

THE IMPULSES PRODUCED BY SENSORY NERVE- ENDINGS. Part 4. Impulses from Pain Receptors.

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THE present investigation deals with the analysis of the impulses set up in cutaneous nerves by painful stimuli and compares the pain discharge with that of other receptors. The older view that pain resulted from excessive stimulation of any cutaneous receptor has been largely abandoned in favour of the idea of special pain receptors and conductors. The specific character of "pain" suggests that these receptors and conductors may differ considerably from those of the other types of cutaneous sensation. For instance, the "protopathic and epicritic" hypothesis of Head and Rivers demands that the nerve fibres concerned with pain must belong to a system phylogenetically distinct from those concerned with touch and the histological work of Ranson has added the view that the pain fibres may be non-medullated. Again, the pain receptor probably differs from many others in the absence of a capsule surrounding the axon termination and for this reason it has been suggested that the discharge of impulses from the pain endings may have some characteristic frequency or grouping of its own. These and similar possibilities can evidently be tested by recording the impulses produced in the afferent nerve fibres by a painful stimulus.

Preliminary observations⁽¹⁾ with the capillary electrometer and amplifier showed that it was possible to record the action currents set up in afferent nerves when the skin was pinched or pricked. The next step was to secure that not more than a few nerve fibres should be in action together so that each impulse might be recorded without interference. Apart from the use of nerves with very few fibres two general methods may be applied in any research of this character, namely (1) to restrict the stimulus to a very small area so that only a few receptors are stimulated; (2) to destroy or put out of action all but a few of the receptors or nerve fibres which will be affected by the stimulus. The former method is suited to the present case since a prick with a very fine needle will produce sensation which is clearly painful, but will scarcely stimulate

a large number of pain endings. The ideal site for the stimulus would be a region sensitive to pain but not to touch, *e.g.* the cornea or the glans, but considerable technical difficulty would attach to working with these regions and it was decided to use a more convenient area of skin surface, bearing in mind that the stimulus might set up impulses in other receptors besides those of pain. Most of the experiments were made on the spinal (decapitated) cat using the preparation of the internal plantar nerve employed by Zotterman and the writer(2) for the study of impulses due to pressure. A few confirmatory experiments were made on the frog; these although much easier to carry out present the disadvantage that we know little about the character of the sensations or sensation provokable from the frog's skin.

Stimulating apparatus. Two methods of stimulation were used. In both a prick was delivered by a fine needle (usually a gilt "entomological pin") clamped in the end of a vulcanite rod (*N*, Fig. 1). In the

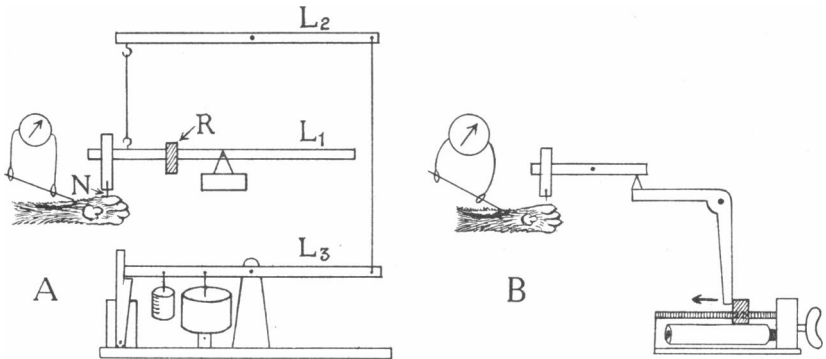


Fig. 1. Stimulating apparatus. A. Constant weight on needle. B. Needle pressed slowly through skin.

first method the rod is fixed at the end of a lever, L_1 , pivoted at its midpoint and carrying a rider R which can be moved so that the weight on the needle varies from 3 to 99 grm. The lever L_1 is connected by a string to another lever L_2 which in turn is connected to L_3 , an arm which can be moved up or down at a constant rate by a weight acting against the resistance of an oil dash pot. In the resting position L_1 is held so that the point of the needle is 1 cm. above the skin. When L_3 is released the needle is lowered smoothly at a rate of about 2 cm. per second and comes to rest on the skin with a weight determined by the position of the rider. When this apparatus is tested on the palmar surface of the finger tip a momentary sensation of touch is all that is produced when the weight on

the needle is only 3 grm. When it exceeds 30 grm. a sharp prick is felt and the duration and intensity of the pain increases with greater weights. In regions where the skin is more delicate pain may be felt with a much smaller weight than 30 grm. The advantage of the method lies in the fact that the stimulus can be graded to some extent by altering the weight, but it has the disadvantage of producing its greatest effect at the moment of contact, when touch as well as pain receptors may be stimulated.

In the second method (Fig. 1 *B*) the needle is pushed slowly into the skin. The rod holding the needle is fixed to a lever which is coupled to a long arm the end of which presses against the sound box carrier of a clockwork driven phonograph. When the phonograph is set in motion the carrier is moved forward slowly by a fine screw and the needle point moves downwards at a rate of 3-5 mm. per minute. In the resting position the needle is set so that its point is just touching the skin. When the finger tip is tested, an ill-defined sensation of contact is experienced when the clockwork is started but this soon gives place to one of pain which becomes more and more intense as the needle is driven deeper into the skin. The pain diminishes slowly after the movement is stopped. This method has the advantage of giving a gradually increasing stimulus and of giving one which is bound in the end to be painful however tough the skin may be.

