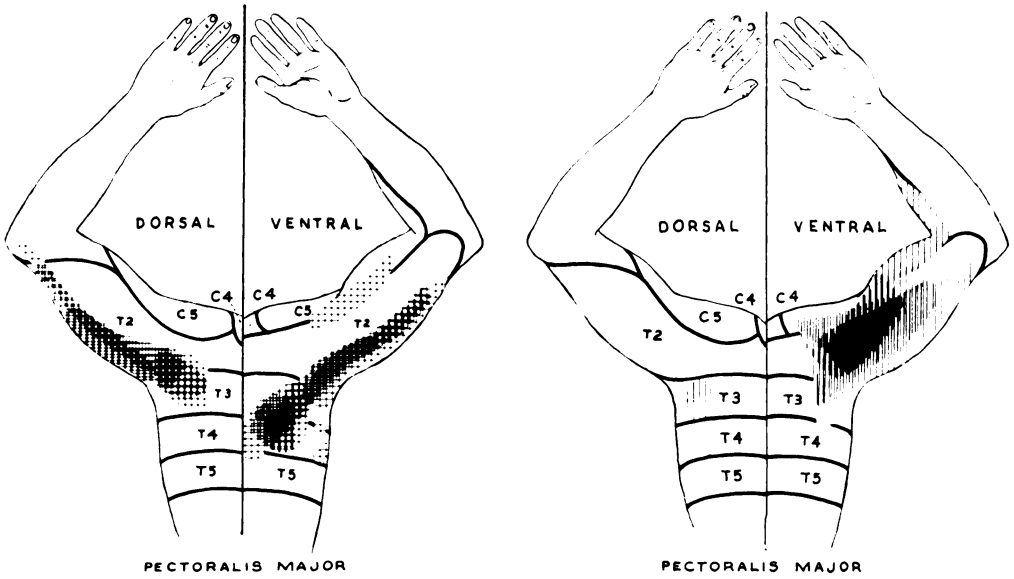

FIG. 5-F

4. *Concomitant Features*

Deep tenderness and muscle spasm: Deep tenderness was present in most cases. This was found uniformly in the regions of radiation, but only variably in isolated areas of referral. Tenderness could be elicited for as long as twenty-two hours following the injection. The area was always smaller than that of referred pain. The greatest discomfort upon deep pressure was felt in muscles which also exhibited spasm. These were often situated at some distance from the point of stimulation. For example, an injection at the level of the sixth cervical segment was fairly consistently accompanied by spasm of the supraspinatus, infraspinatus, or biceps. It will be noted that each of these muscles derives its motor-nerve supply, in part at least, from the sixth cervical segment of the spinal cord.

Alterations of cutaneous sensibility: Hyperalgesia has often been observed to accompany pain arising from visceral and somatic structures [2, 7, 10, 12]. The skin area of increased susceptibility to pricking and pinching is usually reported as lying within the dermatome which corresponds to the cord level of the affected deep tissues. In our own subjects hyperalgesia could not be elicited by pricking or brushing the skin overlying either referred pain, regional deep tenderness, or any other area. On the contrary, pinprick was not felt as clearly over the affected areas as it was in the surrounding regions. Hypo-algesia, therefore, rather than hyperalgesia, was often noted with injections both of interspinous tissues (Fig. 6) and peripheral muscles (Figs. 5-A through 5-F). The hypo-algesia was sufficiently well defined to permit mapping, but its evanescent nature precluded elaborate testing. The region involved was usually concentric, but not necessarily identical, with the area of deep pain, and frequently extended beyond it when limb muscles were injected.

Autonomic concomitants: The pain elicited from muscles was accompanied by a characteristic group of phenomena which indicated involvement of other than segmental somatic mechanisms. These autonomic reactions were most common with injections in the thoracic region, and comparatively rare with injections in the cervical and sacral regions. The manifestations were pallor, sweating, bradycardia, fall in blood pressure, subjective "faintness", and nausea, but vomiting was not observed. Syncope occurred in two early procedures in the series of paravertebral injections and was subsequently avoided by quickly depressing the subject's head or by having him lie down at the first sign of faintness. These features were not proportional to the severity of the pain or to the extent of radiation; on the contrary, they seemed to dominate the experience of subjects who complained of little pain but who were overwhelmed by this distressing complex of symptoms. Most common were pallor and sweating. The sweating was usually generalized; in only a few instances was it confined to the side of the pain.

