APPENDIX I.

## Introductory Review of Literature on the Nature of Pain.

The long history of scientific investigation of pain has revolved around the question of whether it may be established as a separate sense modality, mediated through nerve structures separate from those which mediate other sensations such as touch, pressure, heat and cold. The viewpoint that pain may be so established has been represented historically by Von Frey. It has been traditionally opposed by Goldscheider, who looked upon pain as a non-specific sense, which could be mediated through tactile nerves from intensive summation of their excitations. In more recent research, considerable evidence has been accumulated against a simple, non-specific, peripheral intensity theory such as Goldscheider's. Nevertheless, the position of pain as an independent sense still remains controversial, though increasing evidence has been forthcoming that the concept of pain as a specific modality has been fruitful, although not necessarily final. The evidence marshalled in support of this specific theory of pain and against all forms of non-specific theories has been frequently summarized (9, 25, 30), and may be briefly outlined in the following paragraphs.

Very early, the experiments of Blix (4) and Goldscheider (14), expanded by Von Frey (11), called attention to the punctate nature of distribution of cutaneous sensation. Von

Frey, in particular, reported the existence of minute areas from which pain of a bright, pricking quality, alone could be aroused. Later, Woolard, Weddell and Harpman (32) were able to stain and identify distinctive nerve terminals in the human skin from such a spot, where only pain was appreciated.

Further evidence has pointed to the fact that nerve blocks due to drugs, asphyxia or disease, have shown a differential effect upon pain as distinct from other sensations. Thus, Clark, Hughes and Gasser (7) were able to demonstrate that pain, alone, prevails when cocaine had anesthetized nerves to the point where C class fibres, alone, were functioning. Examples are also available (24), in which spinal cord lesions have shown a dissociation between pain and other sensations. This independence of pain from temperature and touch has been reported by Stookey (25), after surgical transection of spinothalamic pathways.

Hardy and Wolff (29) with their coworkers have reported extensively on the action of certain analgesic drugs. They found that many of these drugs could specifically raise the threshold for pain while they lowered, or left untouched, the threshold for the perception of touch, hearing, smell, two-point discrimination and vibration.

Some evidence of the separation of pure pain receptors from pressure receptors is given by Neff and Dallenbach (20), who found clear differences in the chronaxies for pressure and pain. Moreover, it has been shown by Adrian, Cattell

and Hoagland (2) and by Cattell and Hoagland (6) , that intensive stimulation of areas sensitive to pressure and touch, up to the limit of the corresponding nerve fibres to conduct, never arouses pain. These experiments have often been cited as fatal to Goldscheider's viewpoint.

In spite of this impressive evidence, a specific theory of pain still encounters many difficulties which have been presented by Nafe (18), Hebb (15) and others. Many questions still appear to be unanswered. First, the problem of specific pain receptors has given difficulty. Ever since Von Frey, free nerve endings have appeared to be the only possible receptors. They are the only terminations sufficiently widely distributed to account for the pain sensitivity of skin, muscle and viscera. They are found in pain-sensitive areas such as the cornea and have been repeatedly associated with pain in the histological studies of Weddell (27, 28). However, Erlanger and Gasser (10) have also indicated that free nerve endings must be capable of mediating pressure. Thus, it would appear that both pressure and pain could be aroused through stimulation of free nerve endings. This gives some difficulty to a specific receptor theory of pain, though it may be supposed that specifically functioning receptors do not necessarily look different - at least to our present histological methods.

This failure to clearly identify the pain receptors is a direct reflection of the ignorance which exists concerning the fundamental nature of the algesic stimulus. Several

kinds of stimuli of an electrical, mechanical, thermal or chemical nature are adequate to elicit pain. Goetzl, Burrill and Ivy (13) have reviewed algesimetric methods and have noted many improvements which have been made recently in securing adequately controllable, satisfactory stimuli for pain. None of these methods, however, has given any information about the nature of the stimulus for pain. Such ignorance of the nature of the algesic stimulus is, as Boring (5) says, "Consistent with the equivocal status of pain as an independent sense". It is, in many ways, the direct basis for the peripheral intensity theory (even broader than that of Goldscheider) which regards pain as due to intense stimulation of any modality. This view of pain is still occasionally expressed although, as Stone and Jenkins (25) have pointed out, negative evidence against such a theory continues to accumulate. Nevertheless, the lack of knowledge of the nature of the adequate stimulus for pain has been particularly damaging to specific theories and has made them vulnerable to such alternate formulations.

A second incompleteness in the sensory modality concept of pain has been the failure to establish the peripheral pathways and higher centres. Surgical section of spinal tracts does not clearly abolish pain permanently, and no specialized cortical areas or pain nuclei in the diencephalon or lower brain stem have been demonstrated.

A third difficulty has been raised by experiments of

Heinbecker, Bishop and O'Leary (16). They have shown that application of single, mild, electric shocks to the skin or cutaneous nerves elicits a pressure sensation. When these shocks are increased somewhat in intensity and applied briefly, but repeatedly, the resultant sensation is described as prick. Pain that is definitely unpleasant, pervasive, demanding avoidance, does not appear until the shocks are raised again in intensity and repeated for some time. These observations Heinbecker, Bishop and O'Leary took to indicate that painful experience resulted from central summation and could not be due to stimulation of a specific receptor. To answer this and similar objections, specific theories have often posited that threshold pain need not necessarily be unpleasant. The concept is formed of a sort of non-painful pain.

This last difficulty brings up a problem which has long confused the issue - the problem of the general "quale" or feeling state of pain, which is so characteristic, so insistent and unpleasant. The specific theorists in the attempt to establish pain as a separate modality, with all the distinctive criteria of a sensory modality, have been forced to separate their concept of pain more and more from the concept of pain in common human experience. This process undoubtedly cleared the air, so that further research of great value was possible. Yet it is possible to go too far in this direction, and to relegate to the unworkable a much broader

concept of pain, which lies closer to the main problems involved. One example of this narrowing of the concept of pain is furnished by Wolff and Wolf (31) who make a sharp distinction between the "perception of pain" and the "reactio fo pain". The "perception of pain" becomes the awarness of certain distinct qualities of direct experience which are frequently described as (1) a clear, bright, pricking pain, (2) a slow, burning, diffuse pain and (3) a deeper-feeling, aching pain. The threshold for this "perception of pain" is then measured by noting the intensity of radiant heat stimulation which will first produce a clear, sharp, sticking sensation, distinct from the surrounding heat. Essentially this is what Wolff and other adherents of a specificity theory have meant by pain.

The "reaction to pain", however, becomes something much broader and in many ways closer to the more common view of pain. Wolff and Wolf (31) say: "Included in the category of reaction to pain are not only disagreeable feelings, vocal and facial expressions of displeasure and alterations in sweating in the skin, but also, for example, the elevation of blood pressure which Hines and Brown utilized in their "cold pressor" test. Tachycardia and tapping of the feet are other reactions." Thus included not as pain, but as the "reaction to pain", are practically all the criteria by which the presence of pain is ordinarily inferred. Since, according to this concept, the "perception of pain" and the "reaction to pain" may be dissociated by various means, it

becomes necessary to accept as pain a sensation which is associated with none of the "reactions to pain". That this concept of sensory pain leaves out a large part of the experience is noted by Wolff and Wolf (31) who state, "the sensation pain is often associated with a reaction of anguish or displeasure and, indeed, these strong feeling states may predominate in the pain experience, becoming to the one who suffers the most relevant aspect of pain."

Dissatisfaction with this narrowed concept of pain, together with the weaknesses shown in both of the classical theories, have led to new formulations. Nafe (18), for example, who has raised many of the objections noted above, has offered an entirely different view of the neural mechanism of pain. He has completely rejected a specific receptor theory for all cutaneous sensation. Instead, he suggests, all the different forms of cutaneous experience are centrally determined, by the differentation of patterns of impulses arriving from the periphery. According to this theory, pain becomes a non-specific sensation produced by the pattern of neural activity aroused by noxious stimuli. For certain kinds of pain this neural pattern, he holds, could result from extreme vasoconstriction. To support this, he points to the repeated correlation between vasoconstriction and pain which he has shown experimentally (19). This, of course, is true, but as Stone and Jenkins (25) point out, "it has long been known that pain is accompanied by vasomotor and other autonomic

changes; although these have been taken to be the result rather than the cause of the pain."

Wolff and Hardy (30)also give examples in which it would seem that the neural pattern associated with vasoconstriction must be aroused, yet no pain is reported. They write (30), "Epinephrine, when locally applied to the surface of the pain sensitive middle meningeal artery caused its walls to contract so vigorously that the end result was a vessel which had but a fraction of its former diameter, yet no pain was elicited by such a spasm." Furthermore, Clark, Hough and Wolff (8) and others (21) have shown that histamine, which acts as a strong vasodilator of cerebral arteries, is capable of producing pain experienced as headache.

Such observations, together with the known facts about (1) the punctate nature of cutaneous sensation and (2) the selective loss of different sensations as a result of nerve blocks, are against Nafe's complete disavowal of all specific receptor mechanisms. In spite of this, he has pointed out many of the weaknesses of a strict specificity theory and has especially attacked the concept of pain necessary for such theories. To him, pain must be referred to the central nervous system, because in the peripheral nerve the nearest we come to pain is prick, which he calls, "a sudden and intensive pressure." His idea that pain should be given the status of an internally aroused experience, due to a particular pattern of neural activity, is still a lively one.

Hebb (15) also has reviewed much of the data relevant to pain and has pointed out the inadequacies of the two classical theories, which have been noted above. Moreover,, he emphasizes the important role in the mediation of pain which many investigators (7, 22, 23) have assigned to the smallest type of afferent fibre. This well-established fact directly opposes a theory that high intensity of peripheral stimulation is the basis of pain, because the impulses from these small fibres are the slowest and weakest of all types. However, many considerations make it unlikely that a simple specificity theory need be the only alternative. Hebb suggests, instead, that the two theories are not mutually exclusive and writes:"Let us suppose that the pain fibres do no inevitably mediate pain, but that the slow impulses and the central connections of these fibres are such that they are peculiarly effective in producing sudden massive discharges in somesthetic nuclei at the thalamic or cortical level, with a widespread effect."

According to this viewpoint, pain becomes a central process of a high-intensity, wide-spread, disruptive nature. Hebb suggests that such a concept achieves a partial synthesis of opposing theories. Although peripheral intensity must be discarded as the sole determinant of pain, yet central intensity becomes crucial. Also, the pain fibres, though non-specific in that they must always mediate pain, are nevertheless specific in the sense that, innately, the pain process is most adequately

aroused by the neural activity they initiate. This activity, it appears, would be characteristically of low amplitude, slow and poorly organized such as is known to result from (1) C fibre functioning and (2) certain pathological conditions which result in neural hypofunctioning. Such a pattern, arising from peripheral noxious stimulation, could release central firing from the control that Adrian (3) has shown normal sensory impulses to have, and thus result in the disruptive pain process.

Hebb has pointed out that this hypothesis is incomplete since conditions, like syringomyelia, which must bring about a stage of neural hypofunctioning do not result in pain, but rather the absence of pain. Also, there are many indications that all pain is not carried through C fibres. Gasser (12) cites evidence that pain is carried by both myelinated and unmyelinated fibres. Adrian (1), also, showed that the slower impulses travelling in A fibres apparently are associated with pain. These findings are difficult to fit into Hebb's theory, though there is some reason to assume that we may be confused with two types of pain - a bright, sharp pain carried in faster, myelinated fibres and a duller, aching, longer-lasting pain which is associated with C fibre activity. As Morgan (17) points out, "pain remains in cocainization when only A fibres are left and in asphyxia when only C fibres are functioning". Here, at least, there seems some support for thinking of two types of pain being mediated by these two groups, since the pain that is left longest in cocainization

is bright and

sharp, whereas in asphyxia the dull, aching type of pain persists longest. Undoubtedly, this last pain is the one which appears to have the most profound, generalized autonomic and behavioral effects. This type of pain is presumably closest to the concept of pain held by both Nafe and Hebb.

The above review rather clearly indicates that there is, at present, no generally satisfactory theoretical account of the nature of pain. In such a situation a different attack on the problem, yielding evidence of a different nature, might well be expected to clarify the picture considerably. An opportunity for such a fresh attack is afforded in those rare cases in which there appears to be a complete absence of pain in the human subject. This is especially so if this deficiency makes its appearance as being almost specific to pain. Once even a single case of this kind has been satisfactorily established, there are implications for the general theory of pain. Certainly, the theoretical concepts regarding the nature of pain and the mechanism of its arousal must be such that they can logically admit the existence of such a phenomenon. In the case of a simple peripheral intensity theory this admission does not appear to be possible. For, according to this viewpoint, how could touch, warmth, cold, hearing, vision, smell remain approximately normal and yet the intensest stimulation in any of these modalities fail to elicit pain? A strict specificity theory, on the other hand, could, with difficulty, admit this phenomenon and would offer an explanation

in terms of either (1) lack of receptors, (2) lack of specific peripheral or spinal tracts or (3) deficiencies at a cortical or thalamic level. Consequently, further study of a well-established case of insensitivity to pain by such means as the skin biopsy, for example, could offer a direct test of these hypotheses.

In view of these considerations, it would appear that the study of this phenomenon might prove of great value. The few examples which have so far been studied have been reviewed in detail in the introduction to this paper. The present investigation is concerned with one more such case, but attempts to demonstrate the absence of pain more rigorously than has hitherto been done. For this reason, the demonstration has been carried out on three levels: (1) Verbal report, (2) Behavioral response and (3) Autonomic response. If response to noxious stimulation is invariably absent on all these levels, then it will be asserted that there is complete absence of pain.

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# PREFACE.

The anomaly of a human subject exhibiting a congenital, universal insensitivity to pain is of more than incidental interest in the scientific study of pain. It is, indeed, a rare phenomenon which appears to offer opportunities for insights, not available in more routine investigations. For this reason, the author wishes to especially acknowledge his debt to Dr. R.B. Malmo, who made this study possible. Dr. Malmo was not only instrumental in securing the cooperation of the subject of the study, but freely offered the fine experimental laboratory facilities available at the Allan Memorial Institute of Psychiatry.

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# INTRODUCTION.

It has been frequently observed that wide individual differences exist in what Wolff and Hardy (25) have called the reaction to pain. However cases, in which the usual behavioral and physiological responses to noxious stimuli are apparently totally absent, are rare and strange enough to have aroused considerable scientific interest. Many of these cases not only exhibit absence of reaction to pain, but through verbal report have led investigators to infer that the direct perceptual experience of usually painful stimuli is markedly different from normal.

Several cases have been reported in scientific literature (4, 5, 6) of the appearance of general cutaneous anesthesia in which pain has been involved along with touch, temperature and pressure sensations. Circumscribed analgesias have been observed frequently. However, these examples of disturbances in pain sensitivity appear to be in a different category from the rare reports appearing later of individuals showing more specific lack of reaction to pain. Schilder and Stengel (21), dealing with patients with brain lesions, report having observed ten cases of what they termed "asymbolia for pain." This is described as a dulling of the appreciation of pain - a condition which was usually spread over the whole body, and always associated with an incomplete and insufficient pain reaction. In six of their cases, typical sensory aphasia was also present. The nature

of the brain damage observed in autopsies led the authors to conclude that a lesion in a particular region of the left parietal lobe (probably in the gyrus supramarginalis) was the basis of asymbolia for pain. Dearborn (9) gives the personal history of a man who did not experience, and could not recall having experienced, any pain except headache, and who for nineteen months appeared on the vaudeville stage as, "Edward H. Gibson, The Human Pin Cushion." Critchley (8) mentions briefly having examined a young man who had been referred to him by a physician because of his apparent insensitivity to pinprick and other painful stimuli. This, Critchley confirmed by driving a pin hard into the patient who did not flinch and stated that though he could feel the prick, "it was nothing very much." He (8) also reports a similar case which has been described by Weir Mitchell, of a legal friend of his who had never felt pain keenly at any time in his life, though he had once bitten off the end of his own finger after it had been crushed. He had also undergone operations for lancing an abscess and bilateral removal of cataracts without anesthetic..

Ford and Wilkins (10) describe three children, aged 7 to 9 years, in whom they believed there was no true analgesia, no lack of pain as a sensation, but rather a lack of reaction to pain - an indifference to pain. These children in clinical tests of sensibility could appreciate light touch, distinguish between warm and cool test tubes, and

also between the head and the point of a pin. Yet their reaction to noxious stimuli, such as deep pricking with a pin, squeezing of the tendo Achilles and pinching of the skin, deviated markedly from a normal behavioral reaction and also showed the absence of psychogalvanic response. Their personal histories were replete with examples of behavioral indifference to damaging stimuli, with the qualification that in two of the cases some pains of visceral origin appeared to produce a normal reaction. The possibilities of (1) defect in the sensory pathways of the spinal cord or peripheral nerves, (2) syringomyelia, (3) mental deficiency, (4) hysteria, and (5) masochism as explanations of this condition are examined and rejected. These authors (10) consider the hypothesis that some defect in the thalamus might deprive pain of its disagreeable affective significance, and also the possibility that deficient cortical development in areas described by Schilder and Stengel (21) might account for their results. They state in conclusion, "We are inclined to believe that we are dealing with a congenital defect of development involving in a selective manner the neural mechanisms concerned in our reaction to pain and comparable perhaps to color blindness, congenital word deafness and congenital word blindness, which are also regarded as selective defects of development."