A. *Experiments on cats.*

The experiments on cats will be described first. The animal was decapitated under chloroform anæsthesia and the hind limbs were immobilised by nerve section. The medial branch of the internal plantar nerve was dissected out as far down as the point where it is crossed by a small blood vessel about 1 cm. from the end of the toe. The upper end of the nerve was cut just below its entry into the main trunk of the internal plantar. A diagram of the nerves concerned is given in Part 3 of the present series. The nerve supplies the skin on the medial side of the inner toe; the skin on the side of the toe pad is hairless and not very tough and it was in this region that the stimulus was applied. The hairs in the neighbourhood were all cut short.

The animal was placed on an insulated stand inside the metal preparation box and the leg was fixed to a smaller stand carrying the electrodes. The lateral side of the inner toe was supported by a rigid platform to prevent it moving under the pressure of the needle. The interior of the preparation box was warmed; the nerve was constantly irrigated with Ringer at 37° C. and between the observations it was taken off the

electrodes and covered with lint soaked in Ringer and kept warm by a small carbon lamp 2–3 cm. away. With these precautions the nerve usually remains in good condition for more than an hour.

Twelve animals were used and in all of them occasional impulses passed up the nerve in the absence of any kind of stimulation. The frequency of this “resting” discharge is low (5–40 per second) when the preparation has been set up for ten minutes or more, but may be very high in records taken immediately after the dissection is finished. Fig. 2 shows the confused medley of action currents obtained just after

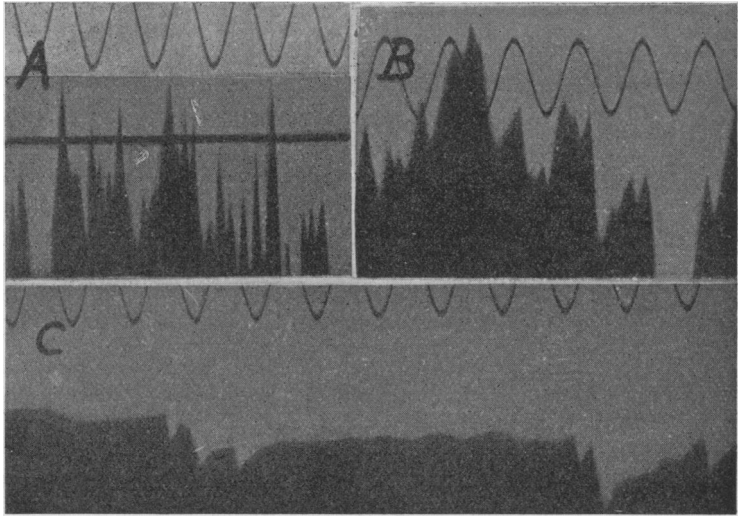


Fig. 2. “Resting” discharge from medial branch of Internal Plantar nerve (cat). A. Exp. 4. Preparation just set up. No stimulation. B. Exp. 1. Preparation just set up. No stimulation. C. Exp. 1. Ten minutes later.

the preparation is set up and the much lower frequency ten minutes later. This initial discharge is presumably due either to pain impulses arising from damage to the skin in the region supplied by the nerve or to the stimulation of other receptors (*e.g.* hairs, temperature, etc.) by the new conditions to which the foot is exposed. After the initial discharge has subsided the resting frequency usually remains at constant value or declines progressively. It has never shown a marked rise in the absence of stimulation.

Results. The film records given in Fig. 3 (Exp. 2) show the nature of the discharge produced by the first method of stimulation (needle

lowered on to skin and allowed to remain there with constant pressure). The dark signal line merely records the movement of the lever L_2 and

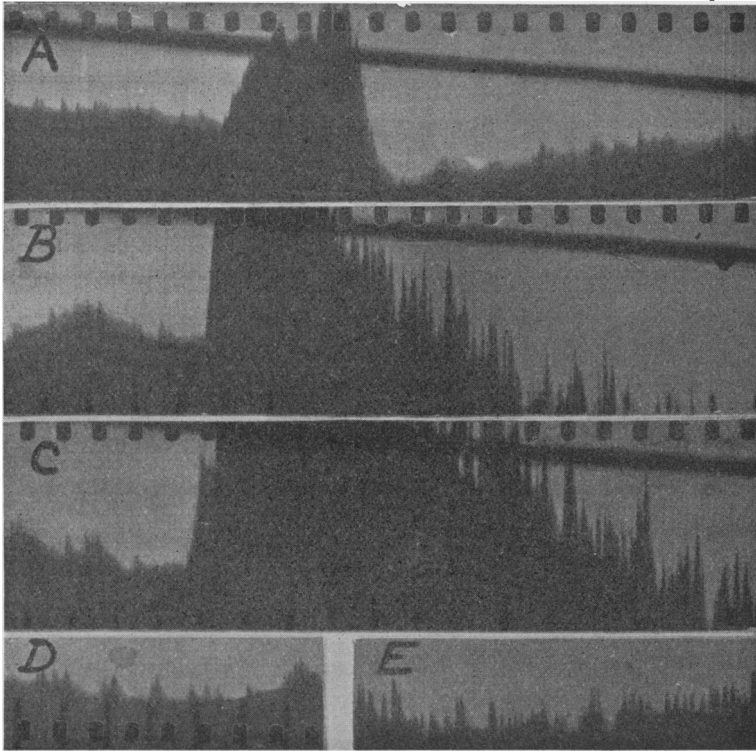


Fig. 3. Exp. 2 (cat). Stimulation by first method (constant weight). Time marker gives $\frac{1}{10}$ second intervals. *A.* Weight on needle 3 gm. *B.* Weight on needle 43 gm. *C.* Weight on needle 99 gm. *D.* Resting discharge before stimulation (same record as *C*). *E.* Same record as *C*. 18 seconds after beginning of stimulation.

does not give the actual moment at which the needle touches the skin, but this last is very clearly signalled by the sudden outburst of impulses in the nerve. There is a resting discharge at a rather higher frequency than usual (about 40 a second) and in the top record, where the weight on the needle is only 3 gm., the contact of the needle with the skin gives an increased frequency of discharge which only lasts for .15 second.

