

**EFFECTS OF TEMPERATURE ON CONDUCTION IN SINGLE
VAGAL AND SAPHENOUS MYELINATED NERVE FIBRES
OF THE CAT**

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There have been several studies on the effects of temperature on the responses in single myelinated nerve fibres, e.g. Bremer & Titeca (1934), Schoepfle & Erlanger (1941), Lorente de Nó (1947), Tasaki & Fujita (1948), Hodler, Stämpfli & Tasaki (1951), Tasaki (1949, 1953), Tasaki & Frank (1955), and more recently Inman & Peruzzi (1961) and Ishiko & Loewenstein (1961). However, although a great deal of valuable information has arisen out of the above investigations, there are still certain gaps in our knowledge, notably on the comparative effects of temperature on fibres of different diameters. For example, it is known that the absolute refractory period ends at the end of the spike at all measured temperatures (Adrian 1921; Amberson, 1930; Tasaki, 1949), but practically nothing is known as to how it varies in fibres of different diameters at different temperatures. Nor is there any information about the relative rates of recovery of excitability or conduction velocity after an impulse in fibres of different diameters.

Further, there is no information about the maximum frequency of discharge that fibres of different diameters can conduct through a region of cooled nerve at different temperatures. Such information would be valuable because cold block is used extensively to block certain reflex effects, and the interpretation of such experiments would be greatly aided by such knowledge. Some information concerning this and other aspects of conduction in nerve fibres has been obtained and is presented in this paper. In the previous paper (Paintal, 1965) it was shown that temperature has no differential blocking effects on fibres of different diameters. In this paper it will be shown that it does have a differential effect on certain other aspects of nerve conduction and recovery processes.

In this paper the expression 'absolute refractory period' has been used in the sense given to it originally by Adrian, i.e. it is the least interval after

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a previous impulse when a second one can be initiated and propagated (Adrian, 1921). In the present experiments it has been measured by determining the least interval between two impulses (generated at normal body temperature) at which both can be propagated through a region of cooled nerve, and when the second impulse is blocked it is assumed that it has run into the absolute refractory period of the first impulse.

METHODS

The results of this paper were obtained from the same series of experiments using immersion cooling as were described in the previous paper; all the methods used were therefore the same (Paintal, 1965).

The temperature coefficients were calculated in the usual way, i.e. $Q_{10} = (x_{t+10})/x_t$, where x_t and x_{t+10} are the respective values of a parameter x , 10° C apart.

Sources of errors

Errors in estimating conduction velocity in the cooled nerve. These errors did not affect the results of the first paper (Paintal, 1965) and were therefore not considered in it. As already mentioned (Paintal, 1965), the length of the nerve bathed in the coolant was between 9 and 13 mm in 19 experiments and 16 mm in two experiments. At 8° C, the difference in the temperature between the various segments of this stretch of nerve in the coolant was less than 1° C. For example, in one experiment on the saphenous nerve the first millimetre of the nerve in the pool was at 8.5–9° C when the centre of the cooled stretch was at 8° C. One may therefore assume that the various segments of the nerve bathed in coolant were at about the same temperature.

The main source of error is that arising from an estimate of the length of nerve cooled. Thus an error of about 10 % in the estimated length will produce an error of 10 % in the estimated conduction velocity. However, since the conduction velocity at any temperature is expressed as a percentage of the conduction velocity of the fibre at 37° C (Figs. 1–4), it follows that the error will be larger in the higher range of temperature. At the 50 % level of conduction velocity (i.e. 50 % of that at 37° C) the error will be 5 %, at the 10 % level it will be 1 %. The net effect will be to displace a little the curves relating conduction velocity against temperature (Figs. 1–4), either up or down. This should be kept in mind when interpreting the results.

A similar source of error arises from the existence of transition zones between the region of nerve bathed in coolant and the portion at body temperature. Since this part of the nerve is in contact with the surrounding tissue as well as the coolant it will have some intermediate temperature, there being a gradient between the part at 37° C and that at the lower temperature. In the case of the vagus it was found that the temperature of the nerve *inside* the tissues and about 1–2 mm from the edge of the nerve in the cold pool was 30° C at a time when the temperature of the nerve in the pool (surrounded by coolant) was 18° C measured simultaneously; the former was 26° C when the latter was 8° C. At this time the temperature of the nerve immediately outside the pool barrier, i.e. less than 5 mm from the cooled nerve, was 36° C. The actual transition zone was therefore less than about 5 mm. It has been calculated that owing to the transition zones, the conduction velocity of the cooled nerve may have been underestimated by less than about 1 % at 8° C and by about 2 % at 18° C. At higher temperatures the error was probably of the same order.

