MEASUREMENT OF PAIN THRESHOLD AND SUPERFICIAL HYPERALGESIA IN DISEASES OF THE SKIN*

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Clinicians have long noted that in the presence of certain dermatoses the sensitivity of the skin is altered. Qualitative estimations of these changes in sensation have been made through the use of various methods of thermal and tactile stimulation. However, not until recently has it been possible to investigate quantitatively the effect on sensation of various dermatoses.

Ollendorff (1) made a systematic study of the sensibility of the skin of patients with syphilis and other pathologic conditions. In testing normal and abnormal areas of skin she used such methods as stroking with a hair, pin prick, pressure with a probe, and heat. She found that in patients with inflammatory and infiltrative diseases and in the papules of secondary syphilis the sensitivity of the skin was increased. The hyperalgesia demonstrated in the papules of secondary syphilis was so constant and characteristic that she advocated it as a diagnostic measure. Mayr's (2) study of 311 patients with syphilis, in which he used a water manometer to exert pressure on the lesions, showed that the florid secondary eruptions were more sensitive than normal skin.

Since the introduction of the thermal radiation method of measuring pain thresholds on the skin, by Hardy et al (3), studies of pain thresholds on normal skin have been numerous. Schumacher et al (4) studied a group of 200 subjects of both sexes between the ages of ten and eighty and reported an average pain threshold of 220 millicalories per second per square centimeter, with a standard deviation of ± 7 mc/sec/cm^2. The series of 200 subjects studied by Chapman and Jones (5) were found to have much higher and more variable pain thresholds, although their more recent publications describe results more in keeping with those of Schumacher (4). Pfeiffer (6) measured the pain threshold on the pad of the fingertip and on the nail. By blocking the stellate ganglion he separated superficial pain into what he terms "sympain" and "supain", the former being deep pain and the latter bright, burning pain. Bigelow, Wolff and Goodell (7) demonstrated two pain thresholds on the hand following anoxia of thirty-five minutes duration. As one of the pains was elicited a few seconds after the other they suggested that the noxious impulses were mediated by slow and fast fibers (8). A recent study by Bishop (9) of the pain endings in the skin indicates that increasingly intense stimuli applied to one "sensory spot" will give rise to touch, itch and pain. He attributes the difference in the qualities of the sensations to

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the effect of increasing stimuli on a single nerve ending. A summary of the information on pain arising from the skin can be found in the recent review of the subject by Wolff and Hardy (10).

In spite of these extensive investigations little is known of the mechanisms in the skin which give rise to pain or to itch. Rothman (11) considers itching an altered pain sensation. Bishop (12), on the other hand, considers itch to be a different sensation. In view of the importance of the skin as a test organ for pain sensitivity, and with the hope of throwing some light on the types of paresthesia encountered in dermatoses, the following investigation was undertaken. It was specifically desired to determine first, whether or not the pain threshold is altered in skin areas affected by various types of skin lesions, and second, to investigate the degree of hyperalgesia existing in areas of pathological skin.

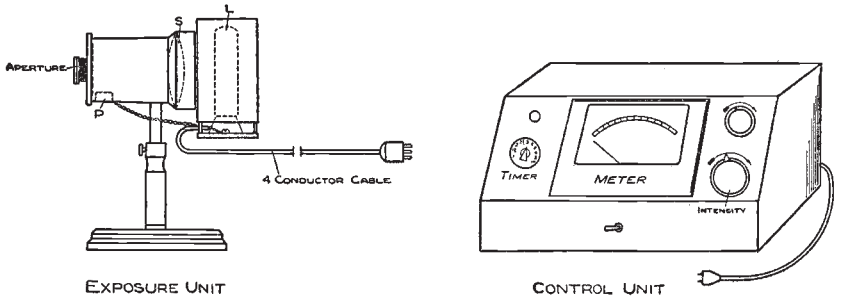

FIG. 1. Pain Threshold Apparatus. P—electronic shutter set at 3 seconds; S—short focus lens; L—500 watt lamp. Control unit contains intensity controls, a meter for reading stimulus intensity, and exposure switches.

METHOD

Figure 1 shows a diagram of the Hardy-Wolff-Goodell Pain Threshold Apparatus used in these experiments. The thermal stimulus is a 500 watt incandescent lamp, the rays of which are focussed onto the area of skin to be tested. The test areas are blackened with India ink to insure complete absorption of radiation and to prevent effects due to penetration of the rays below the skin surface, thus keeping the stimulus a purely thermal one. The radiation is allowed to fall on the skin for three seconds and at the end of the exposure the patient reported the sensation experienced.