When the weight is increased to 43 and 99 gm. (Fig. 3 *B* and *C*) a persistent discharge is set up, and Fig. 3 *E* shows that the frequency is still considerably above normal after the needle has remained in position for 18 seconds. At the height of the discharge there is great overlapping

between impulses in different fibres and the total frequency is difficult to state correctly, but within a second after the moment of contact the overlapping is much less and the frequency has fallen to 150 per second. The decline in frequency is shown in Fig. 4 which gives the total fre-

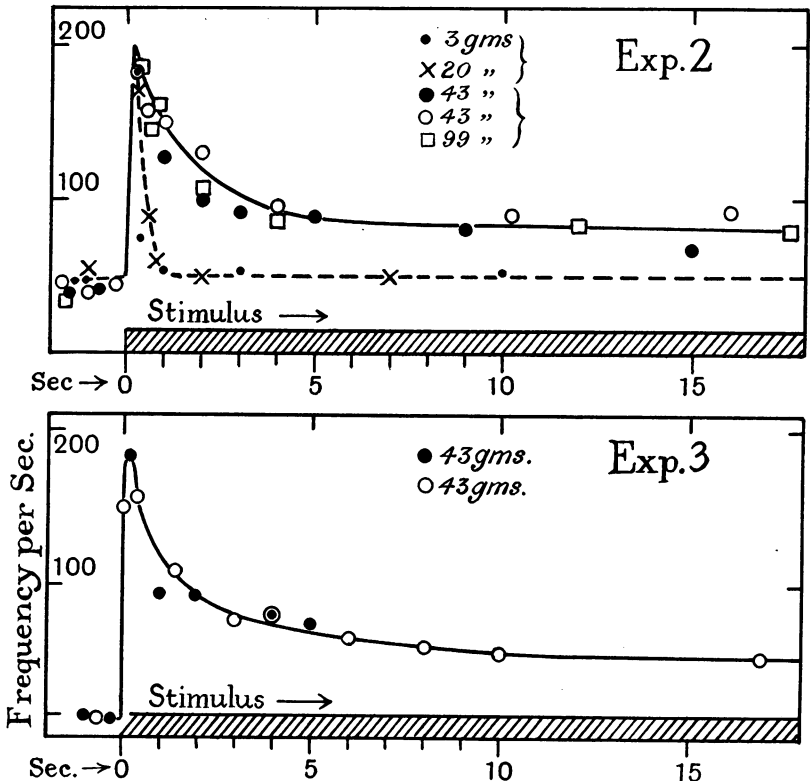


Fig. 4. Decline in frequency of discharge with constant stimulus.

quencies per second in Exps. 2 and 3 with this form of stimulation. The value given for the maximal frequency (200 per second) may be too low but this figure was not exceeded in records on fast moving plates made within $\frac{1}{2}$ second of the moment of contact.

In Exp. 2, it will be seen that the curves fall into two groups. When the weight on the needle is 3 gm. or 20 gm. the discharge has returned to its initial ("resting") frequency within a second, when the weight is 43 or 99 gm. the frequency declines much more slowly and has not returned to the initial value in 20 seconds or more. This grouping is probably related to the fact that on the finger the smaller weights give

only a momentary sensation of touch whereas the larger give a more persistent sensation of pain. Stimuli with 43 or 99 grm. cause a brisk flexion in the spinal cat with nerves intact and with 99 grm. the point of the needle was found to have penetrated the skin 1 mm. or more. Thus the majority of the impulses set up by the strong stimuli after the first second are probably due to the stimulation of pain receptors.

Since the total frequency after one second of stimulation is not more than 200 per second at most, the number of impulses discharged in a second in each nerve fibre cannot be higher than this. The impulses might perhaps be discharged at a much higher frequency in very short bursts with pauses in between, but there is no indication of this in records taken on rapidly moving plates. An example of such records is given in Fig. 5 *A*; it will be seen that the impulses occur without characteristic spacing.