5. *Referred Pain following Sympathetic Block*

Whether the sympathetic nervous system was responsible for pain referral was tested in one medical student. As a preliminary, the interspace of the sixth and seventh cervical vertebrae was injected three times with 6 per cent. saline solution, and the area of pain referral in the left arm was established in the usual manner. Then the left stellate ganglion was blocked with ten milliliters of 2 per cent. procaine. A Horner's syndrome and vasodilatation on the affected side proved the block to be effective. The segmental injection of 6 per cent. saline solution was now repeated, and the resulting pain was identical with the preliminary pain in intensity and distribution. If anything, it rose more rapidly to its peak than before.

6. *Pain Referred to an Anaesthetic Area*

That referred pain may be evoked in areas previously anaesthetized by regional nerve block was shown in one experiment. By means of a preliminary injection of 0.5 milliliter of 6 per cent. saline solution into and slightly to the left of the interspinous ligament

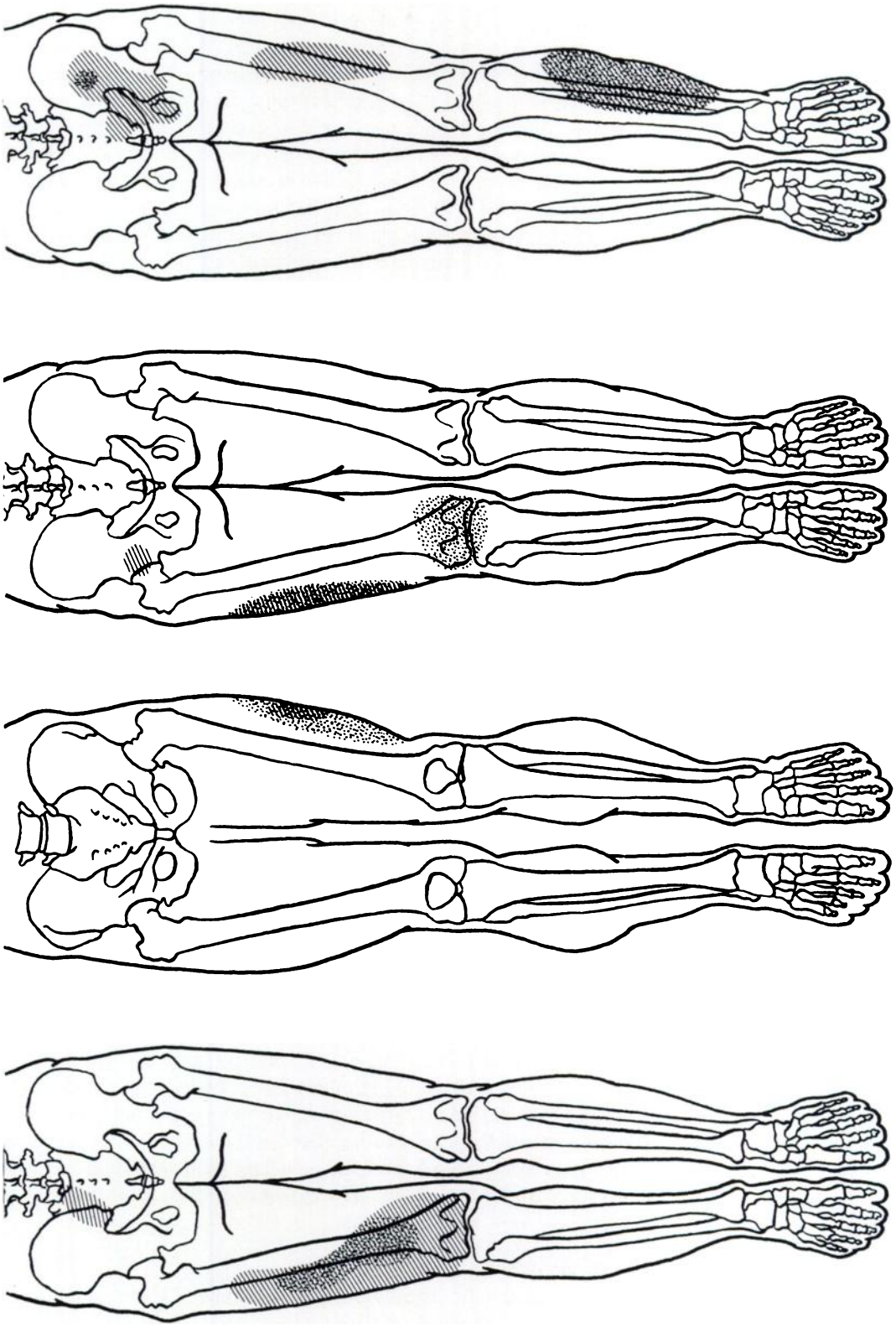

FIG 6

Fig. 6: After intervertebral injections of the first through the third sacral levels with 6 per cent. saline solution (one subject each), deep pain was distributed as shown. Parallel lines indicate areas of deep pain; stippling denotes cutaneous hypo-algesia.

between the spinous processes of the sixth and seventh cervical vertebrae, pain was produced in the ulnar side of the left forearm. Thus, the level of injection for the particular distribution was established in this experimental subject (a medical student). Next, the left brachial plexus was blocked by infiltrating twenty-five milliliters of 2 per cent. procaine. Complete paralysis, with anaesthesia for all modalities including deep pain, was achieved for the entire left upper limb, and a left-sided Horner's syndrome gave proof of effective sympathetic block. Local injections of 0.4 milliliter of 6 per cent. saline solution into the left brachioradialis muscle and into the left thenar eminence failed to induce pain. The sensory and motor paralysis was complete for over thirty minutes.