The above sources of error do not affect the measurement of other parameters of nerve function that have been studied, e.g. absolute refractory period, since this is determined by the coolest part of the nerve.

Lag between recorded and actual temperatures. Another important source of error is that arising from the time taken by the nerve to attain a steady temperature, i.e. the possible lag between the recorded and actual temperatures of the fibre in the nerve. As stated already (Paintal, 1965), although the temperature readings were taken only after the reading had remained steady for at least a minute, there could have been a lag in view of the curves with falling and rising temperatures respectively (Fig. 1). However, such results as those of Fig. 1 can be best explained on the basis of some hysteresis type of behaviour. In the present

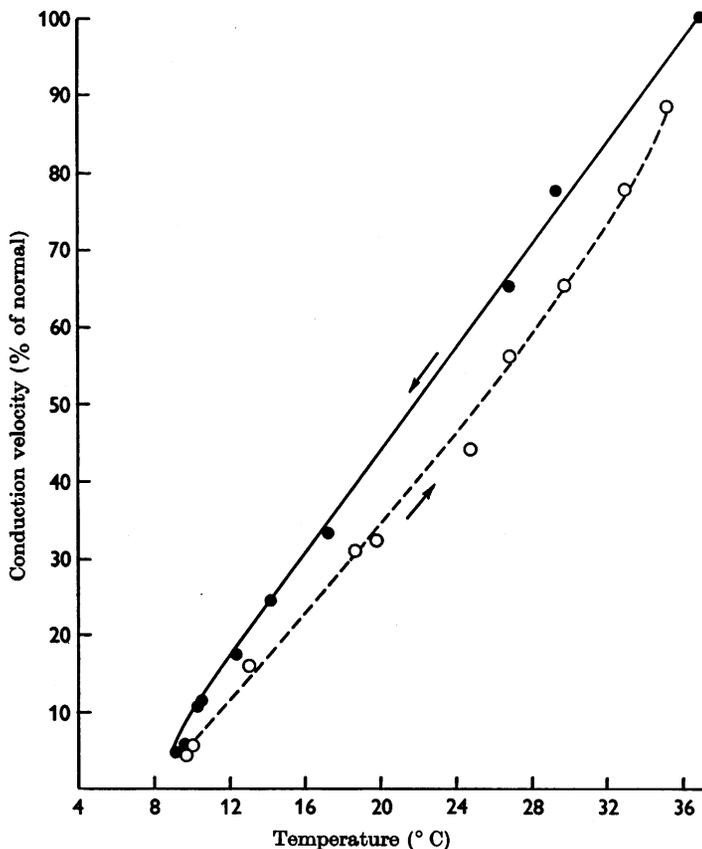


Fig. 1. Conduction velocity of a vagal nerve fibre at different temperatures with falling (—●—●—●—) and rising (---○---○---) temperatures. Normal conduction velocity (i.e. at 37°C) was 30 m/sec. Conduction was blocked at 8.6°C in this fibre but the vagus was cooled to 6.5°C before noting the effect of rising temperature. Length of cooled nerve, 16 mm.

experiments the relation of temperature to conduction velocity and to various other parameters of nerve function were therefore studied only with falling temperatures.

Errors in estimating the absolute refractory period. At low temperatures when the absolute refractory period is large, e.g. 6 msec, there were no errors in measurements of the absolute refractory period of the fibre in the cooled region of the nerve since it could be determined by noting the interval between the two stimuli applied through the single pair of stimulating electrodes. Errors could affect measurements only in the higher temperature ranges, e.g.

between 24 and 37° C when the absolute refractory period is small (Fig. 6) because, owing to the slowing of the 2nd impulse during the relatively refractory period (Fig. 5A), the arrival times of the two impulses at the cooled region must exceed the interval between the two stimuli by an amount depending on the interval between the stimuli; the smaller the interval, the greater the difference. Therefore, when the interval between the stimuli was less than about 6 msec an allowance was made for the extra time taken by the second impulse to reach the cooled nerve. This was simple since the conduction distance between the stimulating electrodes and the cold pool was known and the conduction velocity of the 2nd impulse could be determined by reference to the recovery curve (Fig. 5A). However, it is possible that the absolute refractory period determined in this way may have been under-estimated a little since the recovery curve (Fig. 5A) reflects the average conduction velocity of the 2nd impulse from the stimulating to the recording electrodes, and Tasaki has found that the conduction velocity in the initial part of the conduction distance is less than that in the latter part (Tasaki, 1953, p. 86). However, in the present experiments, in the case of two fibres, it was found that there was no measurable difference between the conduction velocity of the impulse in the proximal and distal parts of the conduction distance of about 63 mm. In this experiment there was no pool and the entire length of the vagus was in contact with the tissues except at the stimulating and recording electrodes. Two pairs of stimulating electrodes were used, one pair being placed 27 mm from the recording electrodes and the other at 63 mm.