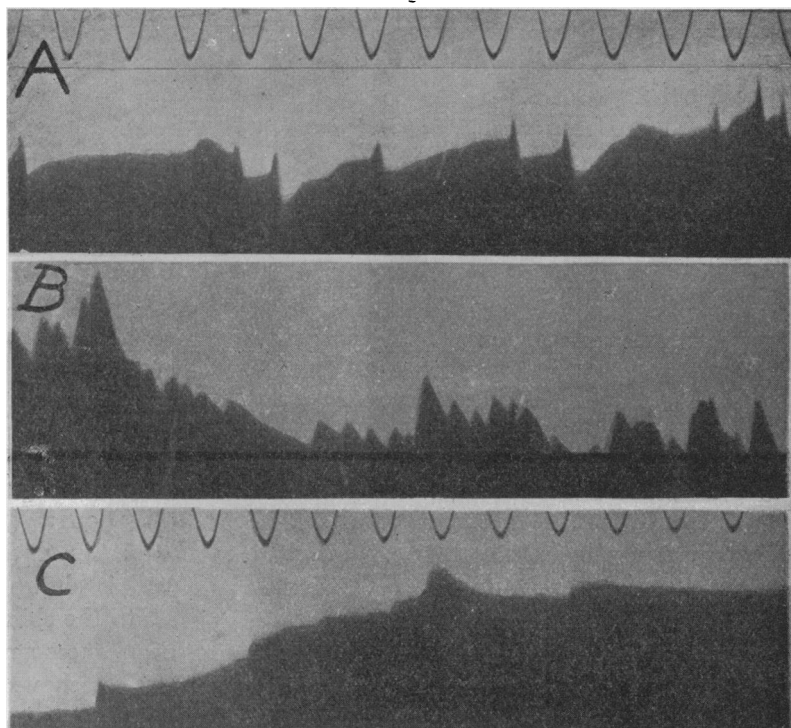


Fig. 5. Plate records (cat). Time marker gives $\cdot 01$ second intervals. *A*. Exp. 4. Stimulation by first method. 34 grm. weight for half second. Diphasic action currents. *B*. Exp. 5. Stimulation by second method. Needle driven in slowly for 20 seconds. Monophasic action currents. *C*. Exp. 5. Before stimulation.

More decisive information is given by the second method of stimulation in which the needle is pushed slowly through the skin; in this case there can be no question but that most of the impulses arise from pain receptors. Fig. 6 (Exp. 5) shows the evolution of the discharge under

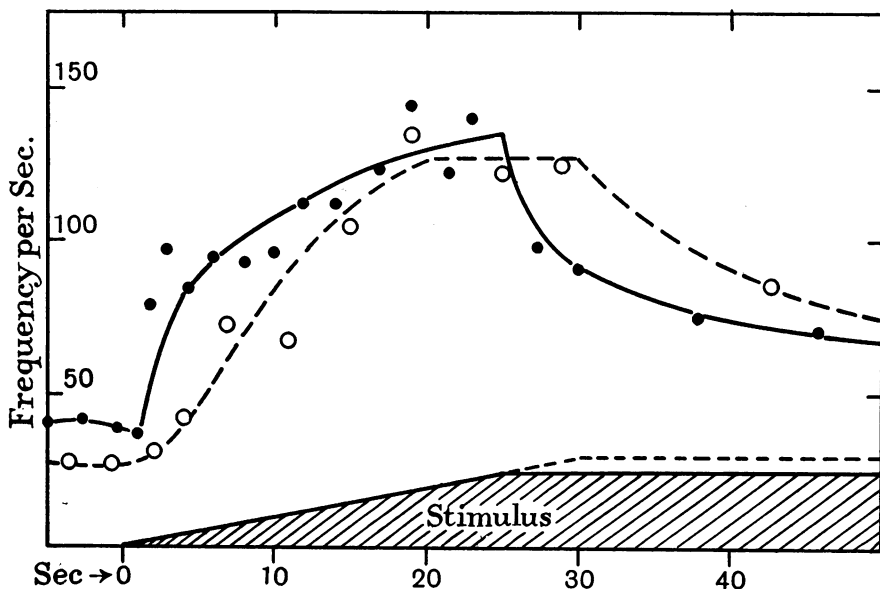


Fig. 6. Exp. 5. Gradual increase in frequency as needle is driven into skin.

this method, the curves being constructed from two continuous film records. The frequency of discharge rises gradually from the resting value and after the downward movement of the needle has proceeded for 20 seconds the frequency reaches a more or less steady value of about 140 per second. It is difficult to count this in the film records owing to the crowding together of the impulses, and records taken on rapidly moving plates at 20 seconds from the beginning of stimulation gave a higher frequency, 180–200 per second. One such record is shown in Fig. 5 *B*. Since the needle has penetrated .5 to 1 mm. into the skin in 20 seconds and since with the finger-tip under like circumstances acute pain is reached at that stage, the majority of the impulses shown in Fig. 5 *B* are certainly due to pain receptors. Indeed the curves in Figs. 4 and 6 giving the rise and decline in the frequency of the impulses are in surprisingly close agreement with the rise and decline in the pain sensation produced by the two forms of stimulation applied to the tip of the finger.

Time relations of pain impulses. The view that pain impulses are carried by nerve fibres different in character from those subserving other species of sense suggests that possibly the time-relations of the individual impulse may be different. In particular, if the pain fibre is non-medullated the rise and decline of the "pain" impulse should be much the slower. The time relations of a typical pain impulse may be determined from an analysis of the monophasic responses recorded when the needle is thrust slowly into the skin. Fig. 5 B gives a record of this kind and an analysis of two of the impulses is shown on an extended time scale in Fig. 7. For comparison with it an analysis is given of mono-

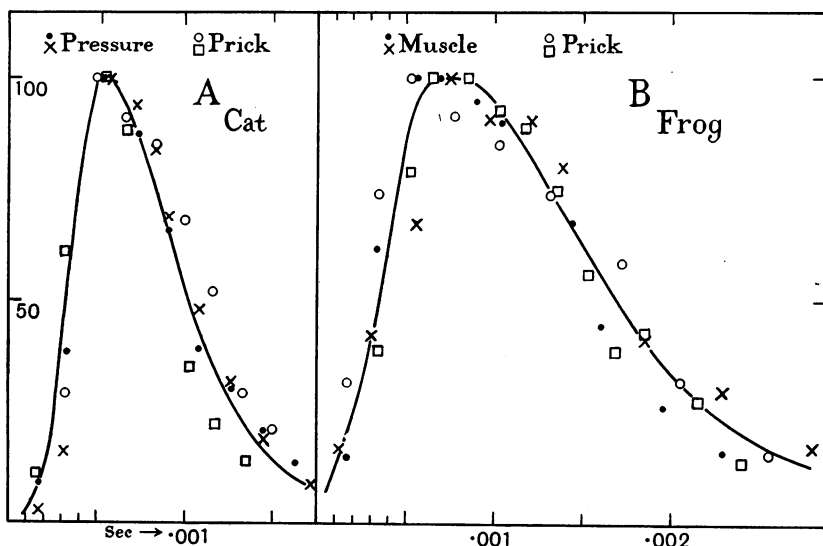


Fig. 7. Time relations of impulses produced by different receptors in the frog and cat. All monophasic. Temperature in frog experiments between 12 and 14° C.