More recently Kunkle and Chapman (14) report the case of a twenty-five year old corporal cook in the United States

Army Air Forces. In addition to the personal history and the application of common clinical tests for pain, they report additional experimental data from the use of five newer techniques:

(A) Muscle Ischemia: Circulation to the lower arm is arrested by a cuff encircling the upper arm. Their subject was able to clench his hand into a fist 80 times at a rate of once per second without reporting pain. Usually the severe pain of muscle ischemia is noted after 30 to 50 such contractions.

(B) Cutaneous Pain Threshold Determination: Use of the Hardy, Wolff and Goodell (11) technique indicated a greatly elevated threshold. Only moderate warmth and, in some tests, a slight pricking sensation were reported at intensities which are normally severely painful and capable of blistering the skin.

(C) Esophageal Distension: A small rubber balloon introduced into the esophagus and inflated with air failed to produce pain report at pressures well beyond normal.

(D) Histamine Headache: Intravenous injection of .2cc. of 1:1000 histamine phosphate failed to produce the usual headache.

(E) Cold Pain: Immersion of one of the subject's hands in water at $5^{\circ}$ C. failed to produce the commonly observed aching pain. In two trials, however, the subject showed the following rises in arterial blood pressure: (1) Systolic - 18 mm., diastolic - 4 mm. (2) Systolic - 20 mm., diastolic - 22 mm. Tachycardia was also shown. The authors look upon this case

as a sensory defect which must be placed centrally, possibly at the thalamic level. Thus, they allow for the possibility of incomplete reaction to pain such as their subject showed in a blood pressure rise during the cold water test; while, at the same time, awareness of pain seems absent, together with the usual behavioral reactions of restlessness, withdrawal and wincing.

Previous reports of this type of disorder, as summarized above, are few and brief. Though they have aroused considerable interest, they have suggested little that has had a very marked effect on theories of pain. To a large extent they have been a presentation of personal case histories, supplemented, in some instances, with the application of well-known clinical tests for pain. These tests do not easily lend themselves to any control data other than the past experience of clinicians. Certainly no other control data has been offered. Further difficulties are involved, when, as has been the case many times, the subjects show evidence of such widespread neurological damage that the facts relevant to pain are inextricably mixed with a variety of sensory and motor disorders (4, 5, 6, 21). It is also likely that in the past literature we have in reality a variety of cases, who for different reasons have exhibited the curious anomaly of a general insensitivity to pain.

Nevertheless, a well-established case of this type, studied under standardized laboratory conditions with a good

background of control data, appears to be a unique testing ground for theories of pain. This is especially so if the anomaly presents itself uncomplicated by too many other evidences of neurological and psychological disorder. This advantage was present in the following investigation, unaccompanied by many of the disadvantages noted in earlier studies. Then, too, there was available an unusually large amount of reliable background data from hospital records dating back to the time the subject[1] of this report was 21 months old. The subject was also in a favorable age range, intelligent and willing to cooperate in the study. Earlier reports have not presented a consistent enough picture to clearly establish the absence of response to noxious stimuli according to the following three criteria of pain: (1) verbal report of painful experience, (2) overt behavioral reactions such as wincing, withdrawal or restlessness, and (3) physiological response as seen in blood pressure, heart rate or respiratory changes. In this study, there appeared to be an opportunity to establish more clearly the possibility of a human subject exhibiting absence of pain according to all these three criteria. Once this has been done the implications to theories on the nature of pain become of far-reaching importance. The case of an individual who from birth shows a complete, universal, indifference and lack of reaction to pain must be a remarkable example of organic defect, the answer to which may lie at the heart of the psychology and physiology of pain.

# CASE HISTORY.

General History: The subject was a young woman, 22 years of age, white, and Canadian-born of British ancestry. At the time of this investigation in the summer of 1948, she had completed second year university. She then joined a research group at the Allan Memorial Institute, for summer employment as a general assistant in filing records, and correcting and administering psychological tests. It was also understood that simultaneously with this other work a study was to be made of her apparent analgesia - a project which received her full cooperation. Throughout this period she showed herself to be very capable, cooperative and displayed remarkable initiative in her work.

She was born by normal delivery of healthy, highly educated parents and had one brother, one year her junior. Her father, a physician, died when she was eleven and her mother remarried about seven years later. Her early education started in a French nursery school and was accompanied by language teaching from a German governess. Later, she attended the ordinary city elementary school, but received most of her secondary education in private boarding schools. Although during this period of schooling she was often in conflict with her mother and her studies frequently interrupted by illness, she appears to have progressed satisfactorily, making friends and entering into student activities. She appears to have been a highly excitable child, who, at an early age, resorted to pounding her nose and to biting tongue and hands

in response to frustration. Later adjustments were satisfactory and present the picture of a slight, active, highly self-reliant person.

Medical History: The childhood of the subject is particularly marked by frequent hospital admissions and by the very early discovery of her apparently complete indifference to common pain-producing stimuli. At the age of 21 months, she was hospitalized for incision of a large, soft abscess over the occipital bone. The case history at the time reports that the child was not sensitive to pain. When three years old, she was admitted three times for treatment of osteomyelitis of the right os calcis. No complaint of pain or tenderness could be elicited from the patient. During this same year, a pinch graft operation was performed on the right leg which had received a third degree burn when the child had knelt on a hot radiator to watch some children playing in the street. At the age of five, tonsillectomy and adenoidectomy were performed. In 1935, four separate hospitalizations occurred, one in which the diagnosis was acute pyelitis, the other three treating osteomyelitis at the lower end of the left femur. Notes in the hospital records repeatedly mention lack of pain sensitivity which is reported to have existed since birth. After 1935, the subject's progress was less interrupted and no further hospitalization occurred until she was 17, when she spent six months in hospital for treatment of spinal osteomyelitis and surgical treatment of a knee.

Interview Material: Early in the study, interviews with the subject were held to further complete information about her insensitivity to pain. This material, together with incidents of her medical history, present a consistent picture of a remarkable lack of response to noxious stimuli. Multiple scars are visible on hands, legs and feet which have been produced by cuts, bites and scratches, many of which were unnoticed. After a day on the beach she has to inspect her feet carefully for cuts. She claims on many occasions to have received deep cuts from shells which she has not noted until after this inspection. At no time has she ever reported any form of ache or pain, such as headache, earache, toothache, stomach ache or menstrual pain. The whole of her ordinary activities of living from birth have repeated, again and again, this same theme of tissue damage which has gone unnoticed or looked upon indifferently. Frost-bites in winter are frequent. Burns from hot objects and from over-long exposure to the sun have also been numerous. Although no damage from burns has been as serious as the incident of kneeling on a hot radiator at the age of five, nevertheless, she has had sunburn on the back of the legs, which, going unnoticed and unprotected from clothing, became infected. It is also interesting to note that she reports never having felt the sensation of itch. From her life in boarding-schools and university she has had ample opportunity to observe the behavior of others in response to the itch from sunburn,

measles, chicken-pox and urticaria. She, herself, often simultaneously with others, had experienced the same causes for itching, yet she reports never having felt any particularly different sensation and no occasion for behavior such as she observed in friends. Kunkle and Chapman (14) also noted the absence of itch in their patient, which is interesting in view of Rothman's (20) work in which itch appears as a form of slow pain.

The subject looks upon this defect in pain sensitivity as some organic deviation quite beyond her knowledge or comprehension. She shows at present some reticence in telling friends of this deviation from normal, but felt that a study of the anomaly could be interesting, worthwhile and worthy of her cooperation. There is evidence of a curiosity as to what feeling could produce the pronounced pain reactions she has observed in others. She also believes that to a large extent her sensitivity to painful stimuli is returning. This belief, it appears in interviews, is largely due to the greater success she has had in later years in avoiding serious tissue damage. Later evidence makes it appear much more likely that this is due to more adult behavior patterns and to learning to use other cues as a warning of potentially damaging stimuli. The sensitivity to pain which she apparently lacks does not appear absolutely indispensable either for normal personality development or as a warning signal of potential tissue damage to the organism. Nevertheless, this defect along with a marked sus-

ceptibility to cutaneous infection has proven very inconvenient, dangerous and potentially fatal.

Neurological Examination: This examination of the subject was made on July 10th, 1948, by Dr. F.L. McNaughton of the Montreal Neurological Institute.[3] He reports: "Examination of the cranial nerves is normal with the exception of the following observation: On testing the corneal reflex there is occasionally a very slight movement of the eyelids when the cornea is touched and it is difficult to be sure that this is not a reaction to an approaching and threatening object. To the ordinary method of testing one would say that the corneal reflexes are both absent. She does feel very light touch on the conjunctiva and possibly on the cornea as well. On her face and elsewhere on the body, she can distinguish between the touch of the finger alone and the touch of the finger associated with pinprick. At first, she thought I was digging in with a finger nail and when asked says that she simply felt something sticking into the skin, but she experienced no pain with it. The same is true when a hypodermic needle is inserted into the epidermis. She feels it penetrating the layers, but experiences no pain. Supra-orbital pressure with the finger causes no discomfort whatsoever. A stick can be inserted up through the nostrils without causing any discomfort or any tendency to sneeze or withdraw. The same is true on touching the external auditory canals or the eardrum lightly with a stick. There is no tickle sensation from either nasal orifice. The gag reflex

can be elicited only by stimulating low down in the posterior pharyngeal wall.

There is fair muscular development, no localized wasting or weakness, and coordination tests are well performed with either hand or arm.

The deep reflexes are normally active and equal. The abdominal reflexes are active and equal, and the plantar responses, while very slight, seem to be flexor in type.

Her ability to distinguish between touch alone and touch associated with pinprick has already been noted. There is no reaction to heavy pressure on the tendo Achilles of either leg. She can appreciate even very weak vibration as tested with a tuning fork. Position sense in the toes also seems perfectly normal.

She is able to distinguish between hot and cold objects anywhere on the body surface, even when the difference between the two temperatures is not great.

The ciliospinal reflex was tested, but no definite change was noted. There were very frequent alterations in diameter of the pupil at all times.

Summary: Examination does not reveal any evidence of organic neurological disease, such as syringomyelia. There are several bony deformities which have resulted from the osteomyelitis. The lateral malleolus of the left leg is abnormally large, though she has never had osteomyelitis of this region and suggests the possibility of a Charcot joint.

However, there is no unusual mobility or crepitus of this joint. There are no trophic changes in the fingers or toes and no unusual scars or calluses on the feet. The remarkable feature is the complete absence of any experience of pain or of the usual reactions to it.

Histamine Test: Subject was given .1cc. of 1: 1000 histamine solution (Parke-Davis) intravenously, producing slight taste sensation in mouth, and throbbing sensations, with specks before the eyes. There was increased pulse rate, and throbbing of the neck arteries at the same time. No headache was produced."

Electroencephalographic Examination: A routine EEG investigation was made with the technical assistance of Mrs. L. Ghent of the Allan Memorial Institute.[3] This involved complete monopolar and bipolar coverage of the scalp and sphenoidal lead recording. No pathological wave forms were revealed.

Psychological Test Examination: This examination was carried out by Miss J. Coulter and Miss T. Gordon of the Allan Memorial Institute.[3] A general investigation of intelligence was made with the Wechsler-Bellevue Intelligence Scale and the Wechsler Memory Scale. Personality structure was explored using the Rorschach, Thematic Apperception Test, Cornell Index (Form N2), McFarland and Seitz's Psychosomatic Inventory.

The results indicate a person of "very superior" intellectual efficiency according to the Wechsler-Bellevue Scale, which gave a verbal scale of IQ of 119, a performance scale IQ of 132 and a full scale IQ of 128. No gross

disturbance of function was noted, although the subject did less well on the verbal than on the performance section of the test - the reverse of the usual situation. Although the Wechsler Memory Scale MQ of 106 was undeniably lower than the level expected from the intelligence rating, the performance suggested lack of attention control rather than any primary impairment of memory.

The two personality inventories did not reveal any gross personality disorder. The Rorschach record, however, was extremely productive, there being 90 responses in all. Actually, many more would have been possible, but the subject voluntarily curtailed responses after a time for she felt it too onerous a task, both for herself and the examiner. This performance bespoke a very considerable associative wealth, although there were frequent blockings and delays exhibited in the rate of production. No diffusion, or vague responses occurred, nor was there any over-emphasis upon anatomical associations. Thus, anxiety would not appear to be a critical problem.

Consideration of these responses suggests that this is a withdrawn individual, whose fantasy world is extremely rich and satisfying. Although, in some respects, the record was somewhat bizarre the individual's critical judgment, contact with reality and ability to appreciate the conventional point of view were quite adequate. Nevertheless, she is not readily able to gain insight and is a detached person, unable to

relate herself to others satisfactorily.

The TAT stories were chiefly concerned with the two main themes of the home and relations with men. Some basic rebellion against the home is shown, in which the need for a mother figure features predominantly. The subject projects a desire for independence in vocational and social terms, but when she tries to achieve these she is quickly faced with conflicts of guilt and uncertainty about these decisions.

It must be emphasized that no marked personality disorders were revealed. Nevertheless, emotional insecurity and immaturity do appear strongly to an observer, though they may be no more than could be expected from the unusual features of her early history. Perhaps the main overt characteristic which is noted by friends is the extreme activity she exhibits. She runs from one place to another and shows a strongly self-willed drive. This hyperactivity does not seem to result in general restlessness, for her control and patience during many of the phases of this investigation were remarkable.

## EXPLORATORY DATA.

General: Early in the study an informal survey was carried out, using varied forms of cutaneous stimulation. Always, the subject was asked to describe the resulting experience as simply as possible. She easily recognizes light touch with the finger, describing it as warmish, not pointed, and touching lightly. As finger pressure is increased, she notes increasing deep

pressure and also decreasing pressure as the finger is relaxed. Touching one hair of the arm lightly elicits touch sensation, while pulling a hair is like heavier touch. Cool water is easily recognized and described as a cool, pleasant sensation. The ring of pressure and temperature gradient where the finger enters the water is also noted. Water at $0^{o}$ C. in which the hand is placed for periods from 5-8 minutes is described similarly by the subject, the cool sensation appearing more intense at first and gradually disappearing. At no time was any report given of an aching, crushing or unpleasant feeling. No behavioral signs of pain were ever shown.

Report of prick sensation may be easily elicited, but is never accompanied by any description of painful feelings. A prick from a very sharp needle is reported as a sharp, pricky, highly localized, and may be distinguished from a dull point. There seems to be a tendency for the prick sensation to appear rapidly and then fade out. A pin point, pressed on the skin at the base of a nail, is described as showing immediate prick which dies away. Further pressure is felt only as pressure and is a matter of indifference. Cutaneous electric shock, caused by discharge between two closely placed terminals of an inductorium pressed against the skin, is also readily perceived as sharp or pricky.

A three litre beaker, in which about 500 ccs. of near boiling water had been placed, was used in an exploratory test of heat sensations. If the beaker is grasped near the

top, the subject describes the experience of a warm pleasant feeling, diffuse in nature. As the hand is moved down on the outside of the beaker, she claims feeling of gradation from general pleasant warmth to a sharper prickier sensation. This prick sensation is described as one which rises rapidly in intensity up to a certain point, after which it appears to stabilize and then to decrease until it has completely faded out. In other tests, in which a finger is immersed in hot water ($58^{o}$ - $60^{o}$), the subject reported this same intensity change over a period of 15 seconds. Preliminary test by the experimenter of the same water resulted in forced withdrawal at five seconds with accompanying painful experience.

Concern with this apparent rise and fall of a pricky sensation or change in the quality of heat, led accidentally to another demonstration of abnormal reaction to noxious stimuli. A modified Hardy-Wolff apparatus was used with a lamp setting at 200 watts and a 3.5 $cm.^{2}$ area of blackened forearm was exposed. In the normal three second period of stimulation, this setting is below the threshold for pain. On this occasion, however, the shutter was held open, so that the time course of this intensity change in prickiness could be followed. The subject reported a rising feeling of warmth and increasing prickiness up to about 21 seconds, when this sensatio stabilized and began to decline. At 45 seconds, the subject reported the absence of any sensation, even warmth. On a repeat trial on the other arm, again the same rise and fall of intensity was noted. The peak of prick sensation occurred

later, but, as before, all sensation had gone at 45 seconds. The same procedure was then repeated on the experimenter. The result was a rapidly increasing feeling of warmth, which after 7-8 seconds, showed a sharp, pricky quality. This sensation increased rapidly, causing extreme pain and forced withdrawal in 12-15 seconds. This observation was repeated by the experimenter and other observers, always with the same result. It was only after the removal of the India ink, which had been used to blacken the exposed skin, that the result of this stimulation on the subject could be observed. On each arm, there appeared a large blister, covering the area which had been exposed. The subject was reporting absence of all sensation while this tissue damage was occurring and at no time showed any behavioral signs of withdrawal, restlessness or wincing.