Early in this period, a second interspinous injection of 0.5 milliliter of 6 per cent. saline solution was given at the identical site of the preliminary injection. Despite the regional anaesthesia of the arm, this second interspinous injection was followed by a dull, aching, deep pain in the ulnar side of the left forearm, only slightly less intense than the pain which had resulted from the preliminary injections in the non-anaesthetized limb.

DISCUSSION

Noxious stimulation of the back muscles at different levels provokes pain in distributions which vary but little from individual to individual. Although the overlap between successive levels exceeds even that seen in dermatomes, the regional patterns suggest a segmental organization. The muscles in which the referred pain is apparently felt all derive their approximate motor-nerve supply, and possibly their sensory-nerve supply, from the segment stimulated by the paravertebral injection. By no means, however, are all the muscles attributed to one segment affected.

Kellgren [4] stated that the pain was "fully segmental in distribution". However, he based his opinion on what appeared to him to be a stimulation of truly segmental structures,—namely, the interspinous ligaments. Sinclair and his associates [10] rightly pointed out the difficulty of selective injections into interspinous ligaments. It is indeed almost certain that paravertebral muscles, rather than ligaments, are being injected, and surface anatomy provides no certain way of verifying the precise segmental representation of these muscles. Kellgren's critics [10] maintained that the saline solution must spread through the tissues and stimulate sensory-nerve "trunks" therein. Whatever their size, sensory nerves or their endings are stimulated, and at each level of injection the afferent impulses enter the spinal cord *via* one, or possibly more than one, posterior division and dorsal root. The number of branches stimulated will be determined by the amount and the diffusion of the injected irritant. The volume injected accounts not only for the intensity of the ensuing pain but also for the extent of its referral. To avoid excessive spread and pain, the amount injected was in our experiments kept within the indicated limits. Whether or not the results obtained should be called truly segmental is, however, an academic question, since sharply delimited segments of sensory organization in the spinal cord are not likely to exist, especially not for deep tissues. The patterns of pain, therefore, may give as good an indication of this organization as one can expect.