phasic impulses taken at random from the records of Zotterman and the writer with the same preparation stimulated by pressure. The pressure in this case was 200 gm. on a disc 11 mm. in diameter and it is very unlikely that this would produce a sensation of pain. Yet the two impulses clearly agree within the limits of experimental error and their duration is much shorter than one would expect from non-medullated nerve fibres. It is difficult to assess the limits of error in these measurements since so much depends on the accuracy of the analysis, but the time relations shown in the figure agree fairly well with those given by

Erlanger and Gasser⁽³⁾ using the cathode ray oscillograph. The latter have shown⁽⁴⁾ that there may be considerable differences in the rates of conduction in different afferent fibres although the duration of the action current is much the same in all. It is therefore quite possible that the pain fibres may possess a distinctive conduction rate in spite of the agreement in the action currents in Fig. 7.

As may be seen from the photographs (Fig. 5), there is very little variation in the duration of different impulses. In certain records there are occasional excursions with a duration about twice as long and an amplitude (when analysed) about one-fifth as great as that of the usual impulses. These have been met with in records of moderate pressure as well as in those of pain and they are not more frequent with painful stimuli. When present their frequency is low (*e.g.* 20 per second). They can scarcely be due to impulses travelling in incompletely recovered nerve since they may occur by themselves in a quiet period. It is possible that they may be identical with the "delta" process of Erlanger, Bishop and Gasser⁽⁵⁾. Whatever they are there is no reason to suppose that they are the typical product of the pain receptors in the skin.

Grouping of impulses. As far as the grouping of impulses is concerned there is nothing to distinguish a discharge of pain impulses from that of impulses due to moderate pressure. In both the total frequency will depend on the number of receptors in action, but if the area covered by the stimulus is such that the total frequency is about 150–250 per second the records would be indistinguishable. This may be seen from a comparison of the present figures with those given in Part 3. In both the impulses are more or less evenly spaced and show little variation in amplitude apart from the larger excursions made up of two or three impulses occurring simultaneously. When two impulses are very close to one another the second is never markedly smaller than the first as it would be if both occurred in the same fibre and there is no sign that the discharge ever takes the form of a rapid series of impulses in each fibre followed by a pause and then another rapid series in the same fibre. Regular rhythms have been observed in two only of the experiments. In one (Exp. 4) a prick of 20 grm. weight applied for 1 second gave a regular series with a period of $\cdot 03$ per second and the same stimulus applied for 5 seconds gave a regular period of $\cdot 037$ per second. Both records contain other impulses which cannot be grouped into regular series. In the other experiment (Exp. 6) there were periods of $\cdot 029$ and $\cdot 04$ second in the same record taken when the needle had been resting

on the skin with a weight of 43 grm. for 20 seconds. In the same preparation a weight of 8 grm. for 3 seconds gave a regular discharge with a period of .0163 second. This result is interesting as showing that a stimulus which is probably non-painful may evoke a higher rate of discharge than one probably painful. The total frequency is however so low, even when the needle is being pushed slowly through the skin, that there can be no doubt that the discharge of impulses produced by a painful stimulus is not characterised by a specially high frequency in each nerve fibre. Judged both by the total frequency in the nerve and the occasional regular rhythms, the usual frequencies in the individual fibre correspond with that found by Zotterman and the writer for the pressure receptors, and are of the same order as those found by them for the receptors in the frog's muscle.

In most of the records it has not been possible to trace any regular rhythms, but here, as in the case of pressure stimuli, a sufficient explanation may lie in the fact that a single nerve fibre leads from a number of pain endings which may interfere with the activity one of another. Owing to the absence of regular rhythms it is impossible to say how far the frequency in each nerve fibre varies with the intensity of the stimulus. When the pin is pushed slowly through the skin the rise in total frequency is no doubt due in part to an increase in the number of fibres in action, though the fairly uniform distribution of the impulses (*e.g.* in Fig. 5 *B*) suggests that each fibre is maintaining a high rate of discharge.

B. *Experiments on Frogs.*

For many reasons it is very much easier to carry out experiments of this kind on the frog instead of the cat. The nerves are more easily dissected out, they need not be kept at 37° C. and the whole routine of the experiment is much simpler. A difficulty lies however in interpreting the results. In the case of the frog, it is much less clearly possible for the observer to discriminate between stimuli applied to its skin as to their being painful or painless. Further, the skin-receptors of the frog are morphologically much less diverse than those of mammals¹. Nevertheless, it seems unlikely that the nerve impulses evolved by pricking

¹ According to Gaupp (6) there are only two forms of sensory ending; one consists of an arborisation of naked axis cylinders about the cells of the epidermis, the other is more highly differentiated, occurs only in certain parts of the skin surface, and consists of a small group of cells in the corium surrounding the terminations of a medullated nerve fibre. The latter is generally regarded as an organ of pressure or touch ("Macula tactus").

the frog's skin with a needle, whether or no they give rise to a reaction truly describable as "pain," differ considerably from the pain impulses in mammals.