Threshold Measurements: A closer investigation was made on the effect of thermal stimulation by using the Hardy-Wolff apparatus to obtain thresholds for warmth and pain. For the warmth threshold, a blackened surface of the volar aspect of the forearm was used as the test area. This area was then placed directly against the 3.5 $cm.^2$ opening of the Hardy-Wolff apparatus and the subject blindfolded so that no light was visible. A series of stimulation of 3 secs. duration, spaced at 30 sec. intervals, was then presented. These started at zero watts and increased in steps of 25 watts until a point was reached where the subject signified that the lamp was on.

The threshold thus represents a point, expressed in terms of wattage input to the lamp, at which the subject first perceives warmth in the exposure area during a stimulation period.

This was found to be a difficult judgment to make in spite of its apparently simple nature. The onset of warmth is so gradual that the area, between the point where the subject is sure there is no stimulation and the point where warmth is certainly felt, is very broad and diffuse. A group of 16 controls tested in this way showed an average threshold of 113 watts with a standard deviation of 25.0. The average threshold of the subject obtained in nine widely spaced trials was 184 watts with a standard deviation of 39.5. There appears, thus, some evidence that the threshold for warmth in the subject is moderately elevated. The subject's response here however, unlike that to pain, is qualitatively the same as that of the control subjects.

Several attempts were made with the subject to measure the threshold for pain using the standard method described by the Hardy, Wolff and Goodell (11). At first it proved impossible to measure any threshold as pain was never reported, although stimulus intensities sufficient to cause blistering were given. No behavioral reaction of head withdrawal or wincing was ever shown. This failure to give a verbal report of pain which is used as the basis for the determination of threshold is most unusual. Kunkle and Chapman, however, report the same thing occurring in their patient. It would seem to

indicate an indeterminately high threshold for pain. Nevertheless, the exploratory observations with hot water showed that there was a change in the quality of sensation as temperature increased. If this was so, then the necessary requirements for obtaining a Hardy-Wolff pain threshold appear to be present. Using this example of hot water and several trials with the Hardy-Wolff apparatus, the subject was asked to watch for a change in the quality of sensation during the periods of stimulation as the lamp intensity was increased. The change was described as one from soft, diffuse warmth to a more localized, pricky sensation. Eventually it appeared possible for the subject to report this change in quality.

Threshold measurements were then taken using the blackened forehead as the test area. The average threshold obtained with the subject in 12 widely spaced trials was 295 watts with a standard deviation of 20.2. A group of 17 controls showed an average threshold of 263 watts with a standard deviation of 27.4. According to Andrews and Workman (3) a linear relation holds between wattmeter readings and radiometer readings obtained by the standard technique (11). Hence, it may be estimated that the threshold indicated by the subject is approximately .24 gm. cal./sec./cm.$^2$ It appears that some kind of threshold has been established for the subject which is only moderately elevated above the normal threshold for cutaneous pain.

To further examine the nature of this "prick" threshold, it was decided to try the effect of ingestion of .6 grams of

acetylsalicylic acid. The subject's normal threshold was taken in the usual way and a value obtained which agreed closely with previous measurements. At 10.00 a.m., .6 grams of acetylsalicylic acid were administered orally and the prick threshold measured rapidly every 15 minutes up until 12.15 p.m. This single trial resulted in the subject reporting a lowering of threshold. The decrease started out gradually and, in $1\frac{3}{4}$ hours after the time of ingestion, reached a maximum of 52% below the starting threshold. This marked drop in threshold is the opposite effect to that reported by Wolff, Hardy and Goodell (26).

The most likely conclusion seems to be that the subject was deceived by the effect which acetylsalicylic acid is reported to have on the feeling of warmth. Wolff, Hardy and Goodell (26) state: "After the administration of acetylsalicylic acid the subject, during successive threshold readings, became aware of a change in the character of the stimulus. The sensation of heat, which preceded the onset of pain, became relatively more intense and it was with surprise that no pain was experienced. The probable explanation of this phenomenon is that the threshold of heat is actually lowered by acetylsalicylic acid." It is also quite possible that the subject's "prick" threshold was not a true threshold. It may have been that at this point an intensitive change in the character of the heat sensation occurred which the subject, lacking the painful element for a criterion, selected as the basis of her judgments.

Muscle Ischemia: In this test, the upper right arm was snugly encircled with the cuff of a standard clinical sphygmanometer. After the cuff had been inflated to 250 millimeters of mercury pressure, the subject was instructed to exercise the right arm by gripping a hand dynanometer at a rate of once per second. The grip suggested was a firm one of approximately 14 kg. Under these conditions, the subject in four trials gripped the dynanometer 64, 79, 95 and 102 times. This gives an average of 85 contractions performed in as many seconds. No muscle ache or pain was ever reported and no change in the quality of sensation from arm muscles immediately after the cuff was deflated and circulation restored. Lewis (16) found, using similar methods, that pain had a remarkably consistent onset after 24-45 such contractions. This pain in Lewis' experiment, rose rapidly in intensity until it forced arrest of the exercise at a point between 60-80 such contractions.

Corneal Reflex: The corneal reflex of the subject was tested in the usual way. Repeated trials were made and the results recorded on 100 ft. of 16 mm. film. Figures 1 and 2, which are taken directly from the movie film, indicate the response seen. It was such that the corneal reflex in both eyes may be stated as being absent. It was easily possible to touch the cornea repeatedly and to draw the cotton point directly across the eye. The subject at no time reported pain, but reported a touch-like or contact sensation.

# EXPERIMENTAL DATA.

General Procedure: After a large part of the case history and exploratory data had been gathered, a series of experimental studies was begun. These studies may be separated into two main divisions. The first group consisted of a number of experiments using pain-producing stimuli, while in the second group a variety of stimulating conditions of a non-noxious nature were employed. The physiological responses to these varied stimuli were measured by continuous readings of blood pressure, heart rate and respiration. At the same time, all relevant behavioral reactions were observed and notes taken of the subject's report of experience during the experimental period.

The continuous blood pressure records were obtained using a recording sphymotonograph which has been described by Kurt Lange (15). In all procedures, the cuff of this instrument was attached high to the left upper arm of the subject. Heart rate was recorded on one channel of an Offner electroencephalograph, using Lead II of the standard electrocardiogram. The rate was then obtained by simply counting the number of beats over a known period of time. Respiration was recorded using a pneumograph attached to a tambour and pen which marked in the standard way on paper of the EEG machine.

In the general plan, all experimental procedures were divided into three parts. During the first part, the subject was given instructions and prepared so that continuous readings

could be taken of all three physiological measures. The second part was the main experimental section. In every case this started with a rest period followed by the stimulus period and concluded with an after-stimulus rest. In the final part the subject was asked to report on experiences during the experiment. Data obtained from the subject was set against the results obtained with groups of controls made up largely of graduate university students of both sexes, in the same age range as the subject. Throughout this report, data obtained from these control groups will be labelled CONTROLS. Data obtained from the case exhibiting insensitivity to pain will be labelled SUBJECT.

## I. The Effect of Pain due to Local Cooling.

**Procedure:** This experiment lasted 20 minutes divided in the following way: (1) A rest period of 8 minutes, during which time respiration and heart rate were recorded. Systolic blood pressure was recorded only during the last three minutes of this period. (2) Following this, the right hand of the subject was immersed in a three litre beaker filled with ice and water at $0^{o}$ - $2^{o}$ C. The subject was instructed to remain passive during the time when the hand was immersed, allowing the experimenter to accomplish the necessary movement. This period of stimulation lasted 8 minutes, at the end of which time the hand was removed by the experimenter. The ice water covered the hand to just above the wrist and

was stirred frequently. (3) The remaining four minutes form an after-period rest, during which all three physiological measures continued to be taken. This procedure was followed with the subject and with a group of nine controls - four female and five male. The subject had six trials in all, recording systolic blood pressure five times, diastolic once, heart rate twice and respiration once.

Results: No control failed to report the experience of "cold pain" during this experiment. It was usually described as a dull, aching, crushing pain which appeared shortly after immersion of the hand and rose rapidly to a maximum, after which some decrease appeared to occur. The sensation of cold was also reported, but was easily separable from pain. Behavioral signs of pain, such as wincing, restlessness and partially executed hand withdrawals were noted. The subject gave the report of cold and wet. No other sensation was ever described and any feeling of ache, unpleasantness, or pain, was denied. No behavioral reactions, such as were observed in the control subjects, could be detected.

This marked difference in verbal report is associated with a complete separation of the subject from the controls in the results obtained from blood pressure data. The contrast is so great that it becomes apparent from mere inspection of a control record beside one obtained from the subject. This may be done by comparing Figs. 3 and 4, which are typical control systolic pressure records, with the subject's response shown in Figs. 5a and 5 b. The full extent

of the differentiation is, perhaps, best indicated by combining all control records and comparing them with the composite record obtained from the subject during five trials. This was done by labelling the point of hand immersion on each record as zero minutes. With this constant point of reference, single spike readings were then noted for each time point plotted in Fig. 6. These sample spike readings were then averaged for comparable time points over all the records from controls and, similarly, over all the trials with the subject. The composite curves resulting from this analysis are plotted in Fig. 6.

The fact that there are no individual exceptions to this differentiation between combined curves for the controls and combined trials for the subject is indicated in Fig. 7. No control failed to show a marked rise in systolic blood pressure during the early stimulation period (B), while the subject showed no appreciable change. (In some trials the full after period was not recorded for the subject, as no response was ever shown during any of the periods and continued recording of "after stimulation" appeared superfluous). Although the systolic pressure of all controls responded similarly in the early stimulation period (B), some variation is indicated in the late stimulation period (C) and after period (D). Three controls showed a marked fall in blood pressure below the pre-level, with accompanying pallor, cold perspiration and feelings of faintness. The overall affect of this experimental procedure upon the systolic blood pressure of the controls and the subject is summarized in Table I. The diastolic

record of Fig. 5b indicates that the subject also failed to show any marked change in diastolic blood pressure, associated with this form of stimulation.

Heart rate readings were taken from the continuous record by selecting a 10 sec. sample every 30 secs. throughout the record. The number of beats in this 10 sec. period was then counted and multiplied by six to give heart rate in the standard units of beats per minute. Times were made comparable from record to record by labelling the point of immersion as zero minutes and measuring all times from this fixed point of reference. Thus, the values from all the records could be combined by averaging rates which were at equal time units from zero. The actual times at which sample readings were taken and averaged are those for which points are plotted in Fig. 8. This was done for the controls and for two separate trials with the subject, in which heart rate was recorded. The resultant composite curves are shown in Fig. 8. The controls show an immediate rise in heart rate at the time of immersion which lasted about two minutes and then is gradually replaced by a marked retardation. The subject fails to show either of these reactions.

Figure 7, which presents a family of individual curves, again indicates that no control failed to show a marked heart-rate response which completely differentiates them from the subject. In the only control who did not show the acceleration in the early stimulation period (B), the initial rise did take

place, but was replaced by retardation so quickly that the average of Period B still appears as a slight drop. That this individual did not react as the subject did is indicated by the continued fall in heart rate shown in Period C. A further interesting differentiation between the subject and each individual control is seen when the variability of heart rate throughout the total period of the experiment is considered. This data is presented in Table II by noting the range, average and standard deviation of all the heart rate readings for each individual. In both trials, the subject shows a variability in heart rate markedly lower than any control.

This experiment also demonstrated a differential response in respiration on the part of the subject and the controls. The pneumograph record was divided into two parts: (1) Before stimulation and (2) During stimulation. Respiratory rate was then counted over 30 sec. intervals taken continuously through these periods. In both of these periods, the variability of respiratory rate as measured by the standard deviation was lower for the subject than any control. Although no consistent trend toward either acceleration or deceleration of respiration appeared as the result of stimulation, nevertheless the controls were consistently more variable in rate during the stimulation period than before. The subject, on the other hand, showed no change in variability from one period to the other.

The controls, as a group, also indicated greater disturbance in the pattern of breathing as a result of stimulation.

A measure of this was obtained by looking at the pattern of breathing on the record, in each 30 second interval throughout the experimental period. If there were irregularities in amplitude the period was rated plus, if not, then it was labelled minus. The percent respiratory irregularity, for the control group and for the subject, was then obtained by calculating what percentage of the total number of respiratory periods scored had been marked plus. Figure 10 shows that the controls, as a group, show a considerable rise in the percentage of irregular respiration periods after the immersion of the hand in ice water. This effect does not appear in the subject's record.

II. The Effect of Pain due to Local Heating.

Procedure: Same procedure was used in Experiment I, with the following changes: (1) The stimulus used was hot water kept at a temperature of $49^{o}$ - $51^{o}$ C. (2) The time of actual immersion in the water was reduced from 8 minutes to 5 minutes. All records were taken and scored in the same way. This procedure was followed with the subject in two trials and with a group of six controls - four males and two females.

Results: The report from the controls on the effect of the stimulus was that of a sharp, pricking heat sensation of a definitely painful character. This sensation rose sharply in intensity and frequently produced wincing and withdrawal reactions. During the five minute period of stimulation, most of the controls reported that the painful element had dis-

appeared, leaving only a feeling of warmth. The subject reported warmth and a pricking heat sensation which was not described as painful. No behavioral reactions such as withdrawal, wincing or restlessness were ever detected.

The contrasting effect of this experimental procedure upon the systolic blood pressure of a control and the subject is shown in Figs. 11 and 12. The difference, though not as marked as that between Figs. 3, 4 and 5a, 5b, is nevertheless apparent. The composite curves shown in Fig. 13 indicate a marked, differential effect on the controls as a group, compared with the combined trials with the subject. Again, no individual exceptions were shown to this differentiation (see Fig. 14). The overall effect of this experimental procedure upon systolic blood pressure is summarized in Table III.

The composite heart rate response is shown in Fig. 15. The control group shows a rise in heart rate which starts at the time of immersion and keeps on until the time of withdrawal. The subject shows no acceleration at the time of immersion, but a rise is indicated later in the stimulation period, probably due to the warming effect of the water. Individual heart rate records of the controls, however, failed to show a complete separation from those of the subject.

Very little differentiation was noted in the respiratory response, except for the measure of respiratory irregularity which is presented in Fig. 16.

III. The Effect of Pain due to Electric Shock.

Procedure: In this experiment, a series of electric shocks was used as the stimulus. The shocks were obtained from an inductorium and were administered by pressing against the volar surface of the right forearm a small lucite holder which contained two fine electrodes set about 2mm. apart. Systolic blood pressure, only, was recorded during this test. The period of stimulation started with a shock administered to the forearm. Following this initial shock, the electrodes were pressed firmly against the skin every 7-8 seconds. The duration of contact was approximately 2-3 seconds. The time of administering the shock was carefully controlled by the experimenter who synchronized his application of the electrodes with a signal light which flashed every 7.5 seconds. Shocks were continued until 20-26 had been administered. Pre- and after-stimulus periods were recorded in the usual way. This same procedure was followed with the subject and with eight controls - five male and three female.

Results: The controls all reported a sharp, needle-like sensation from the electric shock, with the occasional "flutter" as motor nerves were stimulated. They describe the whole experience as very unpleasant, with a generalized feeling of uneasy tension. Without exception, they showed withdrawal reactions which they appeared unable to control. The subject reported the experience of pricky sensations with the occasional flutter. The behavioral reaction was markedly different,

showing unconcern, relaxation and complete absence of any withdrawal movements.

This difference in overt response is associated with a marked difference in the blood pressure records (see Figs.17 and 18). Every individual control showed a rise in systolic pressure during stimulation which, for the group as a whole, amounted to an average elevation of 19.1mm. of mercury. When each record is sampled by taking single spike readings every 30 secs. throughout the record, the individual results of this experiment may be summarized as in Table IV.

IV. The Effect of Non-Noxious Stimuli.

Procedure: The first test used in this experiment was developed at the Allan Memorial Institute for work with psychoneurotics. The subject was given the necessary instructions, followed by a rest period of 40 secs., during which a pre-test level of systolic blood pressure was obtained. The test proper then started when a frame, showing six white circles against a black background, was flashed on a screen on the wall opposite the subject. These circles were of slightly varying diameter, with the identifying numbers 1 to 6 placed above them. The task was to call out to the examiner the number of the largest circle. In Series I, a sequence of 20 such frames was projected at the rate of one every 5 seconds. The subject was then presented the same sequence again in Series II, at a rate of one every 3 secs., and Series III, at a rate of one every 2 secs. The actual presentation of the frames with the

brief pause between series took approximately six minutes, during which time systolic blood pressure was recorded. The test consisted actually of a simple, but relatively fine discrimination of size conducted under mildly stressful circumstances, in that the subject was progressively more and more pressed to respond rapidly. Records were obtained from the subject and from a group of 14 controls.