RESULTS

All the results described in this paper were obtained from saphenous or vagal nerve fibres that were normally silent or, in the case of fibres with periodic sensory activity (e.g. pulmonary stretch receptors), during their periods of silence so as to ensure that natural impulses did not influence the results.

Effect of temperature on conduction velocity. The conduction velocity of the fibres fell gradually with fall in temperature until conduction through the cooled portion ceased altogether at its blocking temperature (Figs. 1-4). The most notable feature is that when the conduction velocity is expressed as a percentage of the conduction velocity of the fibre at 37° C, the curves of all fibres, slow and fast, look alike (Figs. 2 and 3). The fact that temperature affects conduction velocity in slow and fast fibres in the same way was unequivocally demonstrated by noting the effects of different temperatures on slow and fast fibres in the *same* filament (Figs. 2 and 3). This was observed in several filaments of both vagus and saphenous nerves.

Figure 3 shows that there was some variation in the response of different fibres at lower temperatures. This was due to differences in the blocking temperatures of the fibres and was not related to the normal conduction velocities (i.e. velocity at 37° C) of the fibres (Fig. 3). As shown in Fig. 3 this is because, near the blocking temperature, the conduction velocities of the fibres fall rapidly and so the curves deviate near this temperature.

The shapes of the curves relating temperature and conduction velocity varied somewhat in different fibres even in the same filament. In a few fibres the initial part of the curve had a smaller slope giving an S-shaped

appearance, but in the majority the curves were almost linear (Figs. 1 and 4) or slightly curved (Fig. 2). As shown in Fig. 2 the responses of fibres from normal and abnormal saphenous nerves (cf. Paintal, 1965) differed visibly; the slope of the curve was greater in the abnormal fibres and the Q_{10} therefore was higher (Table 1).

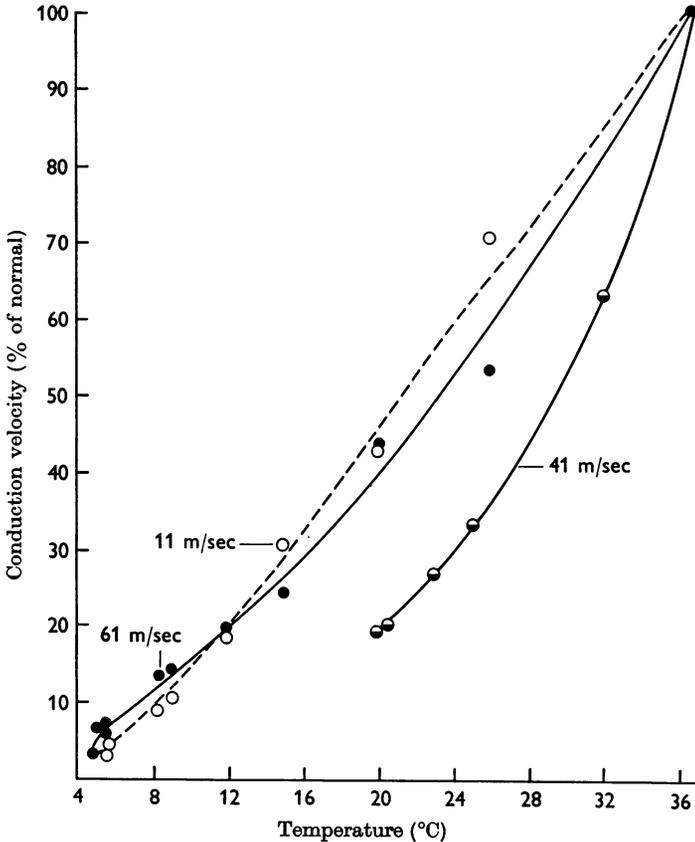


Fig. 2. Conduction velocities of fibres of saphenous nerve at different temperatures. Filled and open circles represent values obtained from two fibres in the *same* filament with normal conduction velocities of 61 and 11 m/sec respectively; length of cooled nerve, 13 mm. The blocking temperatures of these fibres were respectively 4.7 and 5.5° C. Half-filled circles represent values obtained from a fibre with a conduction velocity of 41 m/sec obtained from another experiment on the saphenous nerve with abnormal responses. Conduction was blocked at 18° C in this fibre. Length of cooled nerve, 12.5 mm.