The nerve employed in the present experiments was the superficial branch of the tibial nerve. This sends a branch to the skin on the medial aspect of the leg a short distance above the ankle. All other branches were divided and the nerve was cut just below the knee. The skin was so dissected that an area about 1 cm. square about the point of entry of

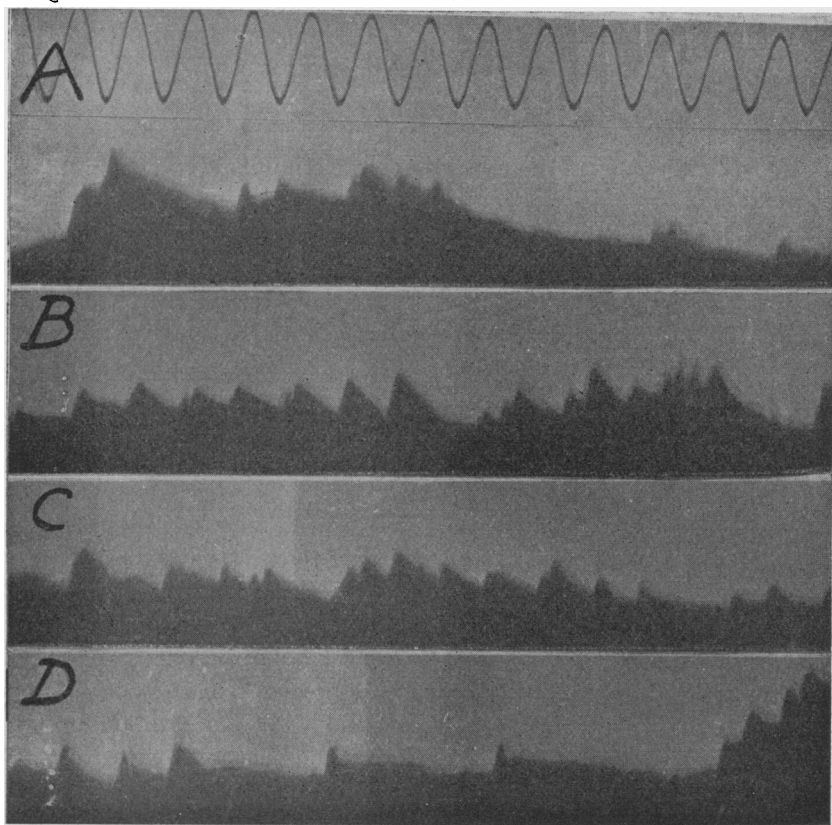


Fig. 8. Plate records from superficial branch of tibial nerve (frog). Time marker gives .01 second intervals. *A, B* and *C*. Exp. 14. Constant weight on needle. Moment of stimulation coincides with release of plate. *A*. Weight $\frac{3}{4}$ gm. The record shows almost the entire discharge. *B*. Weight 10 gm. Regular rhythm in first part of record. *C*. Weight 25 gm. *D*. Exp. 12. Second method. Needle driven through skin for 15 seconds.

the nerve could be laid with the subcutaneous surface downwards on a pad of filter paper soaked in Ringer's fluid. In three experiments the skin and the nerve were removed completely from the frog, in three others one side of the skin was left attached to the leg.

When the nerve is connected with the amplifier and electrometer impulses are usually completely absent unless the skin be stimulated. At most there may be a discharge of two or three a second. The results of stimulating by the first method (constant stimulus) are shown in the records in Figs. 8 and 9 and in the curves in Fig. 10 (Exps. 9 and 10). Four curves are given from two different frogs and it will be seen that they agree very closely. The maximum frequency is just under 150 per second and the records in Figs. 8 and 9 show the absence of any characteristic grouping of impulses.

Records with the second method of stimulation (needle slowly penetrating the skin) are also given in Figs. 8 and 9 and the gradual rise in frequency is shown in the curve in Fig. 10 (Exp. 11). Apart from the absence of a resting discharge, the lower total frequency and the more

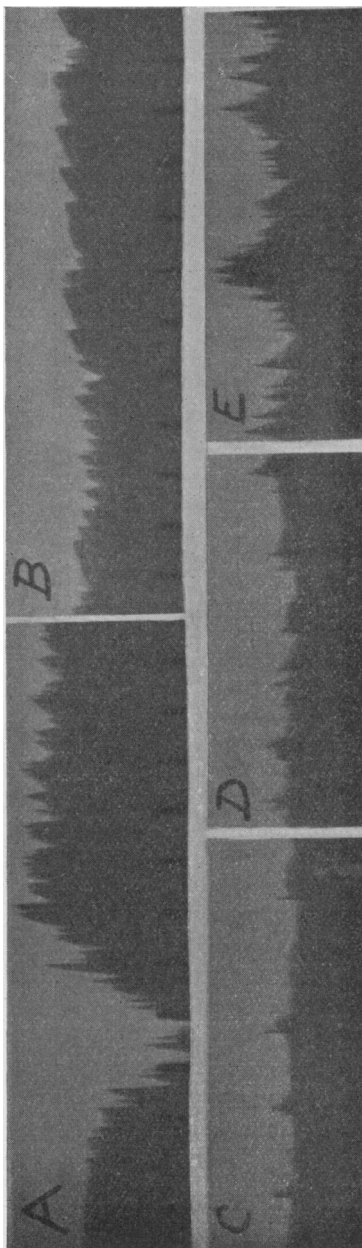


Fig. 9. Film records (frog). Time marker gives $\frac{1}{10}$ second intervals. *A* and *B*. Exp. 10. Constant weight on needle (43 grm.). *A*. Stimulus begins. *B*. $3\frac{1}{4}$ seconds later. Frequency declining. *C*, *D* and *E*. Exp. 11. Needle driven slowly through skin. *C*. 4 seconds after clockwork started. *D*. 9 seconds. *E*. 18 seconds. Frequency of discharge gradually increasing.

rapid decline, these results are in complete agreement with those obtained in the cat.