The second test used was a mirror-drawing task in which the subject was to follow the outline of a printed circle. The line was to be drawn first around the outside of the circumference and then inside, attempting to keep always a distance of 1mm. from the printed circle. A rest period of 30 secs. was given at the beginning, during which systolic blood pressure was recorded. Then followed an instruction period of 90 secs., during which the subject was instructed as to the nature of the mirror-drawing task to be performed. The performance period then followed and was stopped as soon as the subject completed the task or reached the maximum time limit of three minutes. This procedure was followed with the subject and with a group of 17 controls.

In the third test the subject pulled a hand dynanometer at maximum grip until fatigue prevented further contraction. The dynanometer was gripped by the right hand, while systolic pressure was being recorded from the left arm. Instructions were given to pull as nearly as possible at a rate of once per second, until forced to stop from fatigue.

Results: The first two tests of this experiment were known as the Perceptual test and Katoptograph test, respectively, and are so labelled in Figs. 19a and 19b. In both tests, the systolic blood pressure levels for each period were obtained by averaging the values for all the individual spikes on the record during the relevant period. The results presented in Figs. 19a and 19b indicate that the blood pressure response of the subject associated with these experimental procedures follows closely that of the control group average. In the katoptograph test (Fig. 19b) the actual amount of change in systolic blood pressure for the subject was greater than the control average. In the third test, the subject gripped the dynanometer 240 times over a period of four minutes. Figure 20 shows effect of this exercise on blood pressure recorded contralaterally.

## DISCUSSION.

The results of the experimental work show, on the part of the subject, a remarkable absence of response to common pain-producing stimuli. This is true whether we consider the response in terms of: (1) verbal report of painful feelings; (2) overt behavioral signs as wincing, vocal expressions and withdrawal or; (3) physiological response as seen in blood pressure, heart rate or respiratory measures. Although the application of stimuli such as pinprick, cutaneous shock or heat, which are adequate for pain in normals, does produce

report of a pricky or sharp quality, this quality is never described as a painful experience by the subject. It is also unaccompanied by the usual overt reactions or associated physiological changes. These experimental findings are entirely consistent with the picture presented in the case history. Their special interest lies in the way in which theycomplete this picture by demonstrating the lack of physiological response to noxious stimuli in all measures used.

This absence of physiological response on the part of the subject is a significant finding which appears in marked contrast to the response shown by control subjects. These results with control groups may be supplemented by ample evidence from the literature. Nafe and Wagoner (17, 18) with both hot water ($45^{o}$ - $58^{o}$ C.) and faradic stimulation note that the normal response is consistently one of verbal report of pain, associated with vasoconstriction and rise in blood pressure. Hines and Brown (13) showed the blood pressure rise, due to immersion of a hand in water at $4^{o}$ - $5^{o}$ C. to be the normal response for a group of 87 controls. Seventy-six cases,showing hypertensive symptoms, also showed a blood pressure rise which was greater than that of the control group.

In the insensitivity to pain shown by the hysterical patient such physiological responses as the "cold pressor" effect have not been absent, though the experience of pain was denied. Cable and Smirk (7) packed ice around the arm of a patient showing symptoms of hysterical anesthesia.

Although the patient denied pain, a rise in blood pressure of 17mm. systolic and 11mm. diastolic was shown. Also the patient of Kunkle and Chapman (14) who they believed was not hysteric, nevertheless showed a marked cold pressor reaction without reporting pain. They suggested that since at least this part of reaction to pain appeared present, that the defect must lie at a sufficiently high level to allow such a reflex response to occur, while at the same time no pain is perceived. The special significance of this report is that the subject appears to fall in a different category from the patients of either Kunkle and Chapman or Cable and Smirk. It must also be emphasized that this unique absence of physiological response appears specific to pain-producing stimuli. Certainly, normal vasomotor responses can be elicited in this subject, as was shown in the experimental results when non-noxious stimuli of a mildly stressful nature and exercise were used.

Examination of the data presented in this case, with a view to forming hypotheses concerning the nature of the anomaly, leads to many possible considerations. However, much of the evidence points to the location of the defect on an organic level. The lack of response to noxious stimuli has been shown since birth and has been marked by a universality and consistency unusual in cases of psychological disturbance. The psychological examination and interviews, conducted over a period of three months, failed to show any evidence of a marked disorder which could plausibly result in this picture. Perhaps the most convincing aspect of the data appears in the absence of

physiological response which accompanies the subject's denial of pain. The absence of such fundamental reflex actions as the cold pressor effect and the corneal reflex supports the hypothesis of an organic defect. It not only favors the concept of an organic cause, but also points to the strong possibility that the defect may be at the peripheral level. Certainly this level of organic abnormality would logically require first consideration.

Many reports in the literature of pain, dealing with possible peripheral neural mediation, have pointed to the importance of the smallest type of afferent fibres. Wolf and Hardy (24) concluded that pain due to local cooling was mediated through small, non-myelinated fibres of Class C. Ranson and Billingsley (19) have also emphasized the association of pain with fibres of small size. They (19) found that division of the pathway of the fine, unmyelinated fibres which pass from root to cord through the lateral filament of the root also abolishes the pressor reflex, struggling and respiratory changes usual to painful stimulation. In view of this, a great deal of the subject's lack of response to pain might be due to abnormal functioning of the small, unmyelinated, Class C type of fibre.

The recent emphasis that has been placed on the role of hypo-functioning in pain appears to bear directly on this hypothesis. Adrian (1) points out that electrical signs of activity in the pain fibres are often almost negligible - a fact,which, as he says,"Comes as a shock to one's senseof proportion." He (1) writes, "in the nerves from the teeth, for instance,

the usual streams of potential waves are set up by the slightest touch on the intact tooth, but the exposure and laceration of the pulp, the mere thought of which is painful, produces no more than a slight irregularity of the electrical record."

This apparent anomaly is further emphasized by Weddell, Sinclair and Feindel (22) who took biopsies in 39 cases from pathological skin areas in which pain of a peculiarly unpleasant quality could be aroused by needle prick. Without exception, when pain of such a quality could be elicited, the nerve nets and terminals subserving the sensation of cutaneous pain were isolated, instead of interweaving with neighbouring units as they do normally. Thus, in the case of the arousal of this pain, the area was innervated by only one fibre. The result of this is that the peripheral stimulus sets up at the cord a pattern of impulses markedly reduced from the normal pattern. A similar sort of pain may also be aroused by pinprick in an arm which has been compressed well beyond systolic blood pressure for a period of about 30 minutes. The contention of these workers (22) is that, in the arm so cut off by compression, a stage is reached when the conditions shown in their biopsies may be reproduced in the normal arm. This stage is one in which many of the pain fibres and endings will be isolated from one another, due to the gradual dropping out of fibre after fibre from the effects of compression. This condition then gives rise to the characteristic reduction in the nerve impulse pattern reaching the central nervous system.

Hebb (12) has suggested that pain be considered as a disruptive process originating in the somesthetic afferent system and resulting in massive discharges in the somesthetic nuclei. He (12) has pointed out that Adrian (2) and Weiss (23) have shown that normal sensory nerve patterns, regulate and control central firing. It is then only necessary to suppose that if this control pattern from afferent systems is reduced to a very low level that the central, rhythmic firing becomes disturbed. This disturbed synchronous firing may spread to connected nuclei, producing the characteristic generalized phenomena of pain. The reduction to this low level could occur under the conditions Weddell, Sinclair and Feindel (22) report. It could also occur, more normally, in the presence of the weak, slow pattern supplied by C fibres.

This hypothesis regarding the mode of arousal of pain forms a possible basis of explanation of the picture presented in this study. Let us suppose that, in this case, a congenital abnormal influence has acted selectively on the development of the fine, non-myelinated, type of nerve fibre. Let us further suppose that this action has been such that, either functionally or anatomically, these fibres are incapable of delivering the characteristic weak pattern of peripheral impulse shown in normal C fibres and particularly shown when the pain innervation to any area is markedly reduced, but not eliminated. Such a condition prevents the characteristic disruption of central organization and results in the picture shown here,

when the concomitants of pain at all levels of integration are absent. Normally, sharp bright pricky sensations must be associated with the characteristic firing which sets off the pain process. In a case of this type, such sensations might be experienced without ever meaning that pain has been aroused.

Other possibilities, of course, exist for the explanation of our data which differ from the above hypothesis in laying emphasis on central pathology rather than any peripheral mechanism. These central hypotheses consider the phenomena observed as due to deficiencies in (1) the cord, (2) the thalamus or (3) the cortex. A fourth central hypothesis exists if we suppose that some central condition has brought about such a strong organization of central firing, that the disruptive process may not be aroused by the characteristic weak pattern of stimulation, which is normally adequate. Most investigators (10, 14) who have reported on this type of case have favored the concept of a cortical or thalamic defect. It has been emphasized that this has been necessitated mainly because of the partial reactions to noxious stimuli which were observed in their patients.

In the case reported here, many reasons appear to make such central hypotheses less likely and less necessary: (1) The absence of the corneal reflex certainly indicates that a spinal cord defect cannot account for all of the observations made. (2) Thalamic deficiencies have most characteristically produced over-response to pain rather than absence of response. (3) The very basic nature of the responses, which have been

shown to be absent, makes it unlikely that the defect could lie at the cortical level alone. Kunkle and Chapman (14) report that the cold pressor effect could still be partially elicited in a patient who was under nitrous oxide and ether anesthesia. The corneal reflex also persists for a long time under similar types of anesthesia. Although none of these considerations is decisive, it would appear that the possibility of some anomaly in peripheral nerve structure or distribution should be first examined as the most probable.

Further data is needed to confirm any hypothesis which might be made as to the nature of this anomaly. Of prime importance, in view of the peripheral hypothesis suggested, is the skin biopsy as a direct means of searching for any abnormality in the innervation of the skin. Circumstances to date have prevented this further study, though it is hoped that it may be possible to take a biopsy in the near future.

## SUMMARY AND CONCLUSIONS

The case is presented of an individual who, from birth, has shown a marked insensitivity to pain. In the introductory approach to this case the main features are dealt with under the headings: (1) General history, (2) Medical history, (3) Interview material, (4) Neurological examination, (5) Electroencephalograph examination and (6) Psychological test examination.

This preliminary investigation reveals a history which gives a consistent picture of lack of response to pain. Neuro-

logical examination showed no evidence of organic neurological disease, such as syringomyelia, and indicated a defect which appears specific to pain. This examination also revealed the absence of corneal reflexes in both eyes. Psychological tests showed a person of superior intelligence (Wechsler-Bellevue IQ 128). No pronounced personality disorders appeared. The electroencephalographic examination revealed no pathological wave forms. Some evidence is given that the threshold for warmth in the subject is moderately elevated. Exploratory trials with hot water and the Hardy-Wolff thermal stimulator showed that the subject reports some of the pricky quality of heat, without showing any reaction of pain even at high intensities. It has also been noted that other "prick" sensations are reported such as commonly result from application of a pin or electric shock from an inductorium.

The most significant findings appear in the experimental results which showed a complete absence of physiological response to noxious stimuli in all measures used. These measures included recordings of blood pressure, heart rate and respiration, taken during two types of experiments: (1) Using noxious stimuli, (2) Using non-noxious stimuli. In the first type, cold water at $0^{o}$ - $2^{o}$ C., hot water at $49^{o}$ - $51^{o}$ C. and electric shock from an inductorium were used as pain-producing stimuli. In the second type, a size-discrimination test carried out under pressure of time, a mirror-drawing task and exercise with a hand dynanometer were used. Records of physiological response

were supplemented by noting the verbal report of the subject and by observation of overt behavior. The same procedures were followed with a group of control subjects.

The results show absence of pain on the part of the subject according to all three criteria of (1) report, (2) overt reaction and (3) blood pressure, heart rate or respiratory changes. The response shown by the control groups differentiates them, without exception, from the subject. On the other hand, the subject reacted as did the control groups to the non- painful type of stimulating conditions.

The findings of other workers using similar stimuli to produce pain are discussed. An interesting differentiation between this subject and similar cases reported in the literature (14) appears in the absence of such basic reactions as the cold pressor effect and the corneal reflex. These findings support the concept of an organic defect most probably located in the peripheral neural apparatus. The suggestions put forward by many workers with respect to the role of small, non-myelinated fibres in the mediation of pain are examined. Recent findings concerning the role of hypo-functioning in pain are also considered. Together they lead to the suggestion that the reduced pattern of afferent impulses characteristic of pain cannot be elicited in this subject. This could be due either to the unusual number, distribution or functional size of the smallest calibre fibres. The possibilities of central nervous dysfunctioning either in the cord, thalamus or cortex are discussed, but appear less probable in this case.

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TABLE I.

Average systolic blood pressure readings (mm. of Hg) during "cold pain" experiment.

| Period | Controls | Subject |
|---|---|---|
| Pre-Stimulation (Period A) | 115.0 | 117.4 |
| Early Stimulation (Period B) | 141.9 | 117.4 |
| Late Stimulation (Period C) | 128.1 | 115.4 |
| After Stimulation (Period D) | 115.2 | 114.2 |

TABLE II.

Individual heart rate variability during "cold pain" experiment.

| Individual | Maximum H.R. Reading | Minimum H.R. Reading | Average H.R. | Standard Deviation |
|---|---|---|---|---|
| Control | | | | |
| A | 93.0 | 64.5 | 78.0 | 7.38 |
| B | 100.5 | 75.0 | 85.1 | 6.09 |
| C | 102.0 | 84.0 | 93.1 | 3.63 |
| D | 94.5 | 75.0 | 84.0 | 5.37 |
| E | 90.0 | 64.5 | 75.4 | 6.62 |
| F | 94.5 | 48.0 | 71.2 | 14.9 |
| G | 102.0 | 73.5 | 83.4 | 7.15 |
| H | 114.0 | 61.5 | 79.0 | 11.9 |
| I | 90.0 | 58.5 | 71.9 | 6.96 |
| Subject | | | | |
| Trial I | 84.0 | 75.0 | 79.7 | 2.30 |
| Trial II | 100.5 | 90.0 | 92.9 | 2.75 |

TABLE III.

Average systolic blood pressure (mm. of Hg) during "hot pain" experiment.

| Period | Controls | Subject |
|---|---|---|
| Pre-Stimulation (Period A) | 121.9 | 118.5 |
| Early Stimulation (Period B) | 132.2 | 118.5 |
| Late Stimulation (Period C) | 127.6 | 117.9 |
| After Stimulation (Period D) | 123.4 | 117.1 |

TABLE IV.

Average systolic blood pressure readings (mm. of Hg.) during "electric shock" experiment.

| Individual | Period One Before Stimulation | Period Two During Stimulation | Period Three After Stimulation |
|---|---|---|---|
| Control | | | |
| A | 111.0 | 122.7 | 114.6 |
| B | 122.6 | 130.5 | 124.8 |
| C | 151.1 | 176.8 | 153.7 |
| D | 108.0 | 118.6 | 112.1 |
| E | 132.8 | 173.2 | 150.5 |
| F | 121.3 | 146.5 | 138.9 |
| G | 126.0 | 141.8 | 133.2 |
| H | 104.8 | 120.4 | 100.4 |
| Average of Controls | 122.2 | 141.3 | 128.5 |
| Subject | 118.6 | 119.9 | 117.6 |

FOOTNOTES.

1. Throughout this report the case exhibiting insensitivity to pain is referred to as the subject.

2. The reader is referred to Appendix I for historical review of literature on the nature of pain.

3. The author is indebted to Dr. F.L. McNaughton, Mrs. L. Ghent, Miss J. Coulter and Miss T. Gordon for their kind cooperation in this study.

FIGURE 1.

Photograph of subject taken during testing for corneal reflex.

FIGURE 2.