In Fig. 4 the results from ten fibres in which observations were made at all ranges of temperature have been pooled together. The slope of the curve increases with temperature, but it is practically linear between 18 and 37° C and between 10 and 18° C. As shown in Table 1, the Q_{10} varies

in different temperature ranges; between 8 and 18° C it averages 4·8; between 18 and 28° C it averages 2·5; between 27 and 37° C it averages about 1·6 in both vagus and saphenous nerve fibres. The last figure is the same as that obtained from experiments in which the whole mammalian nerve was cooled in this temperature range, e.g. Gasser (1928), Kiraly & Krnjević (1959) (cf. p. 85 in Paintal, 1963). This therefore shows that the present method of studying the effect of temperature on conduction velocity in a small stretch of a nerve fibre is satisfactory even in the higher temperature ranges in which the errors are likely to be greater (see Methods).

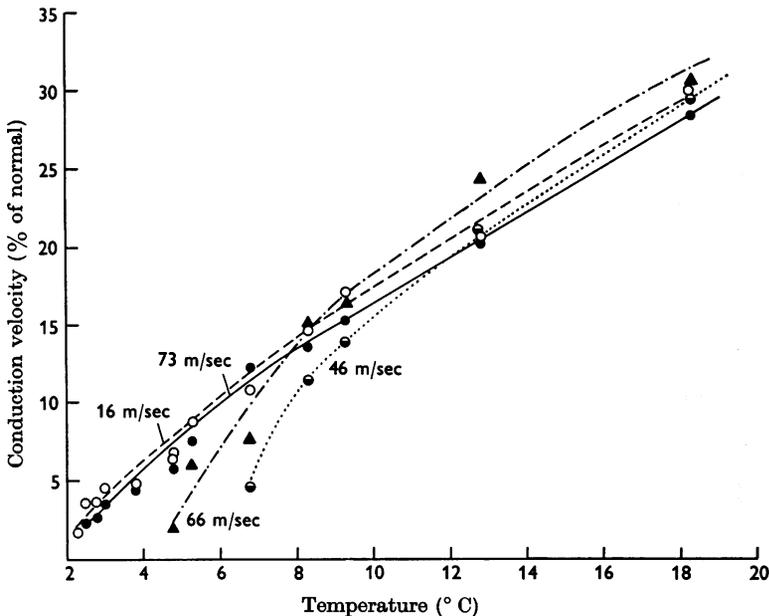


Fig. 3. Conduction velocities of four vagal nerve fibres in the same filament at different temperatures. Normal conduction velocities of the fibres were, filled circles 73 m/sec; open circles 16 m/sec; triangles 66 m/sec and half-filled circles 46 m/sec. The blocking temperatures of these fibres were respectively, 2·5, 2·3, 4·8 and 6·0° C. Graphs show that temperatures affect fast and slowly conducting fibres in the same way. Length of cooled nerve, 16 mm.

The relatively large temperature coefficient in the lower temperature range of 8–18° C is to be expected from what is already known about temperature coefficients of biological processes (Fuhrman & Fuhrman, 1961). This also applies to certain processes that vary linearly with temperature. This is one of the shortcomings of Q_{10} as a measure of temperature dependence. As is to be expected from the above results, the Q_{10} bore no relation to the conduction velocities of the fibres.

The minimum conduction velocity recorded just before block averaged

2.5% in 23 fibres (range, 1.1–3.7%; s.e. 0.13). In six fibres a minimum value of 1–2% was recorded. This shows that nerve fibres can conduct even though their conduction velocity is reduced to 1–2% of normal, i.e. nerve fibres with a normal conduction velocity of 6–100 m/sec can conduct at a velocity of 0.06–1.0 m/sec respectively at low temperatures. In the case of fifteen fibres from two normal saphenous nerves the minimum conduction velocity before block averaged 3.7% (range, 2.0–8.1%, s.e. 0.52).