In these experiments the patients received no prior instruction regarding the test and the following method was found to be the simplest of those which were devised for use with the clinic patient. However, even this procedure was not effective with patients who could not speak and understand English, and there were a few patients who were unable to cooperate because they could not understand the directions regarding the test in the time that could be allotted.

The patient was first given a stimulus well below the pain threshold (about 150 millicalories) on the normal skin. The patient was asked what he felt and in all cases this was either a feeling of warmth or no sensation at all. A second stimulus of an intensity of about 250 millicarlories was given about sixty seconds later,

in the same area, and the patient asked to focus his attention on a sharp prick which would occur at the end of the exposure. In most cases there was no difficulty in recognizing this change in the sensation. The patient was then instructed to report on subsequent stimuli simply as to whether or not this prick could be felt at all. Beginning with a stimulus below the threshold and gradually increasing the intensity it was usually possible to determine the pain threshold with the use of not more than five stimuli. It was important not to overstimulate the test area, particularly that within a lesion, and to give the patient rest and reassurance between tests. Maintaining the cooperation of the patient was of the utmost importance in obtaining reproducible results. Following the above procedure patients had little difficulty in recognizing the pain threshold, a finding in keeping with the results of past studies using this method (3, 4). Usually a single pain threshold measurement was made on the normal skin of each clinic patient, but this measurement was checked if there were doubts as to its accuracy and duplicate measurements were always made on those patients whose thresholds were outside the normal range. Clinic time did not permit more extensive examination of the normal skin of patients.

The intensity of the stimulus was read from a meter calibrated by means of a standardized radiometer, and recorded in absolute units of millicalories per second per square centimeter of heat absorbed on the skin surface. Precautions were taken by frequently checking the calibration of the meter to insure reproducibility as regards the stimulus.

Sixty-five patients with pruritic and non-pruritic skin disorders were studied. They were of both sexes and ranged in age from thirteen to seventy-five years. Observations were made before treatment was instituted or when medication had been discontinued for twenty-four hours prior to testing.

Two types of observations were made.

Series I. Pain thresholds

Pain threshold measurements were made on all patients. These determinations were made on an area of affected skin and on a contralateral or adjacent normal area. Subjects with diseases in which itching was a factor were asked to report on the effect of the radiation on itching.

Series II

While some patients showed a lowered pain threshold associated with hyperalgesia on the diseased skin, in others the pain threshold was unchanged. For this reason a second series of observations was carried out. This series comprised thirty-eight patients representing eighteen dermatoses. Measurements were made to determine the sensitivity of the skin to stimuli above the pain threshold using the method recently introduced by Hardy, Wolff and Goodell (15, 16). These authors introduced the concept of a scale of painfulness against which experimental and spontaneously occurring pains can be compared. The basis of this scale is the fact that there are twenty-one just noticeable differences in pain sensation between the threshold pain and the ceiling pain or maximum per-

ceivable pain. The unit of painfulness is taken to be equivalent to two just noticeable differences and is called the "Dol". In these experiments a stimulus evoking a four *dol* pain (pain of moderate intensity) was applied to an area of normal skin. A series of stimuli were then applied to the affected skin and the patient asked to compare the intensity of these pains with the four dol pain evoked on the normal skin. The measurement was completed when the patient reported a test pain to be the same intensity as the four *dol* pain. The test pains were produced at intervals of about twenty seconds and the standard pain was repeated only after an approximate balance had been reached in order that the patient might be able to make a finer comparison. It was not always necessary to repeat the standard pain as the patients had little difficulty in remembering

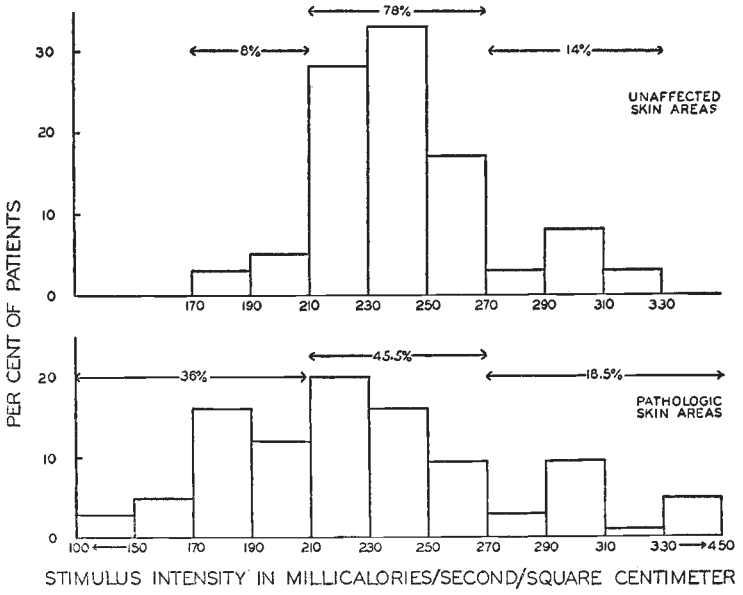

FIG. 2. Distribution of pain threshold measurements for 65 patients. a) (Upper diagram) Unaffected skin areas. b) (Lower diagram) Pathologic skin areas.