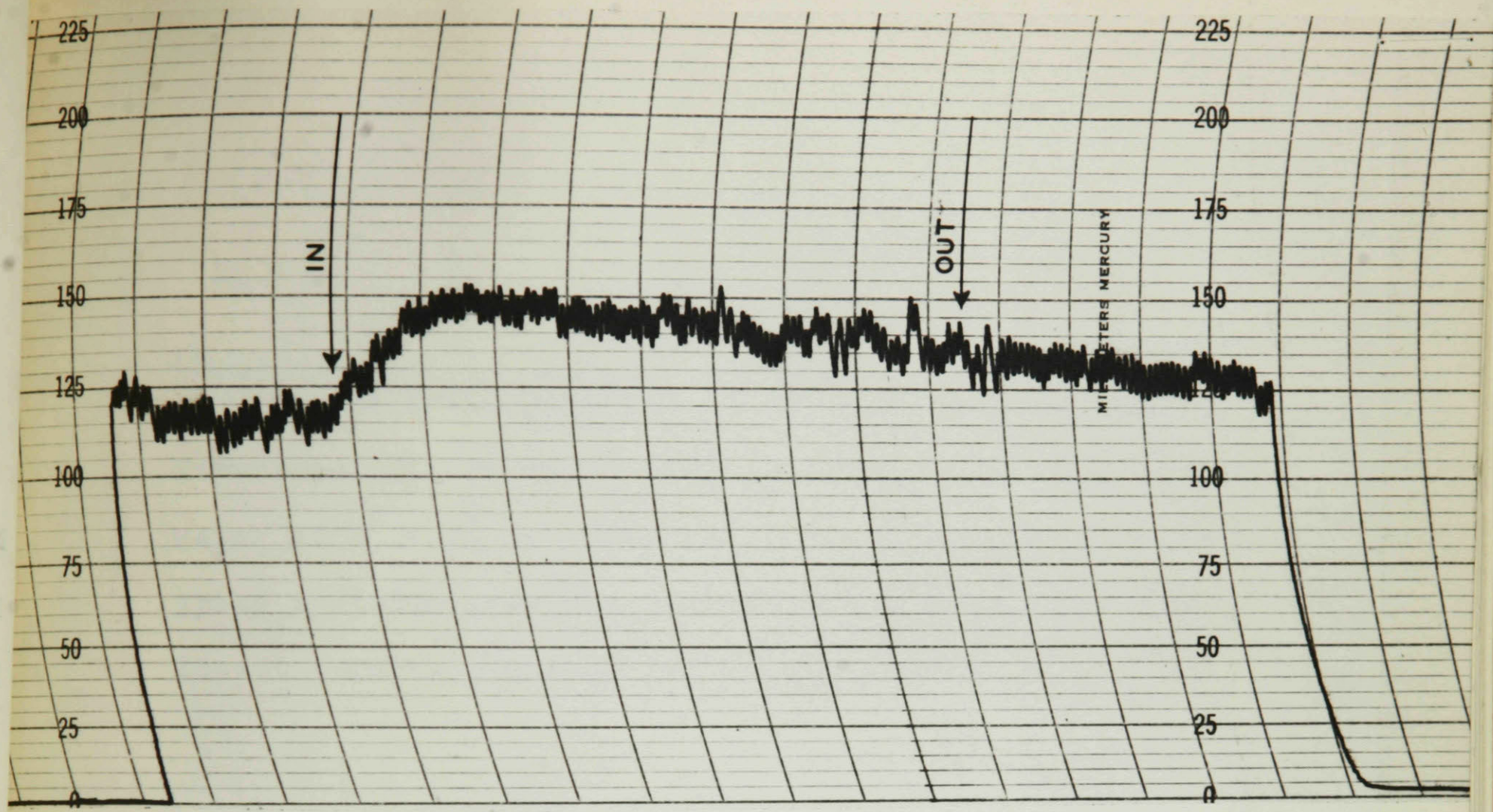
Photograph of subject taken during testing for corneal reflex.

FIGURE 3.

Systolic blood pressure record taken on control during Experiment I. IN marks the time of immersion of right hand in water at $0^{\circ}$ - $2^{\circ}$ C. OUT marks the time of withdrawal. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.

FIGURE 4.

Systolic blood pressure record taken on control during Experiment I. IN marks the time of immersion of right hand in water at $0^{\circ}$ - $2^{\circ}$ C. OUT marks the time of withdrawal. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.


225
200
175
150
125
100
75
50
25
0
IN
OUT
MILLIMETERS MERCURY

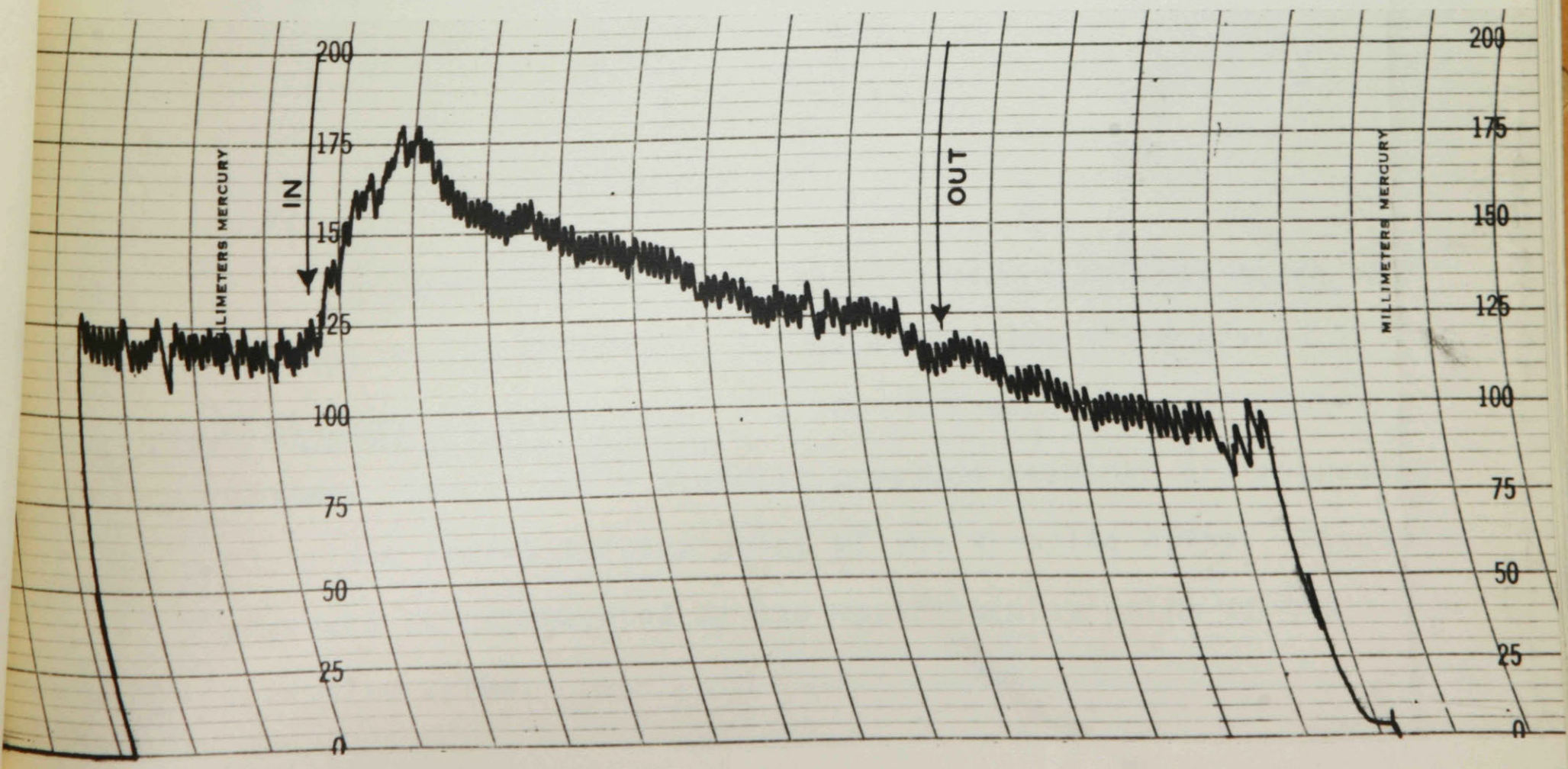
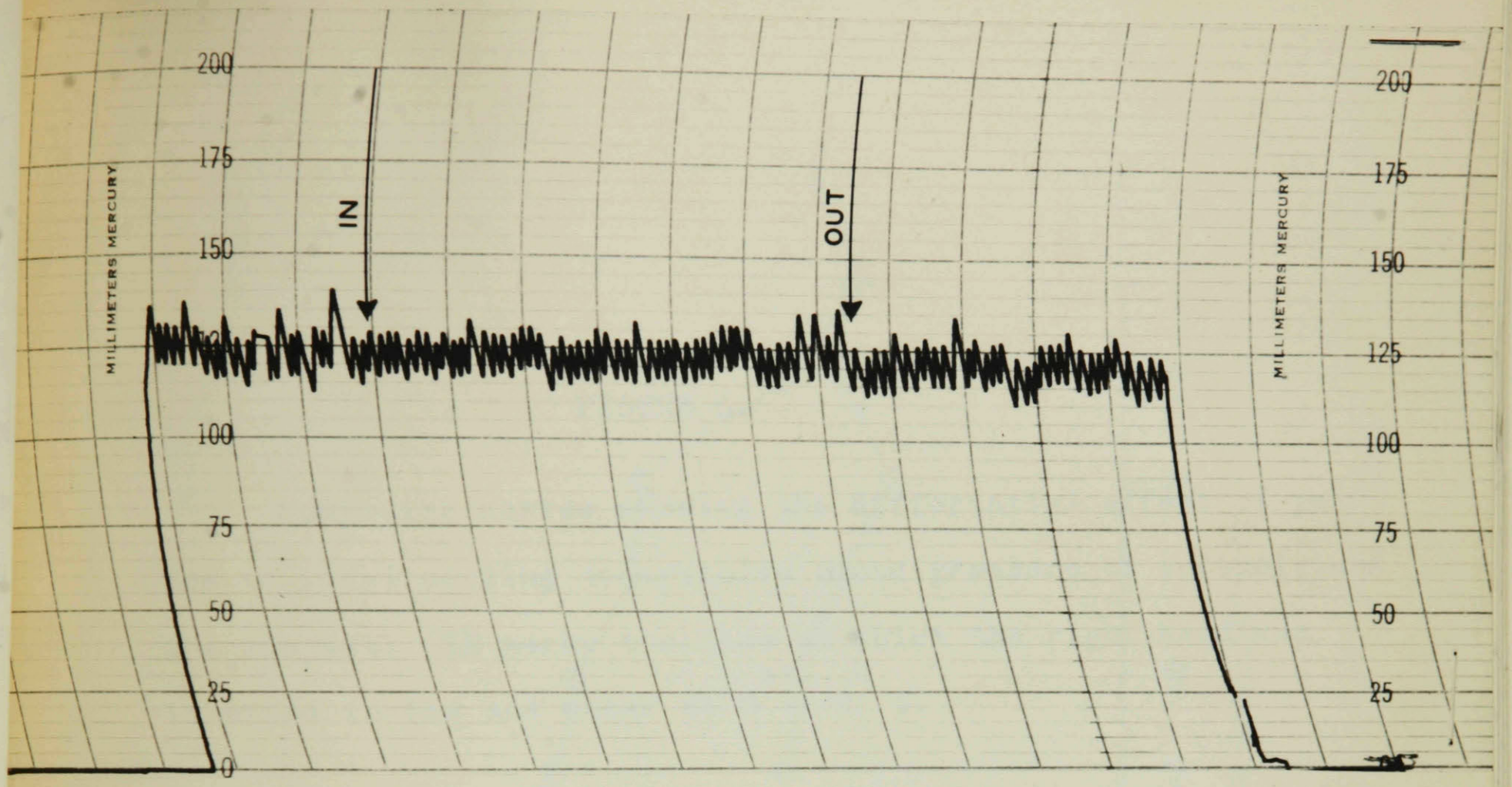

200
175
150
125
100
75
50
25
0
IN
OUT
MILLIMETERS MERCURY

FIGURE 5a

Systolic blood pressure record taken on subject during Experiment I. IN marks time of immersion of right hand in water at $0^{o}$ - $2^{o}$ C. OUT marks time of withdrawal. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.

FIGURE 5b.

Diastolic and systolic blood pressure records taken on subject during Experiment I. IN marks time of immersion of right hand in water at $0^{o}$ - $2^{o}$ C. OUT marks time of withdrawal. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike. Diastolic pressure is represented by the upper turning point of the diastolic spike.


200
175
150
125
100
75
50
25
0
IN
OUT
MILLIMETERS MERCURY

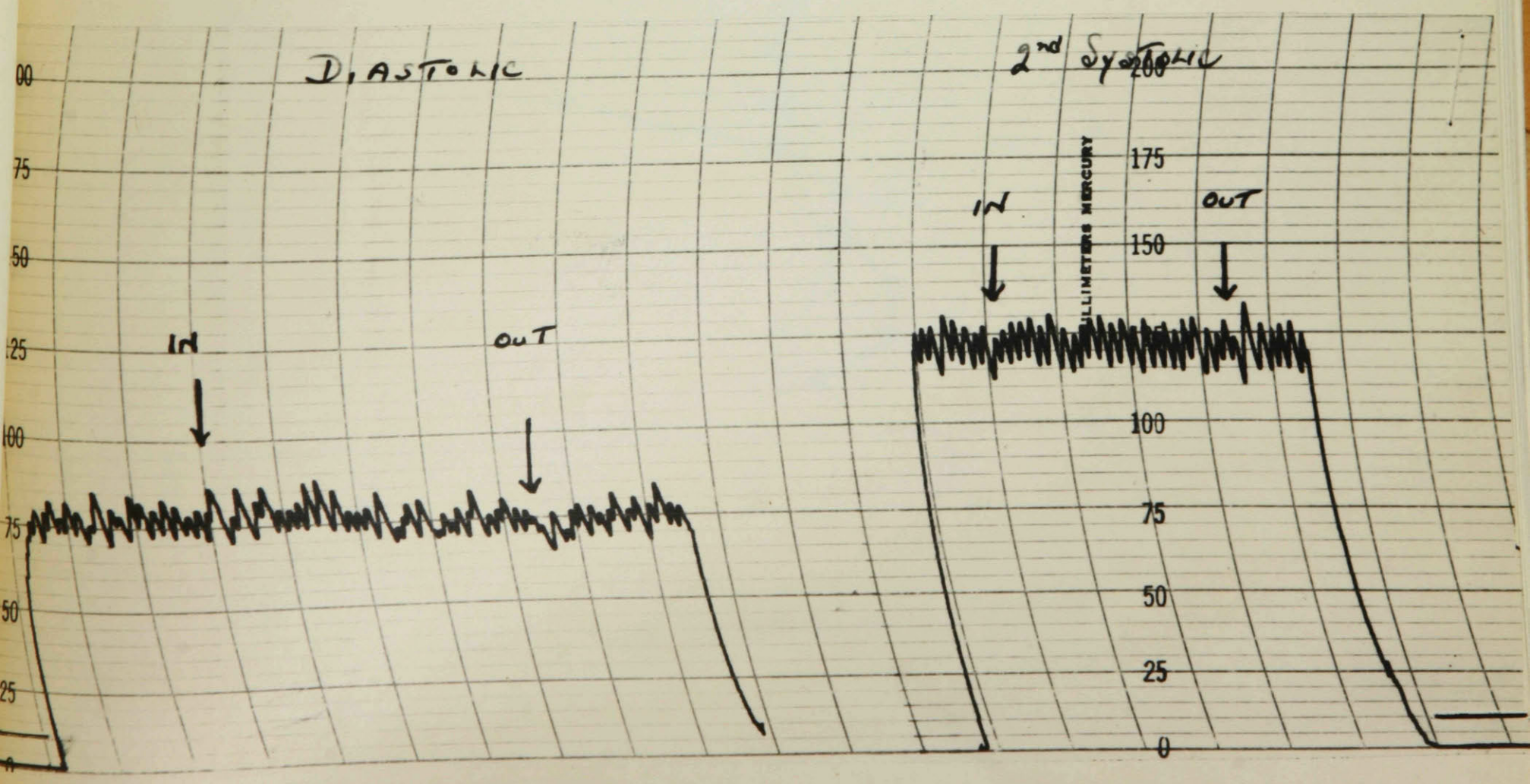
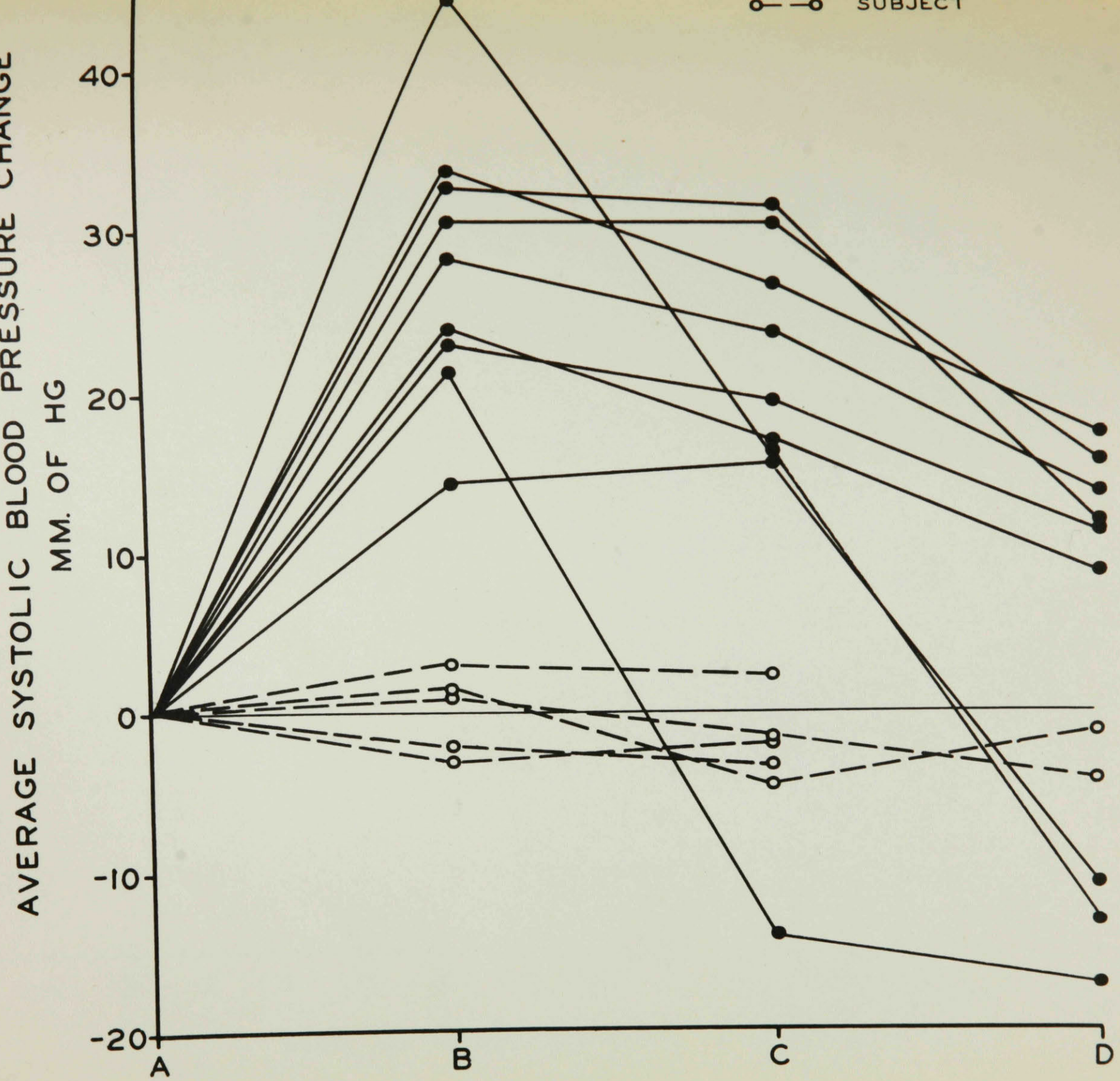

DIASTOLIC
IN
OUT
2nd Systolic
IN
OUT
MILLIMETERS MERCURY
200
175
150
100
75
50
25
0

FIGURE 6.