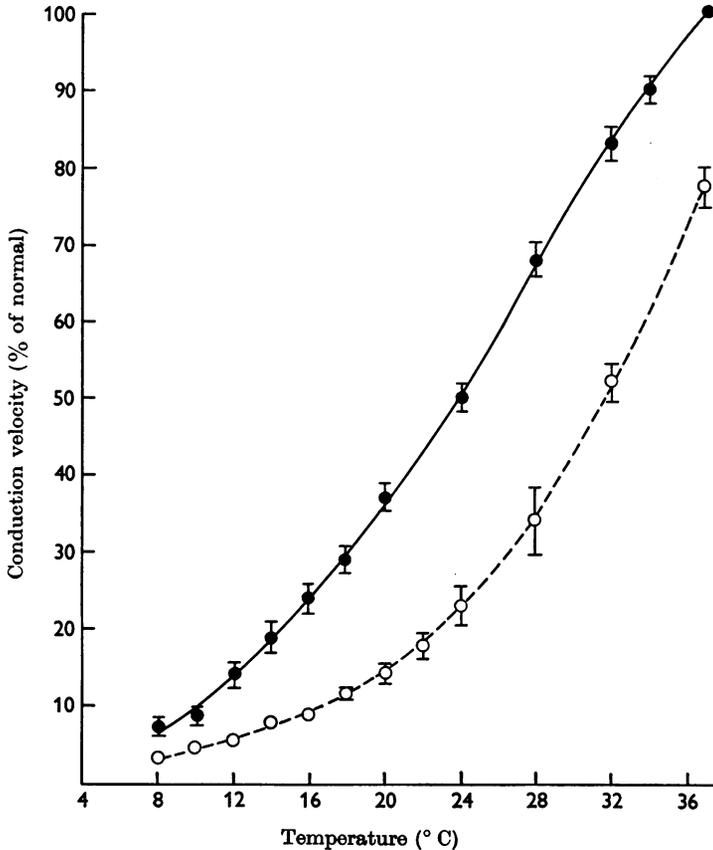


Fig. 4. Average conduction velocities of ten vagal nerve fibres at different temperatures. Filled circles, conduction velocity of the first impulse as in Figs. 1–3. Open circles, conduction velocity of second impulse immediately after the absolute refractory period of the first impulse. Bars represent \pm s.e.; at low temperatures where there are no bars, the s.e. was less than the diameter of the circles.

The average in fourteen fibres from two abnormal saphenous nerves was 9.4% (range, 4.8–14.6%, s.e. 0.8). This difference between the means of normal and abnormal saphenous nerves therefore provides another index of abnormality in the fibres of the two abnormal saphenous nerves studied.

Similar increases in the minimum conduction velocity of vagal nerve fibres were noted after application of tension or pressure, but asphyxia had no effect (cf. Fig. 4*E*, *G* and *J* in Paintal, 1965).

Recovery of conduction velocity. In the present experiments it has been possible to determine only the average conduction velocity of the second impulse in the stretch of cooled nerve. This is because, as shown by Tasaki (1953, p. 86), the conduction velocity of the second impulse is lower in the