Although similar methods of provoking pain were used in Kellgren's investigation and ours, his assessment of segments was based on deep tenderness, whereas our criterion was spontaneous, aching pain. In our experience, areas of tenderness showed no close correspondence to those of aching pain. Detailed comparisons of his patterns of pain with ours cannot, therefore, be made. The discrepancies, such as they are, pertain chiefly to the lower cervical and the sacral segments. Our patterns at these levels differ far more from the conventional dermatomes than Kellgren's do.

It must be emphasized that the spread of pain is felt three-dimensionally, although

only two of these dimensions can be indicated on surface outlines. Thus, in the trunk "areas" the pain may be partly felt within the body cavities and come close to sensations of visceral pain.

While there is a good deal of correspondence between the referred pain of disease and that of these experiments, our findings of associated cutaneous sensory changes differ from other experimental and clinical accounts, especially from the notion of "Head's zones". Hypo-algetic areas of skin, concentric with areas of deep pain, have to our knowledge not been reported except in the tables recently produced by Steinbrocker and his associates and in an article by Sturge, published seventy years ago. The latter author commented on the "numbness" and "heaviness" of the left arm during attacks of anginal pain. Yet the experience is a common accompaniment of any deep ache. In our subjects the hypo-algetic zones followed no clear-cut dermatomal patterns; their relation to the hitherto known segmental innervation of muscle, on the one hand, and that of the skin, on the other, remains somewhat obscure.

The discrepancy between our findings of hypo-algesia and the hyperalgesia almost uniformly reported in the literature is hard to explain. It is possible, however, that the observers' expectation, as well as semantics, may be responsible in so far as the term "numbness" is concerned. In nerve lesions producing both pain and numbness, cutaneous hypo-aesthesia and hyperalgesia of the same area are common. It is often difficult for the untrained patient to make this nice distinction. The over-all experience of unpleasantness may mask the actual reduction of sensory acuity. Nevertheless, it was the intensity of pinprick which our subjects unanimously declared to be reduced in the areas in question.

Regarding the injections of peripheral muscles, we cannot conclude with certainty that more than part of the "full segment" was as a rule activated, a point also made by Travell and Bigelow and by Steinbrocker and his associates.

After brachial plexus block, referred pain in the anaesthetic area was readily evoked by the appropriate axial injection. Thus, there is little reason to believe that peripheral-nerve function, including the axon reflex [11], played any part in this kind of referred pain. The central segmental organization, when adequately stimulated at the spinal level, is fully able to produce and to account for the projection of deep pain to the periphery. In other words, such stimulation is capable of lighting up the relevant area of the body scheme. Sympathetic denervation does not block this mechanism.

The interspinous injections showed that, with an approximately segmental referral of pain, multiple concomitants may be observed which are referable to disturbances within and beyond the various sectors of segmental organization. In the cutaneous sensory system we found hypo-algesia; in the motor system, muscle spasm; in the autonomic system, a wide range of cardiovascular, sudomotor, and gastro-intestinal effects. We are led to endorse Ruch's convergence-projection theory of referred pain and to regard this disturbance as a "central" phenomenon which consists of the setting up of an excitation at the spinal segmental level in the first place. With increasing intensity the excitation spreads beyond the spinal segment to result in a wider referral of pain and in autonomic and emotional disturbance.

SUMMARY

The patterns of deep somatic pain referral were studied with paravertebral injections of 6 per cent. saline solution from the occiput to the sacrum, five subjects being used for each intervertebral level. The distributions were found to approximate a segmental plan, although they overlapped considerably and differed in location from the conventional dermatomes. Pain could not be induced in the radial aspect of the upper limbs and in the feet. Injections into individual peripheral limb muscles showed less regularity in suggesting segmental patterns. As opposed to the hyperalgesia of "Head's zones", areas of hypo-algesia, usually in a concentric manner, were found to overlie the locations of in-

duced deep pain. Sympathetic and somatic (plexus) blocks did not interfere with the segmental referred pain produced by this method, thus suggesting a primarily spinal integrative mechanism. The character of the pain and its autonomic concomitants are described, and the theoretical implications are discussed.

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