Composite curves showing the differential effect of pain due to local cooling on systolic blood pressure of controls and the subject. IN marks the time at which the right hand was immersed in ice and water at $0^{o}$ - $2^{o}$ C.


SUBJECT
AVERAGE SYSTOLIC BLOOD PRESSURE CHANGE
MM. OF HG
40
30
20
10
0
-10
-20
A
B
C
D
TIME SEGMENT

I.B.P. -C

FIGURE 8.

Composite curves showing the differential effect of pain due to local cooling on the heart rate of controls and the subject. IN marks the time at which the right hand was immersed in ice and water at $0^{o}$ - $2^{o}$ C.

CONTROLS

SUBJECT

HEART RATE

90

85

80

75

70

65

-8 -7 -6 -5 -4 -3 -2 -1 0 +1 +2 +3 +4 +5 +6 +7 +8 +9 +10 +11

IN

TIME IN MINUTES

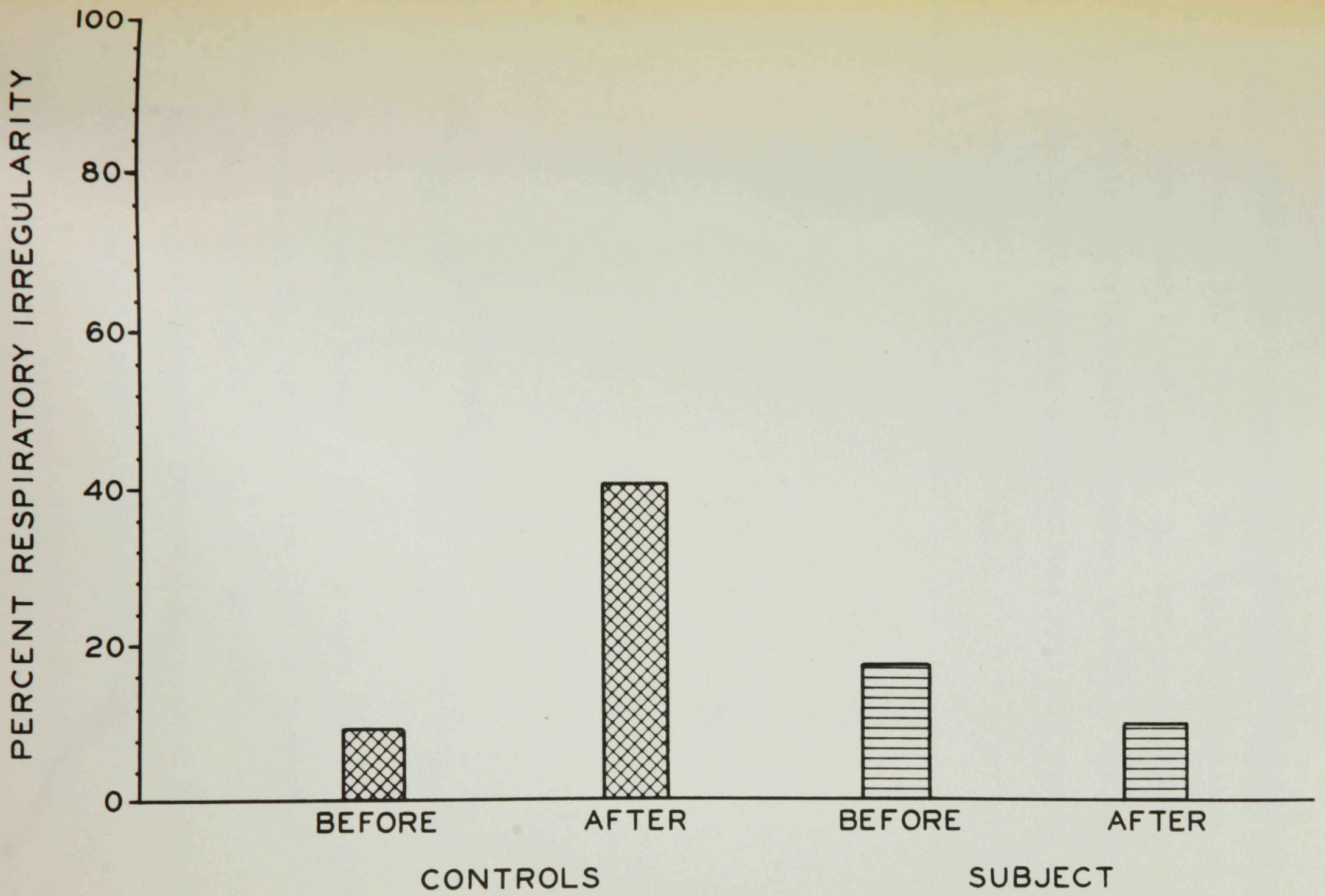
H.R.-C

FIGURE 9.

The effect of pain due to local cooling on the heart rate of (1) individual controls and (2) the subject during repeated trials. Time segment A represents a pre-period prior to the time of hand immersion in ice and water. B represents a period from the time of immersion until 1½ mins. later. C represents a period from 1½ mins. after immersion until the hand is withdrawn. D represents a period after withdrawal. All readings are averaged for the relevant period and plotted as absolute change from the pre-level average (A) which is taken as the base-line.

FIGURE 10.

The effect of pain due to local cooling on respiratory irregularity of controls and the subject. "Before" represents the period prior to the time of hand immersion in ice and water. "After" represents the period after the time of immersion until withdrawal.


PERCENT RESPIRATORY IRREGULARITY
100
80
60
40
20
0
BEFORE
AFTER
BEFORE
AFTER
CONTROLS
SUBJECT

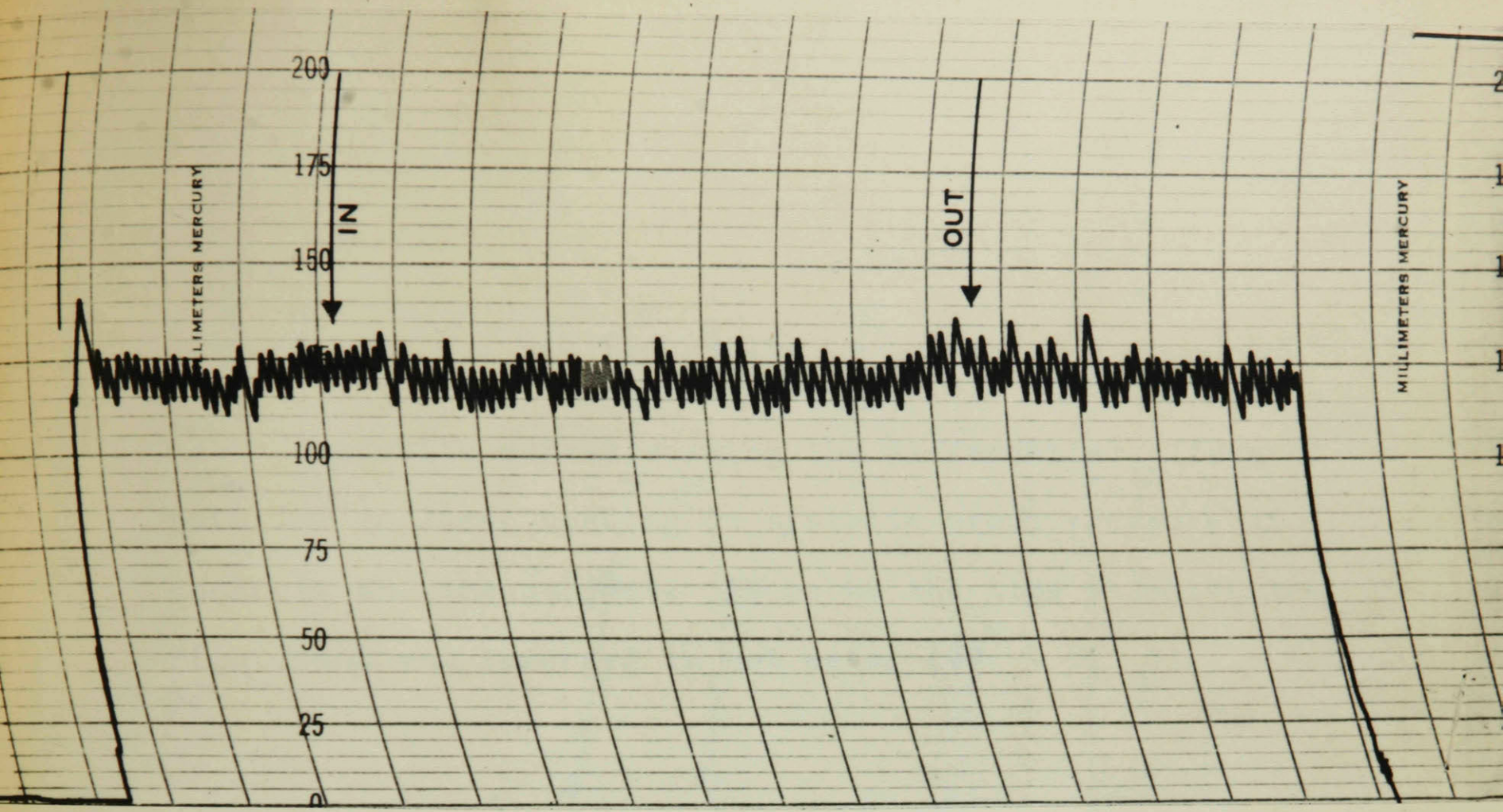
R.I. - C

FIGURE 11.

Systolic blood pressure record taken on subject during Experiment II. IN marks the time of immersion of right hand in hot water at 49° - 51° C. OUT marks the time of withdrawal. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.

FIGURE 12.

Systolic blood pressure record taken on a control during Experiment II. IN marks the time of immersion of right hand in hot water at 49° - 51° C. OUT marks the time of withdrawal. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.


200
175
150
100
75
50
25
0
IN
OUT
MILLIMETERS MERCURY

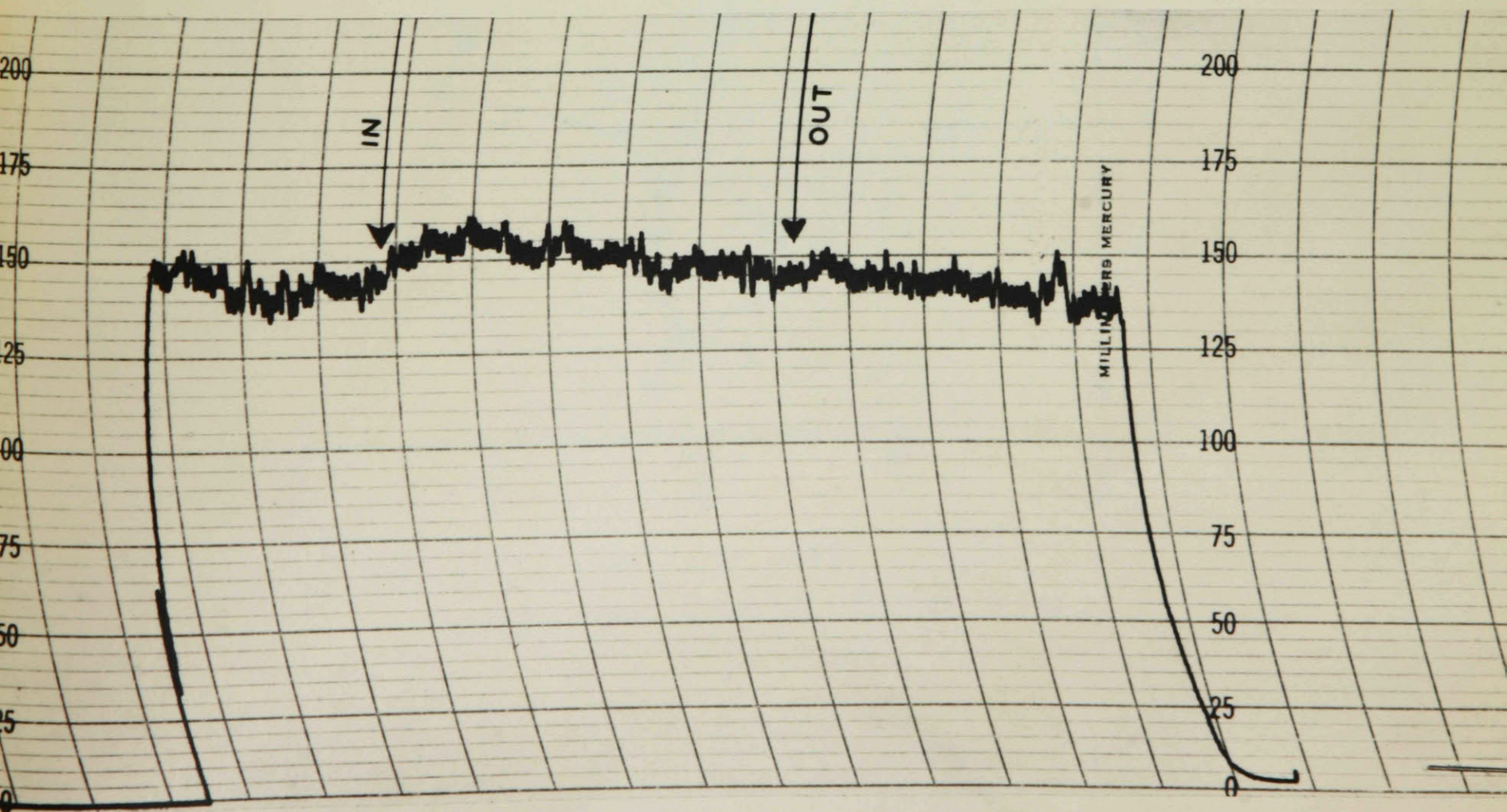
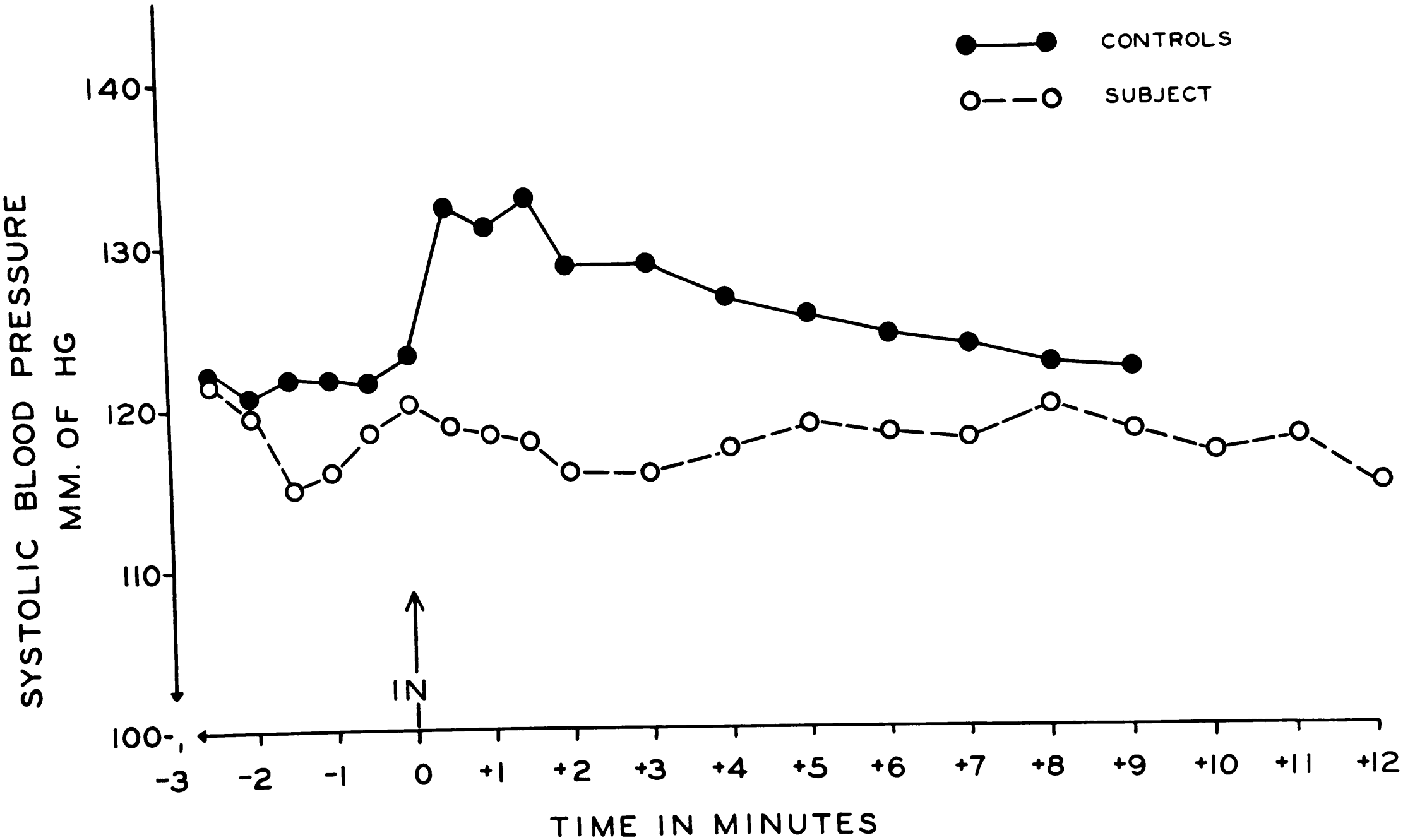

200
175
150
125
100
75
50
25
0
IN
OUT
MILLIMETERS MERCURY

FIGURE 13.