the intensity of this pain for a few minutes and could make reproducible comparisons. It is important in using stimuli above the pain threshold to be sure that a minimal number of exposures be made on one area so as to avoid irritation which would interfere with accurate perception.

RESULTS

Series I. Pain thresholds

The upper part of Figure 2 shows the results of measurement of the pain threshold on the normal skin of sixty-five patients. Sixty-one per cent of the patients fall within the normal range (210–250 mc/sec/cm^2) of pain thresholds described by Hardy, Wolff and Goodell (3) for trained subjects. Eight per cent had lower pain thresholds, and thirty-one per cent had higher pain thresholds.

The average for the group was 235 mc/sec/cm^2, the extreme range being from twenty-eight per cent lower to forty per cent higher. The variation of the pain threshold measurements in this group of clinic patients is higher than that observed on medical students and on trained observers as previously reported (16) but less than that reported by Chapman and Jones (5). It is believed that the measurements herein reported are typical of those that can be expected of clinic patients among whom will be encountered those with language difficulties and difficulty in understanding the purpose of the test. Based on these considerations, the range of stimuli from 210 to 270 mc/sec/cm^2 is considered a normal range of pain thresholds for studies of patients. The distribution is not symmetrical about the mean, there being more patients with higher thresholds. This may be attributed in part to the effect of the dermatosis upon skin which is apparently unaffected. It is well known that leprosy is characterized by anesthesia in the skin, and the one patient with leprosy in this series had a pain threshold in the highest range. Furthermore, the presence of pain elsewhere in the body is known to raise the pain threshold (3), and the sensitivity of the skin over the body surface is probably not uniform. This latter topic is now under investigation.

In the lower part of Figure 2 is shown the measurements of pain threshold on the skin lesions of the sixty-five patients. There is a considerably wider distribution, ranging from 100 to 450 millicalories. Forty-five per cent had pain thresholds between 210 and 270 mc/sec/cm^2 in areas of pathological skin, as compared with seventy-eight per cent on unaffected skin. Thirty-six per cent showed definite hyperalgesia as compared to eight per cent on the unaffected skin. Eighteen per cent showed hypalgesia, a number not significantly different from that obtained on unaffected skin.

In comparing the pain threshold measurements on the unaffected and pathological skin areas, the principle differences are the wider spread in threshold values and the tendency for increased hyperalgesia in pathological areas. For purposes of analysis the group was divided into those patients with active pruritus and those with nonpruritic lesions. Table 1 shows the results of threshold measurements of patients with pruritus. Fourteen disease entities were studied in a total of forty-one patients. Thirty-two per cent of these patients showed a hyperalgesia as well as pruritus. Sixty-eight per cent showed unchanged or raised pain thresholds. Table 2 contains the data obtained on twenty-four patients with nonpruritic lesions representing sixteen disease entities. Twenty-five per cent of these patients showed a lowered pain threshold and twenty-one per cent a raised pain threshold. The majority of patients in either group, sixty-one per cent of those with pruritus and fifty-four per cent of those with nonpruritic lesions, had thresholds within the range of 210 to 270 mc/sec/cm^2.

Series II. Pain sensitivity

The possibility of changes in skin sensitivity not related to changes in pain threshold which was pointed out some years ago (13, 17) was investigated in thirty-six patients. Fifty per cent of these showed a lowered pain threshold and

TABLE I

Change in pain threshold on pathological areas of patients with pruritic lesions at the time of study

NUMBER	DIAGNOSIS	PAIN THRESHOLD		
		Raised	Unchanged	Lowered
7	Contact dermatitis		5	2
4	Atopic eczema		1	3
2	Eczematoid dermatitis			2
1	Psoriasis			1
4	Urticaria		3	1
2	Nummular eczema		1	1
11	Neurodermatitis	2	7	2
2	Seborrheic dermatitis		2	
3	Herpes zoster	1	1	1
1	Post-herpetic neuralgia		1	
1	Drug eruption		1	
1	Pruritus		1	
1	Static eczema		1	
1	Pityriasis rosea		1	
		3	25	13
		7%	61%	32%