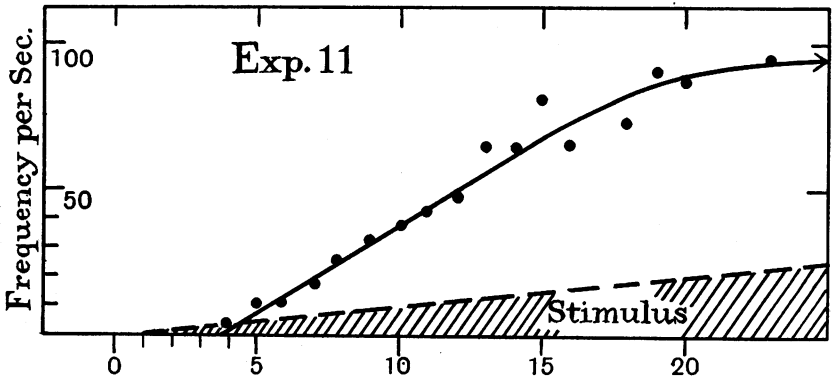
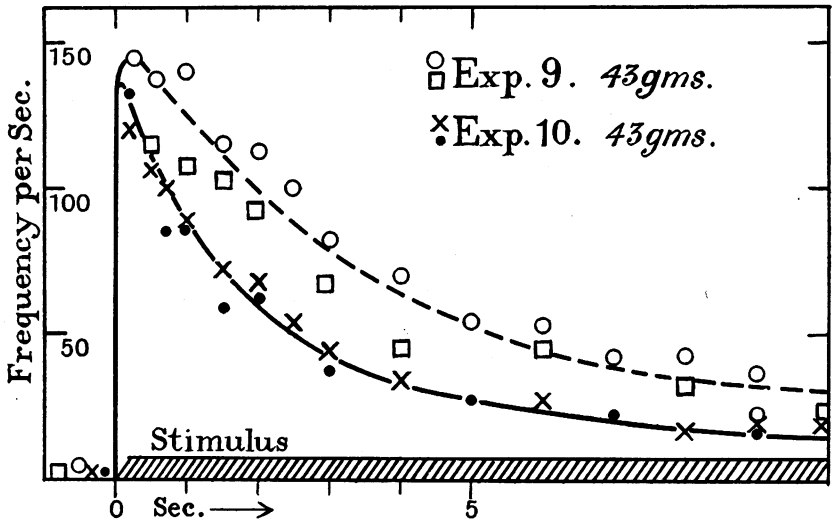


Fig. 10. Impulses from frog's skin. Decline in frequency with constant stimulus and gradual increase with increasing stimulus.

An analysis of typical monophasic impulses is given in Fig. 7 side by side with an analysis from the records of Zotterman and the writer of the afferent nerve impulses produced by a tension of $\frac{1}{2}$ grm. on the frog's sterno-cutaneous muscle. The duration of the impulses is naturally longer than in the mammalian nerve but there is again no difference between the impulses set up in the two different kinds of receptor.

As in the records from the cat, regular rhythms are very uncommon. One with a frequency of 100 per second occurs in the first part of Fig. 8 B, but it cannot be traced in the latter part of the record.

Adaptation. The curves in Fig. 10 show the decline in frequency when the needle remains in position with a load of 43 gm. This decline is much more rapid than that found for the muscle receptors of the frog stimulated by constant tension (cf. Part 2). But the rate of adaptation, *i.e.* the decline in the effectiveness of the stimulus, must be even greater than is indicated in Fig. 10. This appears when we study the effect of altering the strength of the stimulus. In the frog's muscle receptors an increase in tension produces an increased frequency of discharge and the rate of decline of the frequency when the tension is steady is always much the same. On the other hand, in the frog's cutaneous nerves, if the load on the needle is reduced from 43 gm. to $\frac{3}{4}$ gm. the maximum frequency of the discharge is scarcely affected but the rate of decline becomes so rapid that the whole discharge is over in $\frac{1}{2}$ second or less. This may be seen in Fig. 8, where *A* is almost the entire discharge produced by a weight of $\frac{3}{4}$ gm. on the needle and *C* is the initial part of one lasting 3-4 seconds produced by a weight of 25 gm. The same result is shown in Table I, which gives the number of impulses counted in successive periods in another experiment made with continuous film records.

TABLE I.

Exp. 13.

Load on needle	43 gm.	4 gm.	$\frac{3}{4}$ gm.
Period	Number of impulses in successive periods				
Rest: - 1-0 sec.			0	0	0
Stimulus—0 - .05			7	7	8
.05- .1			7	4	6
.1 - .15			5	3	3
.15- .2			5	2	0
.2 - .25			7	3	0
.25- .3			4	2	0
.3 - .35			5	1	0
.35- .4			7	1	0
.4 - .45			3	2	0
.45- .5			2	2	1 (?)
.5 - .75			14	0	0
.75-1.0			15	0	0
1.0 -2.0			31	2	0
2.0 -3.0			25	0	1



Since the initial frequencies are so closely similar it seems unlikely that the longer discharge is maintained by additional receptors brought

into play by the stronger stimulus and having a slower rate of adaptation. Should that be so, the additional receptors must be credited with a latent period of .1 second or more, since otherwise the stronger stimulus would give a higher frequency during the first .1 second. It is more probable that we are dealing throughout with a group of receptors which adapt so rapidly that a $\frac{3}{4}$ gm. stimulus, though initially strong enough to produce the maximum rate of discharge, has become completely ineffective within .2 second, although a much stronger stimulus remains above the threshold value for a longer time.