Composite curves showing the differential effect of pain due to local heating on systolic blood pressure of controls and the subject. IN marks the time at which the right hand was immersed in hot water ($49^{o}$ - $51^{o}$ C).


CONTROLS
SUBJECT
SYSTOLIC BLOOD PRESSURE
MM. OF HG
140
130
120
110
100
IN
-3
-2
-1
0
+1
+2
+3
+4
+5
+6
+7
+8
+9
+10
+11
+12
TIME IN MINUTES

B.P.-H

FIGURE 14.

The effect of pain due to local heating on the systolic blood pressure of (1) individual controls and (2) the subject during repeated trials. Time segment A represents a pre-period prior to the time of hand immersion in hot water. B represents a period from the time of immersion until $1\frac{1}{2}$ mins. after immersion until the hand is withdrawn. D represents a period after withdrawal. All readings are averaged for the relevant period and plotted as absolute change from the pre-level average (A) which is taken as the base-line.

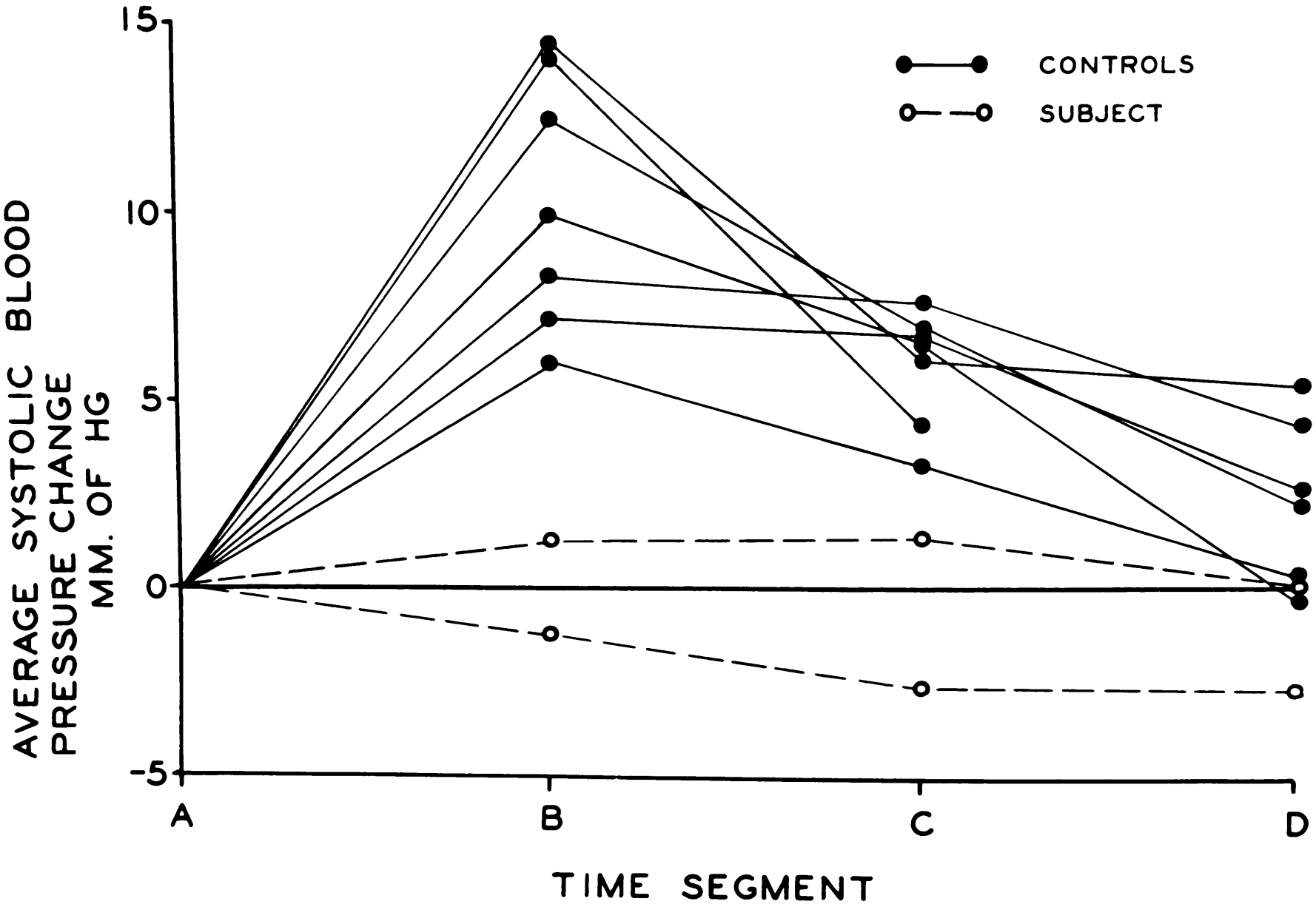
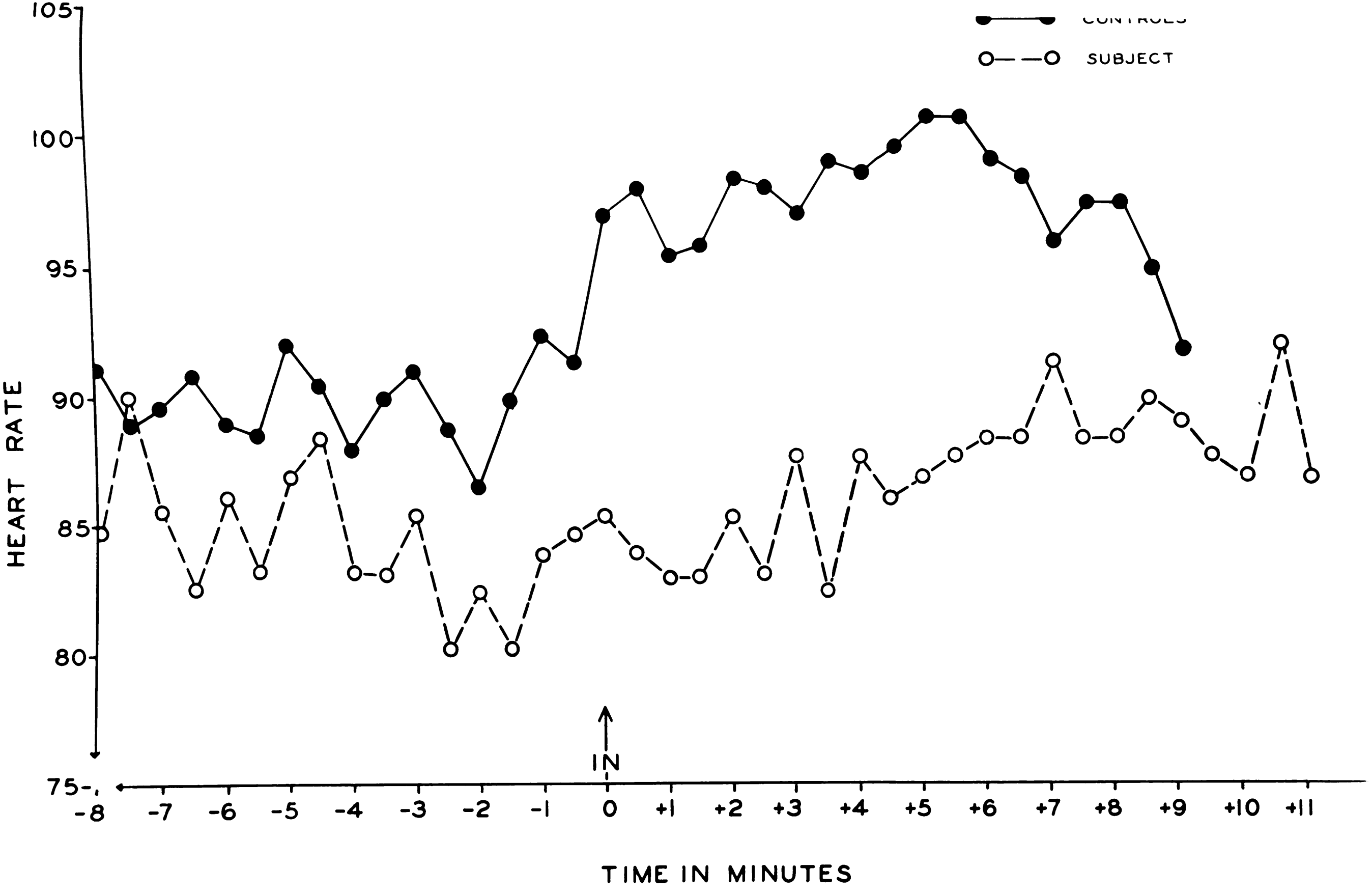

15
10
5
0
-5
AVERAGE SYSTOLIC BLOOD PRESSURE CHANGE MM. OF HG
CONTROLS
SUBJECT
A
B
C
D
TIME SEGMENT

FIGURE 15.

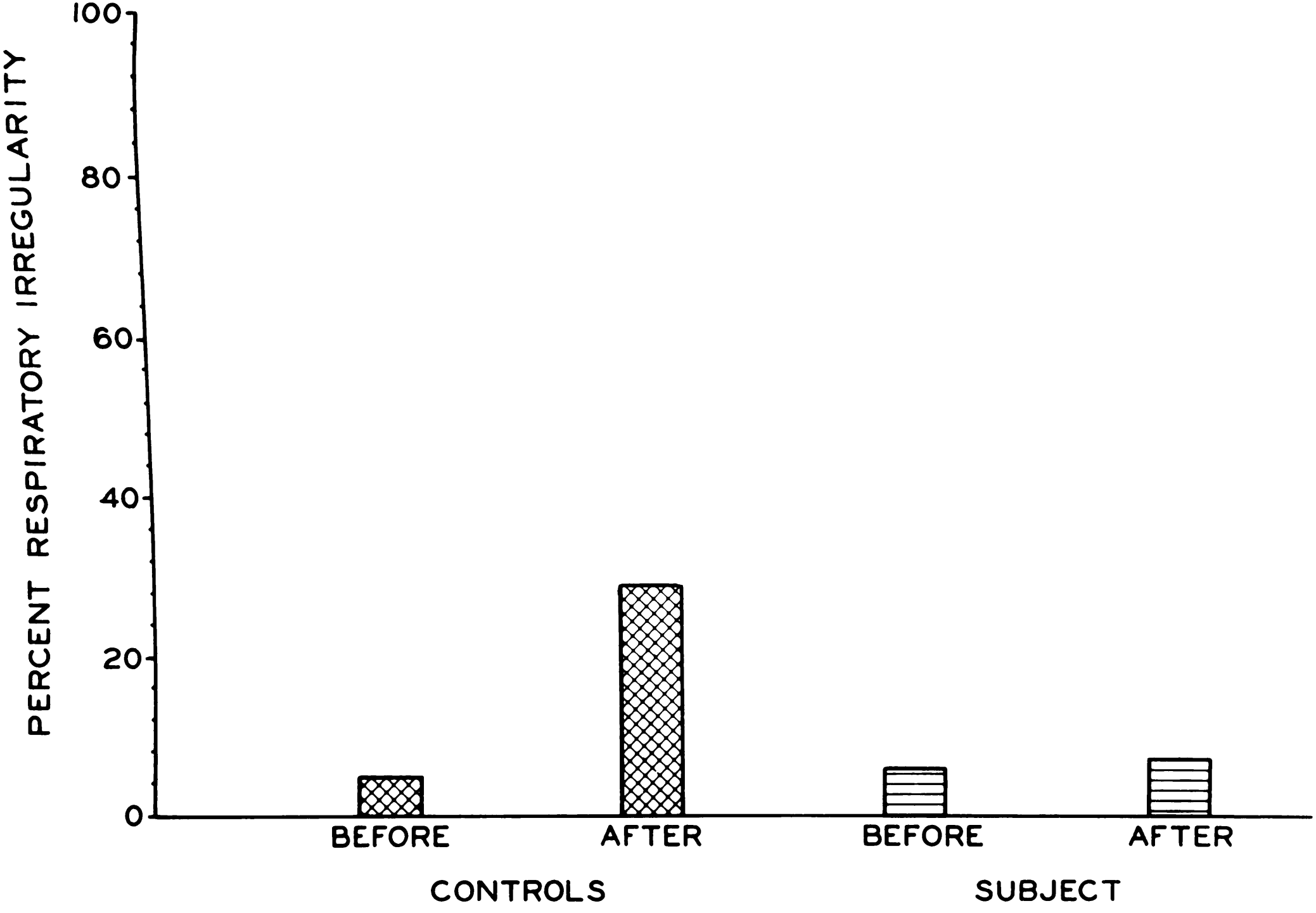
Composite curves showing the differential effect of pain due to local heating on the heart rate of controls and the subject. IN marks the time at which the right hand was immersed in hot water ($49^{o}$ - $51^{o}$ C.).


CONTROLS
SUBJECT
HEART RATE
105
100
95
90
85
80
75
IN
-8
-7
-6
-5
-4
-3
-2
-1
0
+1
+2
+3
+4
+5
+6
+7
+8
+9
+10
+11
TIME IN MINUTES

H.R.-H

FIGURE 16.

The effect of pain due to local heating on respiratory irregularity of controls and the subject. "Before" represents the period prior to the time of hand immersion in hot water. "After" represents the period after the time of immersion until withdrawal.