TABLE II

Change in pain threshold on pathological areas of patients with nonpruritic lesions at the time of study

NUMBER	DIAGNOSIS	PAIN THRESHOLD		
		Raised	Unchanged	Lowered
3	Contact dermatitis	2		1
2	Atopic eczema		2	
1	Eczematoid dermatitis	1		
1	Necrobiosis	1		
3	Psoriasis		2	1
1	Urticaria			1
1	Epidermolysis bullosa		1	
1	Nummular eczema			1
2	Neurodermatitis		2	
3	Herpes zoster		3	
1	Ultraviolet exposure		1	
1	Pityriasis rosea		1	
1	Erythema nodosum			1
1	Sarcoid of Boeck		1	
1	Lepromatous leprosy	1		
1	Secondary syphilis			1
		5	13	6
		21%	54%	25%

an increased sensitivity of an amount comparable to the lowered pain threshold. Nine patients showed no change in pain threshold and correspondingly no change in sensitivity. However, three patients of the pruritic group showed increased sensitivity but no lowering of pain threshold and six patients (four nonpruritic and two pruritic) showed a decrease in sensitivity with unchanged pain threshold.

COMMENT

1. Comparison of pain threshold measurements on pathologic and unaffected skin

Figure 1 shows that fifty-seven per cent of all patients studied had the same pain threshold on affected and unaffected skin. Twenty-nine per cent had lowered and fourteen per cent had raised pain thresholds in the areas of the skin lesions. From these data we conclude that:

a) Tissue damage itself is not a sufficient cause for altered pain threshold. Thickened skin and trophic changes may cause a raised pain threshold (14%) or combine their effects with other skin changes to produce a normal threshold.

b) Lowered pain threshold in the skin lesion is the result of a particular type of tissue damage which keeps the superficial pain endings in a state of hyperexcitability. The nature of this excitability is unknown, but in the cases studied was not due to excoriation of the skin.

c) The small number of patients with raised pain thresholds indicates that skin thickening and atrophy were not common in the diseased skin areas.

2. Relationship of pruritus to pain threshold

It was originally a purpose of this study to establish the relationship between pain sensitivity and itching, and, therefore, the patients have been separated into two groups: those with active pruritus, (Table 1); and patients with no itching at the time of examination (Table 2).

In the group with pruritus sixty-one per cent had unchanged pain thresholds in the pathologic area; thirty-two per cent had lowered and seven per cent raised pain thresholds. Also, the test procedure either initiated or increased the itching in only twenty-two per cent of the patients and had no effect on seventy-eight per cent. We conclude from this:

a) There is no correlation between pruritus and lowered pain threshold or increased sensitivity. This finding although at first surprising is, we believe, in keeping with common experience. Scratching is generally pleasant only on skin that is not hyperalgesic. Also, although the sensations of itch and pricking pain are almost identical in quality, scratching will cause relief in the first instance and increased pain in the second.

b) Itching and superficial pain are not interdependent sensory entities, and although hyperalgesia and itching may occur together they result from different causes.

The group with non-pruritic lesions is characterized by a greater percentage of patients with raised pain thresholds. Although this may be due to atrophy of the pain endings or to skin thickening, it was not possible from clinical examination to specify the cause.

3. Relationship of pain threshold to skin sensitivity

Sensitivity comparisons were made on the unaffected and pathologic skin areas of thirty-six patients. Of these

15 patients had lowered pain threshold and increased sensitivity
3 patients had raised pain threshold and decreased sensitivity
9 patients had unchanged pain threshold and unchanged sensitivity

—

27 patients or seventy-five per cent of the group.

The above changes are those to be expected if the skin is the effective organ in producing the changes in pain sensation. However,

3 patients had unchanged pain threshold and increased sensitivity
6 patients had unchanged pain threshold and decreased sensitivity

—

9 patients or twenty-five per cent of the group.

As there was no demonstrable technical difficulty involved in these measurements it is not proper to dismiss them as accidents or errors. It is believed that the conducting pathways of the pain impulses play an important role in modifying the sensation evoked by stimulation at the periphery. Therefore, these results are interpreted as follows:

a) Normal peripheral endings plus an excitatory state in the path of the noxious impulses from the skin to the sensory cortex may account for the three patients with unchanged pain threshold and increased pain sensitivity. Thus, any impulses passing from the periphery would be facilitated and the pain sensation perceived as more intense.

b) A normal peripheral apparatus combined with a depressed functional state in the nerve pathways can account for the six patients with unchanged pain thresholds and decreased sensitivity above the threshold.