This raises several points of interest. In the first place the receptor with which we are dealing is almost certainly the free intra-epithelial nerve ending, since the maculae tactus are very far apart in this region. It was pointed out by Sherrington⁽⁷⁾ that the free nerve ending provides a suitable "pain" receptor since, *inter alia*, it may be expected to respond, like a nerve fibre, to any form of stimulus which is sufficiently strong. It is interesting, therefore, to find that the pain receptors adapt themselves to a constant stimulus at a rate comparable to that of a nerve fibre and much more rapid than that of a complex end organ like a muscle spindle. Although the time relations are not the same, the present records with different weights on the needle bear a close resemblance to Garten's records⁽⁸⁾ of the multiple discharges produced by a constant current in a nerve trunk.

The varying duration of the discharge is important from another point of view. A prick of 43 gm. undoubtedly provokes a much greater motor response in a spinal frog than does one of $\frac{3}{4}$ gm. The maximal frequencies of the discharges are the same, and therefore the change in the response cannot depend on the frequency alone. If we make the assumption (discussed above) that the stronger stimulus does not bring any fresh receptors into play, the greater response must be due simply to the greater duration of the discharge. If this is so, the pain reaction must be determined by the summation of a number of impulses in the central nervous system and the very brief discharge might be inadequate to excite the appropriate arcs. It is possible that there are other paths open to a brief discharge, and in this way the skin receptors in the frog may conceivably serve a double purpose, calling up "touch reactions" when the stimulus is very weak and "pain reactions" when the discharge has a sufficient momentum to bring the pain mechanism into play.

Whether there is really any qualitative difference in the reactions of the frog to a very light and a very heavy prick it is hard to say, but

it is worth enquiring whether the skin receptors of the cat may not serve in the same way for touch and pain reactions according to the varying duration of the discharge set up. In the cat's pad a light touch with the needle point produces a very brief discharge (cf. Fig. 3)¹ and in man it may give a momentary sensation of contact. There can be little doubt that most sensations of touch are due to specific receptors, but it has long been known that the terminal organs anatomically known as "touch-corpules" are far too sparse to provide of themselves the cutaneous sense of touch (contact). The intra-epithelial nerve endings could scarcely serve for lasting sensations of contact as well as for pain, but it seems quite possible that they may account for momentary sensations which are not painful.

DISCUSSION.

The foregoing analysis has shown that the discharge of the pain receptors differs very little from that of other receptors. The range of frequency in each nerve fibre is apparently much the same, the time relations of the individual impulses are the same and the impulses show no characteristic grouping. The only feature which is at all characteristic is the relation between the strength of the stimulus and the duration of the discharge set up. If we grant that the same receptor may give a very brief discharge with a weak stimulus and a much longer one when the stimulus is stronger, it seems likely that the character of the reaction is determined by the duration of the discharge, and it is conceivable that a momentary stimulation of the pain receptor may sometimes evoke a sensation which is not painful. The suggestion that a summation of impulses must occur before the pain reaction is aroused would provide an explanation for the supposed longer latency of the pain sensation as compared with other sensations. On the other hand, considerable difficulties are introduced by the fact that a single induction shock to a nerve trunk can give rise to pain. Evidently there are some pain fibres which have immediate access to the central mechanism of the pain reaction without the necessity for temporal summation, or else we must suppose that the simultaneous arrival of a number of impulses in different fibres is as effective as their successive arrival in one fibre.

Apart from these speculations it is clear that we must accept the established view of specific pain fibres which produce their effects in

¹ But it is noteworthy that in the cat a pain discharge may continue for a long time (30 seconds or more) with a constant stimulus if the needle has penetrated the skin. Possibly the rate of adaptation is slower for the endings which are more deeply situated.

virtue of their central connections and not in virtue of a characteristic type of impulse or arrangement of discharge.

It is particularly interesting to find that the maximum frequency of the discharge in each nerve fibre is much the same for all the receptors so far investigated, namely about 150 per second in the cat and 100 per second in the frog. This suggests that the limits of frequency are not determined by the structure of the particular end organ but must depend on something common to all end organs, *e.g.* the properties of the naked axis cylinder. On the other hand, the rate of adaptation certainly varies widely as between one type and another of receptive organ.

CONCLUSIONS.

1. Impulses produced in cutaneous nerves by painful stimuli to the skin have been recorded in the cat and in the frog. By the use of a sharply localised stimulus (the prick of a fine needle) the number of fibres in action can be restricted so that individual impulses can be recorded without interference.

2. With a constant stimulus (the needle pressing with a constant weight on the skin) the frequency of the discharge declines rapidly from its initial, maximum value. With an increasing stimulus (the needle slowly driven through the skin) the frequency rises gradually and declines again when the movement is stopped. The intensity of the pain sensation in man follows much the same course.

3. The impulses produced by the pain receptors have the same time relations as those produced by pressure receptors (cat) and muscle receptors (frog). The frequency of discharge in each fibre seems to cover the same range and there is nothing characteristic in the grouping of the impulses.

4. The only distinction which can be drawn between the discharge of the pain receptor and that of other receptors lies in the very brief duration of the discharge with weak stimuli. It is suggested that these brief discharges may not be adequate to evoke the pain response but may serve instead for momentary sensations of contact, the development of the pain response depending on the summation of impulses in the central nervous system.

5. Since the range of frequency in each fibre is much the same for all the receptors investigated, it is presumably determined by some common factor such as the properties of the naked axis cylinder, and not by the particular structure of the end organ.

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