PERCENT RESPIRATORY IRREGULARITY
100
80
60
40
20
0
BEFORE
AFTER
BEFORE
AFTER
CONTROLS
SUBJECT

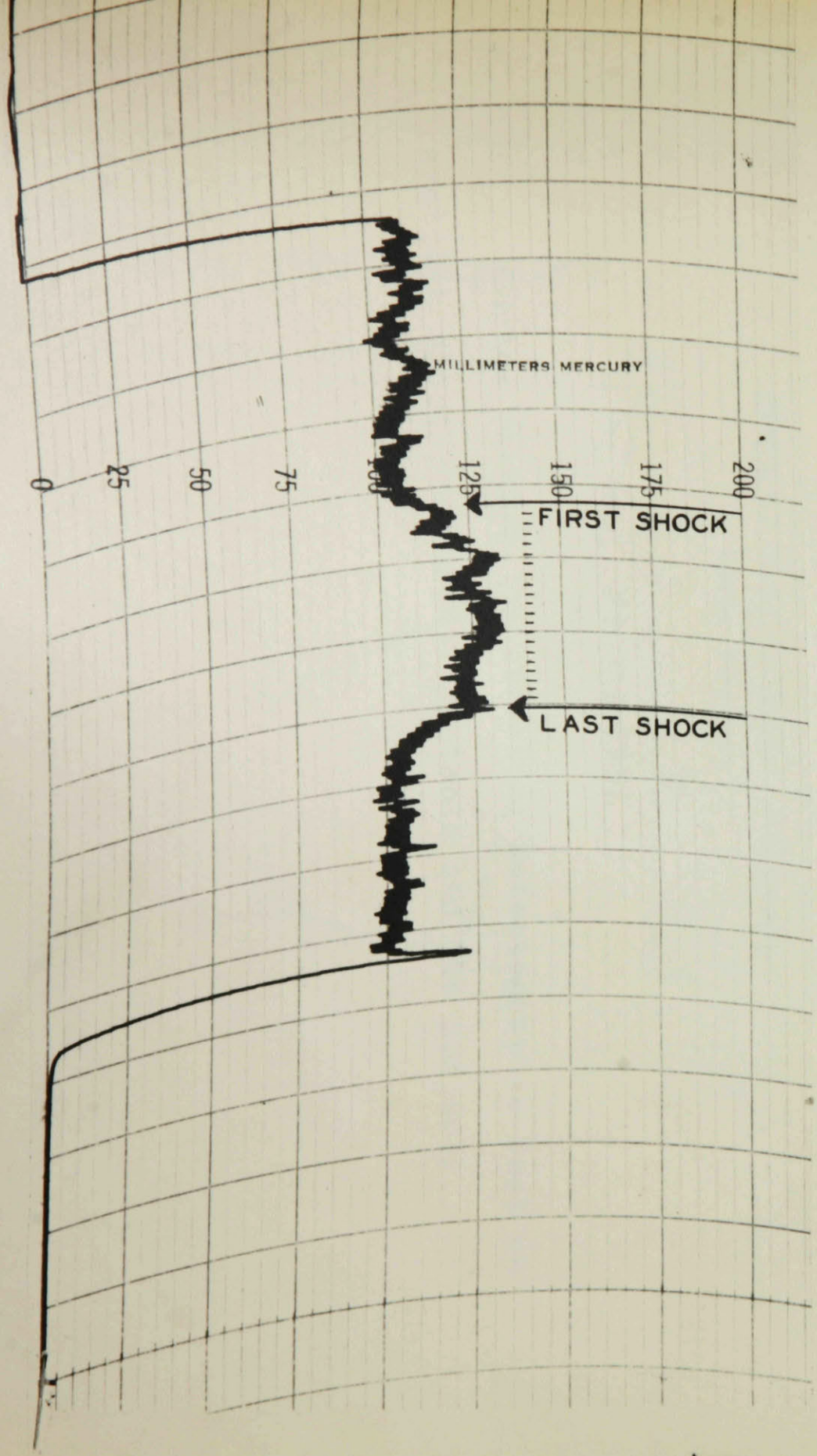
R.I.-H

FIGURE 17.

Systolic blood pressure record taken on subject during Experiment III. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.

FIGURE 18.

Systolic blood pressure record taken on control during Experiment III. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.


MILLIMETERS MERCURY
0
25
50
75
100
125
150
175
200
FIRST SHOCK
LAST SHOCK

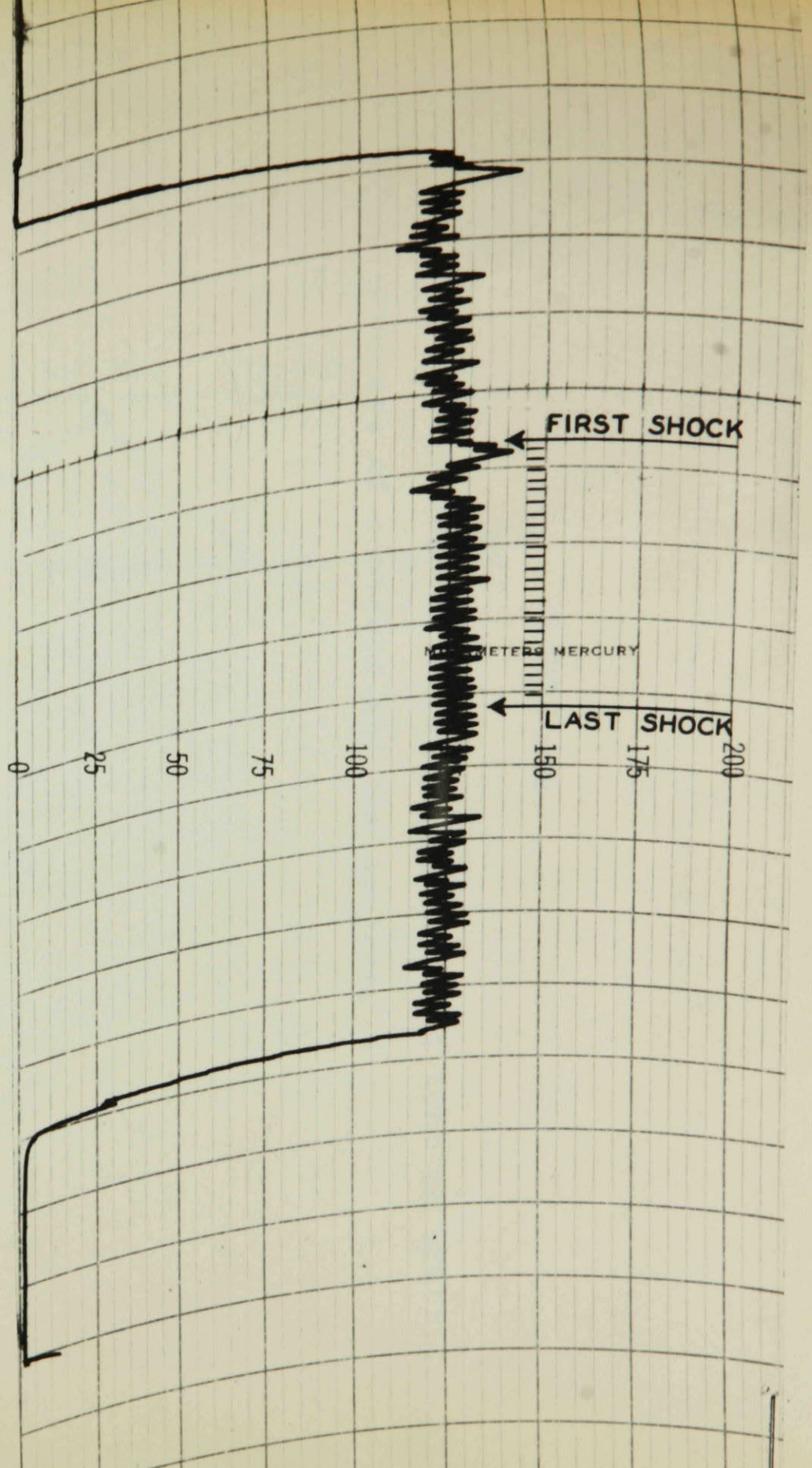
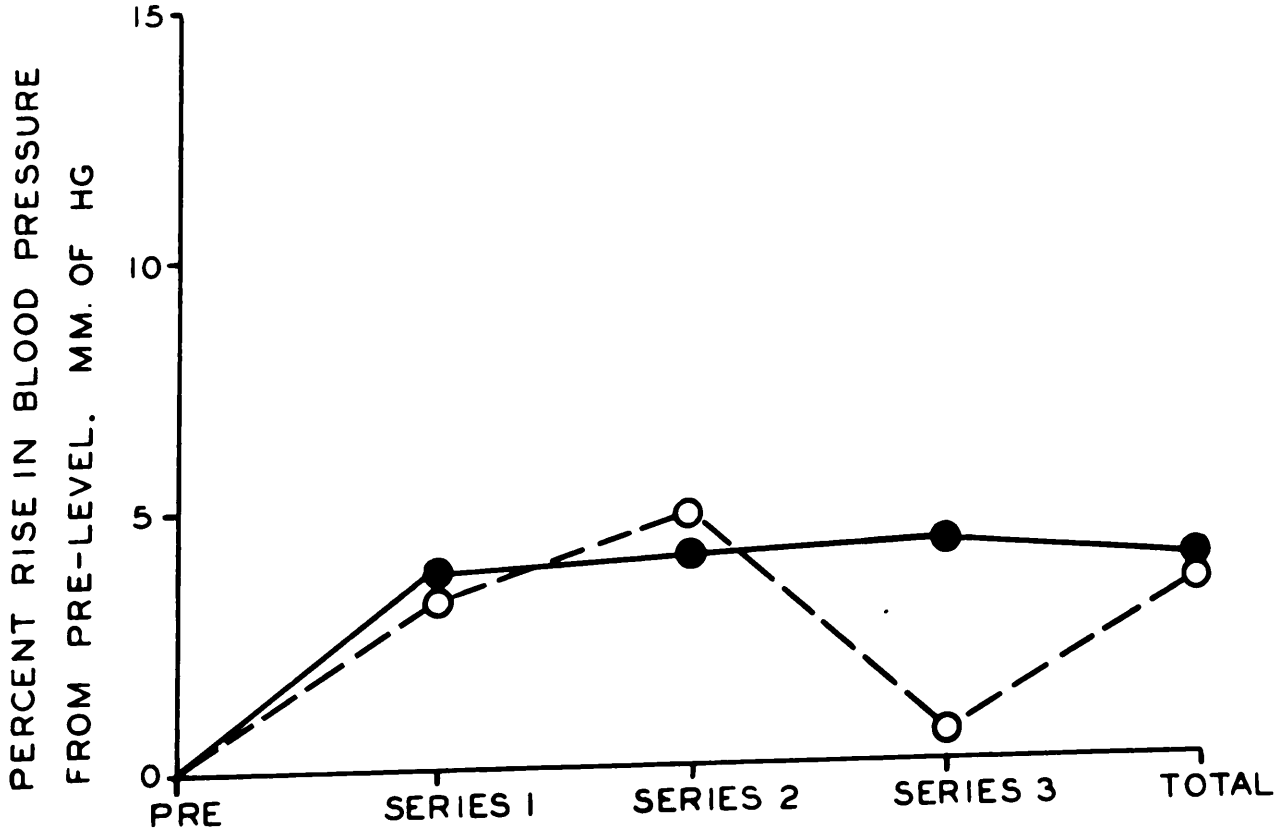

FIRST SHOCK
LAST SHOCK
0
25
50
75
100
150
175
200

FIGURE 19a.

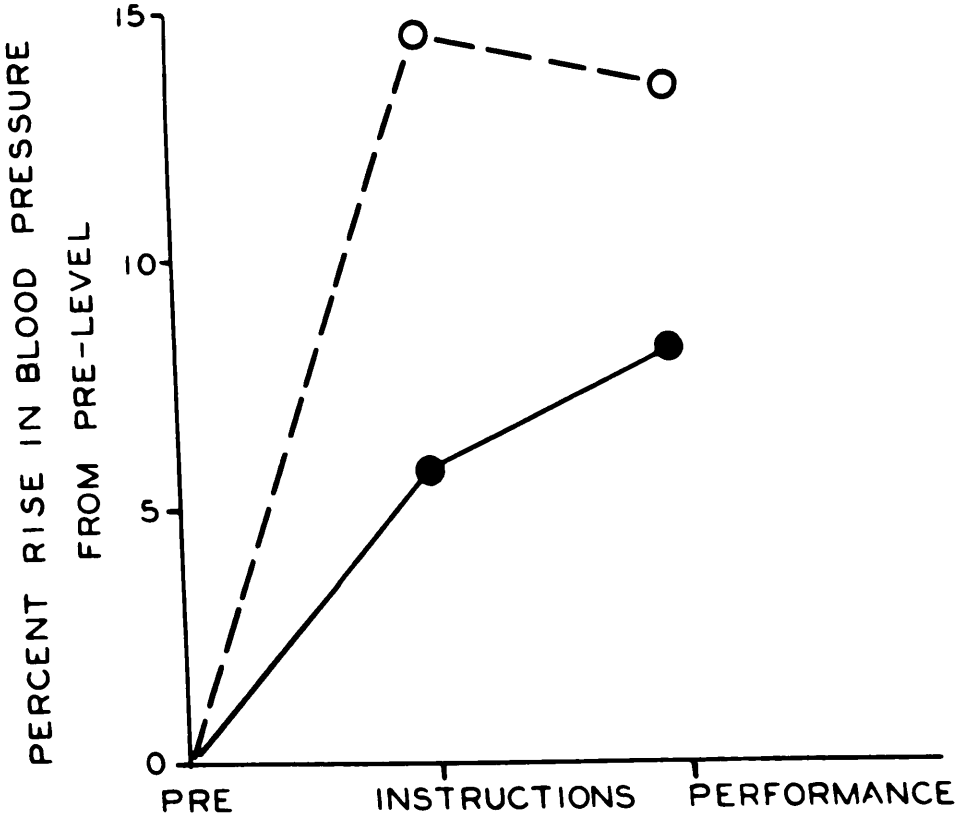
Curves showing the effect of Perceptual test on systolic blood pressure of controls and the subject.

FIGURE 19b.

Curves showing the effect of Katoptographic test on systolic blood pressure of controls and the subject.




PERCEPTUAL TEST




KATOPTOGRAPH TEST

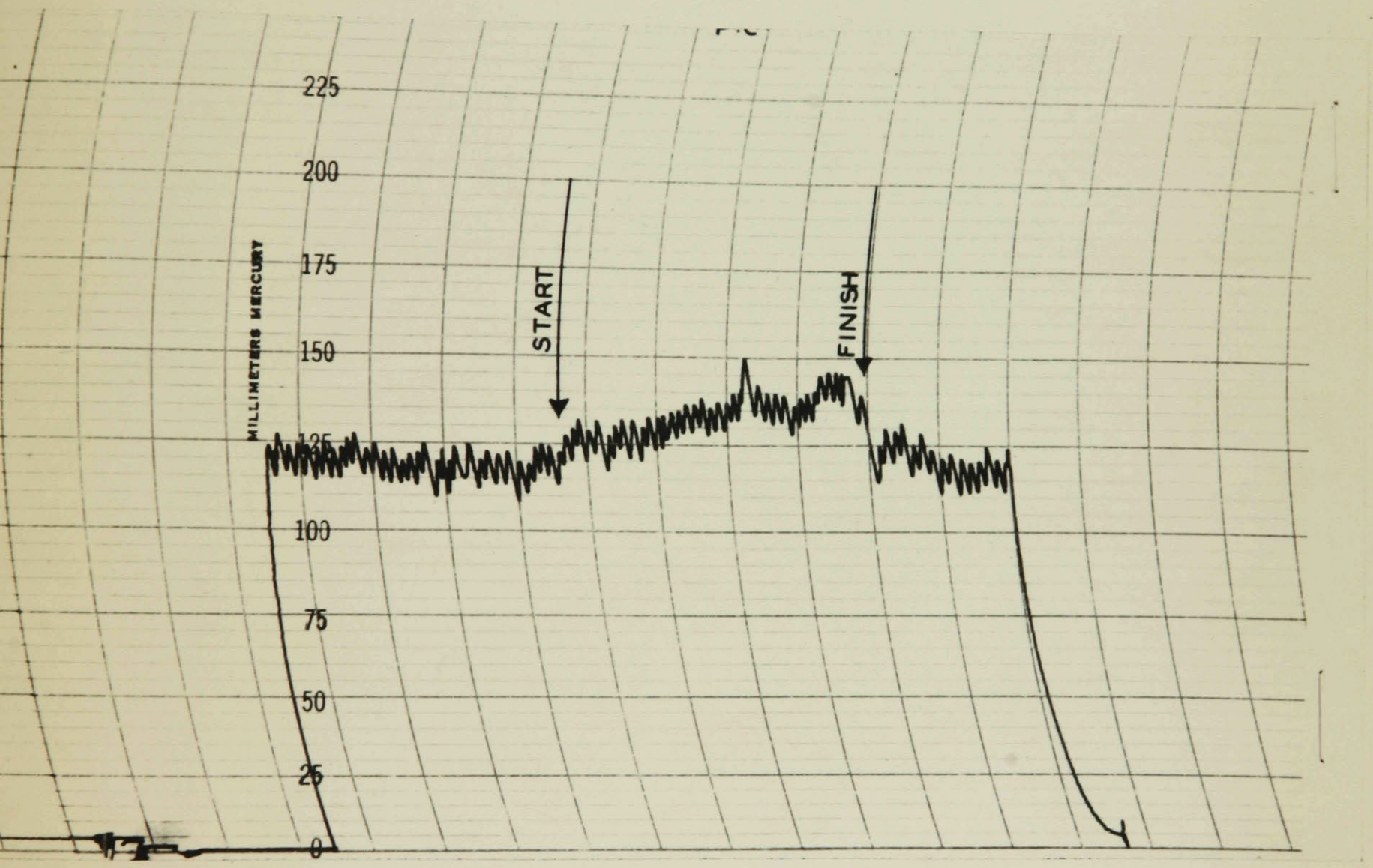
CONTROLS

SUBJECT

BP-PK

FIGURE 20.

Systolic blood pressure record taken on subject during exercise with dynanometer. Single spike systolic pressure readings are represented by the lowest turning point of the systolic spike.


225
200
175
150
125
100
75
50
25
0
MILLIMETERS MERCURY
START
FINISH