SUMMARY

Using a three-second exposure to intense thermal radiation as the painful stimulus, pain thresholds were measured on the unaffected and pathologic skin of sixty-five dermatologic patients. The patients ranged in age from thirteen to seventy-five years and were of both sexes. Eighteen disease entities were encountered, including pruritic and non-pruritic lesions. Tests of sensitiveness to painful stimuli above the pain threshold were made by exposing the unaffected skin to a stimulus causing a four *dol* pain and measuring the amount of stimulus required to evoke pain of the same intensity from the pathologic skin. Results are as follows:

1. Pain thresholds on unaffected skin averaged 235 mc/sec/cm^2, with extreme values of 170 and 330 mc/sec/cm^2.

2. Fifty-seven per cent of all patients had the same pain threshold on affected and unaffected skin; twenty-nine per cent had lowered and fourteen per cent had raised pain thresholds in areas of skin lesions.

3. In the patients with active pruritus sixty-one per cent had the same thresholds in unaffected and pathologic skin areas; thirty-two per cent had lowered and

seven per cent had raised pain thresholds as compared with unaffected skin. In twenty-two per cent of these patients the experimental procedure initiated or increased itching, in seventy-eight per cent there was no effect.

4. Comparisons of pain thresholds and pain sensitivity on unaffected with that on pathologic skin showed parallel changes in pain thresholds and sensitivity in seventy-five per cent on patients; twenty-five per cent had changes in sensitivity but no change in pain threshold.

CONCLUSIONS

1. Tissue damage resulting from dermatoses is an infrequent cause for altered pain threshold, and lowered pain threshold in the area of skin lesion is the result of a particular type of tissue injury which is capable of maintaining a state of hyperexcitability in the superficial pain endings. The nature of the local excitatory state is not understood.

2. There is no correlation between itching and altered pain thresholds; itching and superficial pain are not interdependent sensory entities and result from different causes.

3. Changes in sensitivity to painful stimuli in areas of skin damage generally parallel observed changes in pain threshold. In a small number of cases, sensitivity changes are dependent upon neurological factors of excitability or depression in the nervous pathways and not to local effects in the skin.

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Discussion by Dr. Helen Ollendorff Curth: Dr. Potelunas and Dr. Hardy should be congratulated on having used a precise method for determining the pain threshold in cutaneous diseases. They have, for this purpose, used on affected skin a method which was originally devised for normal skin. It consists of evoking pain through heat.

Have the authors determined the sensibility to temperature of the affected skin as a separate and preliminary study? I am asking this question because years ago at Jadassohns dermatological clinic in Breslau I tested the various dermatoses for disturbances of sensibility. 205 patients were examined and notes of Jadassohn on 305 of his patients were used for the study. My methods for determining sensibility to pain were rather primitive and consisted of needle-pricks and pressure with a blunt probe. Independently, sensibility to temperature was tested with water-filled test-tubes. I found that disturbances of sensibility to pain and temperature did not always go parallel; there even were differences between the disturbances of sensation to hot and cold temperatures. Hardy, Wolff and Goodell also found that certain conditions, i.e. doses of acetylsalicylic acid lowered the heat and raised the pain threshold. In my series herpes zoster as well as chronic eczema—there was no nummular eczema known at that time—showed lowered sensibility to temperature and increased sensibility to pain. This may be the explanation for the authors' findings of unchanged pain threshold in the presence of hyperalgesia or hypesthesia in the same dermatoses, a fact which suggests to them the possibility of central involvement. I believed from my tests that no conclusions as to the involvement of the nervous system could be drawn. The most practical result of my study was the constant finding of hyperalgesia of infiltrated lesions, which in the case of the hypersensitivity of papular syphilids to pressure with a probe proved to be of differential-diagnostic value.

Closing Discussion by Dr. Potelunas: I wish to thank Dr. Curth for her kind discussion of this paper. In answer to her question concerning the effect of heat on various dermatoses I can only say that we did not measure the heat threshold but the pain threshold of the affected skin. The patients reported on the minimal sensation of pain produced by the measurable stimulus. Hardy, et al, have shown in studies on the effect of aspirin on the pain threshold of normal skin that aspirin produces hypalgesia but lowers the heat threshold. (Reference: Hardy, J. D., Wolff, H. G. and Goodell, H: Studies on pain: A new method for measuring pain threshold: Observation on spatial summation of pain. J. Clin. Invest. **19:** 649, 1940).