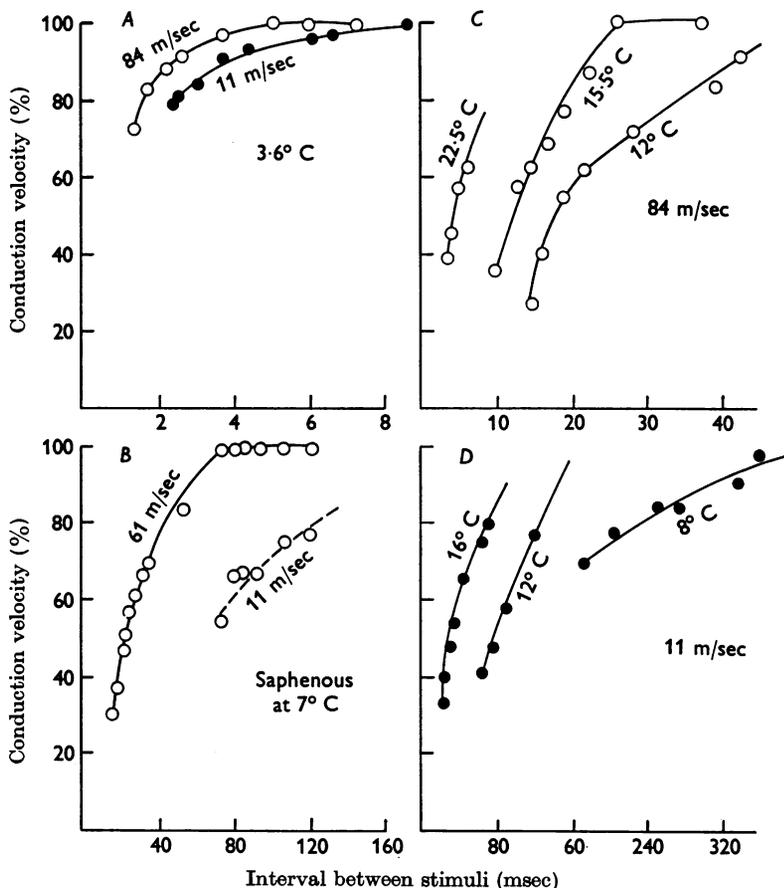


Fig. 5. Graphs showing recovery of average conduction velocity of second impulse. Open and filled circles in *A*, *C* and *D* are values obtained in two vagal nerve fibres in the same experiment with normal conduction velocities of 84 and 11 m/sec, respectively; length of cooled nerve, 16 mm. These graphs show clearly that recovery of conduction velocity is much slower in fibres with lower conduction velocities. Note the difference in the abscissae in *C* and *D*. *B* shows similar results obtained simultaneously in two fibres of the same filament of a normal saphenous nerve with conduction velocities of 61 and 11 m/sec respectively; length of cooled nerve, 13.0 mm.

initial part of the conduction distance. It follows that the average conduction velocity of the second impulse will depend on the conduction distance, but since the conduction distance was about 11–13 mm in most experiments the effect of the small variation in the conduction distance may be ignored.

Figure 5*A* shows that at 36° C, the recovery of conduction velocity up to 95 % of normal is attained by about 3 msec after the first stimulus in the fast fibre with a conduction velocity of 84 m/sec, and by 5 msec in the fibre with a velocity of 11 m/sec. This indicates that the rate of recovery varies a little at 37° C in different fibres, being a little slower in the more slowly conducting fibres. This has been confirmed by recording impulses simultaneously in fast and slow fibres in the same filament.

In contrast, the difference between slow and fast fibres is considerable at low temperatures; the lower the temperature, the greater the difference (Figs. 5*C* and *D*). Thus, at about 16° C, whereas 90 % recovery of conduction velocity is attained by 23 msec after the first impulse in the fast fibre (Fig. 5*C*), in the slow one it is attained only after about 90 msec (Fig. 5*D*). At 12° C the values are respectively 42 and 140 msec in the fast and slow fibres (Fig. 5*C* and *D*). All these features seen in vagal fibres were also seen in normal fibres of the saphenous nerve (Fig. 5*B*). All the curves in Fig. 5 became discontinuous at the lower end owing to the absolute refractory period of the fibres. The lowest point of each curve, therefore, indicates approximately the duration of the absolute refractory period.

The second curve in Fig. 4 (open circles) shows the conduction velocity of the second impulse immediately after the absolute refractory period of the first impulse. This curve which represents the results pooled from nine fibres shows that the relation of the conduction velocity of the second impulse to temperature is logarithmic since plotting the logarithm of this against temperature yields a straight line. The Q_{10} at different ranges of temperature is therefore nearly the same—about 3 (Table 1). The lowest conduction velocity of the second impulse (i.e. relative to that of the first at 37° C) ranged from 1.8 to 4.5 % (mean, 3.0, s.e. 0.2). In no case was it less than the minimum conduction velocity of the first impulse, just above blocking temperature (see above). This, therefore, implies that although the conduction velocity of the second impulse is always less than that of the first impulse at all temperatures (Fig. 4) it cannot be lower than the lowest possible conduction velocity of the first impulse, and that the conduction velocity of the two tends to approximate as the temperature is lowered (Fig. 4).

Although the rate of recovery of conduction velocity after the first impulse is slower in normally slowly conducting fibres (Fig. 5), the actual conduction velocity of the second impulse (relative to the normal conduc-

tion velocity of the fibre) immediately after the absolute refractory period of the first impulse, bears no relation to fibre diameter, being practically the same in fast and slow fibres alike as would be concluded from the pooled results of Fig. 4 obtained from fibres with conduction velocities ranging from 12 to 59 m/sec.

All the above features of the conduction velocity of the second impulse were also noted in the nerve fibres of two normal saphenous nerves.

Conduction velocity of third impulse. In twenty-one fibres the conduction velocity of the third impulse, immediately after the absolute refractory

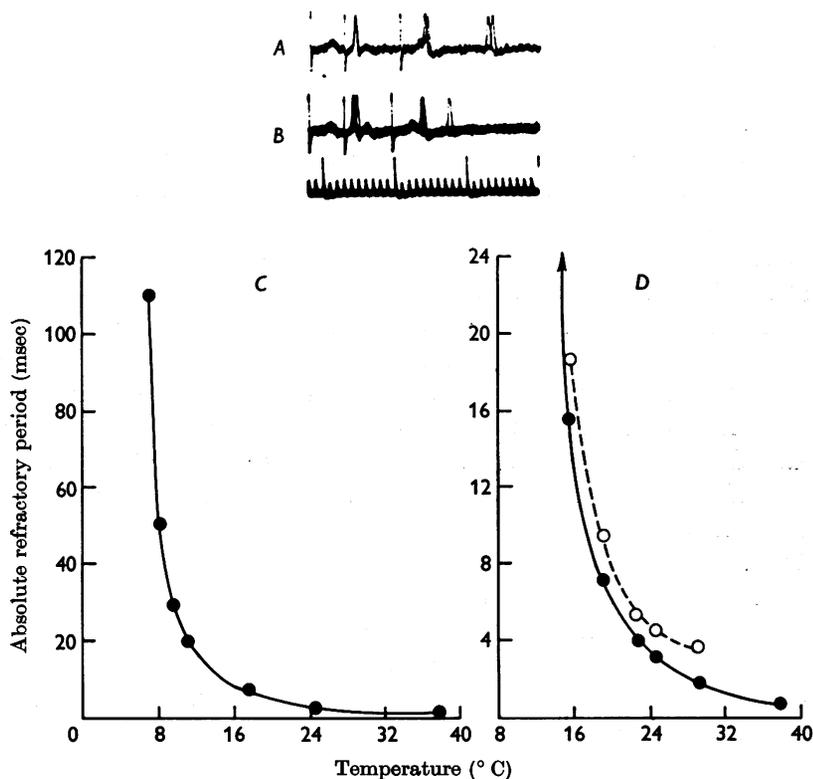


Fig. 6. Absolute refractory period of vagal fibres. *A* and *B* are superimposed sweeps showing that the absolute refractory period after the second impulse is greater than that after the first; in *A* the third stimulus yielded a response in two out of four trials. In *B* the third stimulus was applied within the absolute refractory period following the second impulse; the single response it yielded is due to the absence of a response to the second stimulus in one of the superimposed sweeps. The curves in *C* and *D* were obtained from fibres with conduction velocities of 24 and 12 m/sec, respectively; their respective blocking temperatures were 7.2 and 10.8° C. The arrow in *D* indicates a point at 139 msec recorded at 11° C. Open circles in *D* represent the absolute refractory period after the second impulse. Length of nerve cooled in *A* and *B*, 13.0 mm; in *C*, 11 mm; in *D*, 11.5 mm.

period of the second impulse, was practically the same as that of the second, immediately after the absolute refractory period of the first impulse (Fig. 6*A*). In Fig. 6*A*, the conduction velocity of the second impulse is slightly greater than that of the third because the stimulus of the former was applied a little after the absolute refractory period of the first impulse. In general it was noted that the degree of recovery of conduction velocity at a given interval after a preceding impulse (during the relative refractory period) was the same for various impulses of a train (except the first). Apart from the first impulse, the conduction velocities of all impulses of a train of fixed frequency are therefore the same (Fig. 12*A*, *B* and *E*).

Absolute refractory period. The absolute refractory period at 37° C was determined by noting the least interval between the first and second stimuli at which the second could initiate an impulse at the stimulating electrodes. At lower temperatures it was determined as described in Methods (cf. sources of errors in estimating absolute refractory period), but in every case the nerve at the stimulating electrodes was always at body temperature.

As already known (Adrian, 1921; Amberson, 1930; Schoepfle & Erlanger, 1941; Tasaki & Fujita, 1948; Tasaki, 1949), reduction of temperature increased the absolute refractory period of the cooled nerve fibres. Typical results are shown in Fig. 6. This kind of relation of the absolute refractory period to temperature was seen in all the fourteen vagal and saphenous fibres studied. In all cases the curves rose steeply as the temperature approached the blocking temperature of the fibres (Fig. 6). The actual values of absolute refractory period in the lower range of temperature depended on the blocking temperature of the fibre, so that in two fibres with the same normal conduction velocity, the absolute refractory period was greater in the fibre with the higher blocking temperature. The most noteworthy feature of the present experiments is the new finding that the absolute refractory period depends on the normal conduction velocity of the fibres, being greater in the normally slowly conducting fibres. This was proved conclusively by comparing the absolute refractory periods in fibres with the same blocking temperature but with different conduction velocities. In fact it was found that even if the blocking temperature was lower in the slower fibre by a few degrees, it still had a greater absolute refractory period than the faster fibre (Fig. 7). Figure 10*A* also provides some evidence of this, but it must be remembered that the ordinate in this figure is not merely the reciprocal of the absolute refractory period (cf. below).

In Fig. 8*B* and *C* are shown the absolute refractory periods of nine vagal fibres, mostly sensory, with practically similar blocking temperature ranging from 6.2 to 8.2° C. It is clear that, at all three temperatures, and below

TABLE 1. Temperature coefficients (Q_{10}) of some parameters of conduction in nerve fibres

Physiological variable	8-18° C				18-28° C				27-37° C			
	No. of fibres	Range	Mean	s.e.	No. of fibres	Range	Mean	s.e.	No. of fibres	Range	Mean	s.e.
Conduction velocity of fibres:												
Vagus	6	2.8-7.8	4.8	0.8	10	1.9-4.3	2.5	0.2	10	1.4-1.9	1.6	0.05
Sphenous (normal)	—	—	—	—	8	1.7-3.8	2.4	0.2	8	1.3-2.3	1.7	0.1
Sphenous (abnormal) (cf. Paintal, 1965)	—	—	—	—	6	2.5-4.1	2.9	0.3	6	1.6-2.4	1.9	0.1
Conduction velocity of second impulse immediately after absolute refractory period of first impulse (vagus)	7	2.6-4.7	3.4	0.3	7	2.2-5.0	3.1	0.4	6	2.1-3.1	2.7	0.2
Absolute refractory period (vagus)	7	5.2-16.3	12.2	1.5	8	2.5-5.5	3.6	0.3	6	2.1-4.4	3.2	0.5
Peak frequency of discharge (vagus)	5	6.2-25.0	12.3	3.3	7	2.3-4.3	3.2	0.1	—	—	—	—

25 m/sec, the absolute refractory period varies inversely with the normal conduction velocity of the fibre. All three curves tend to flatten out beyond a conduction velocity of 25–30 m/sec which means that in the faster fibres, i.e. with conduction velocity greater than about 30 m/sec the difference between the absolute refractory periods of different fibres will be small or insignificant. In fact the variation in individual fibres is large enough to mask any actual relation between conduction velocity and absolute refractory periods in the faster fibres (Fig. 8A).

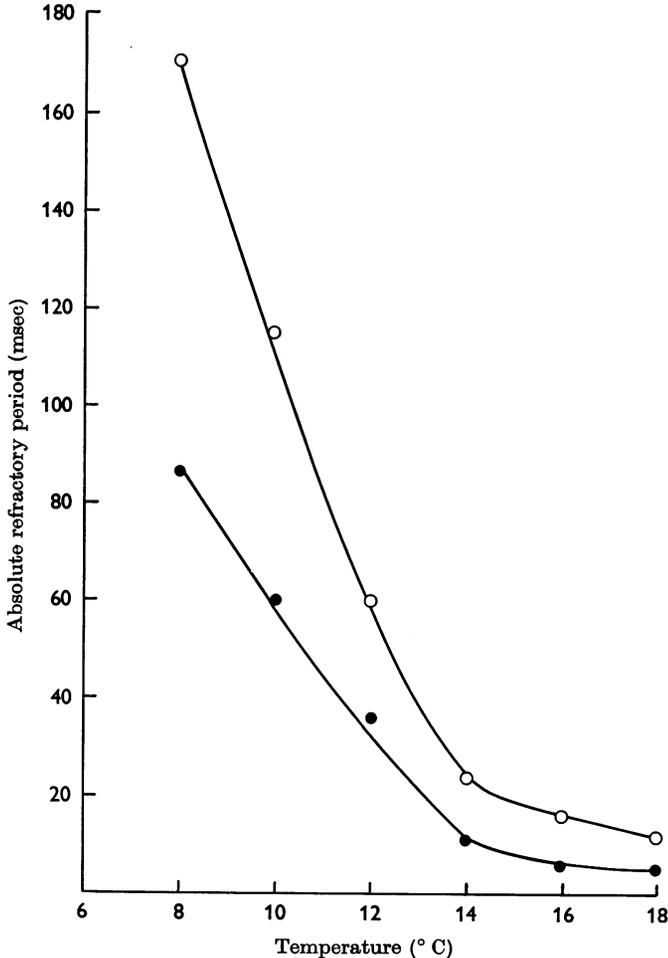


Fig. 7. Absolute refractory periods of two fibres at lower temperatures recorded simultaneously in the same filament of the vagus. The blocking temperature of the fibre with a normal conduction velocity of 38 m/sec (filled circles) was 7.5° C, that of the slower one (11 m/sec; open circles) was 3.5° C. Graphs therefore show conclusively that the absolute refractory period is greater in the more slowly conducting fibre. Length of cooled nerve, 16 mm.

In order to rule out variations in individual experiments the absolute refractory period was determined in thirteen fibres of the vagus in the same cat. The absolute refractory period was recorded between 16 and 17.7° C and corrected to 17° C assuming a Q_{10} of 3.5 (Fig. 8A). Comparing Fig. 8A with the graph of the results obtained at 16° C (Fig. 8C) shows that

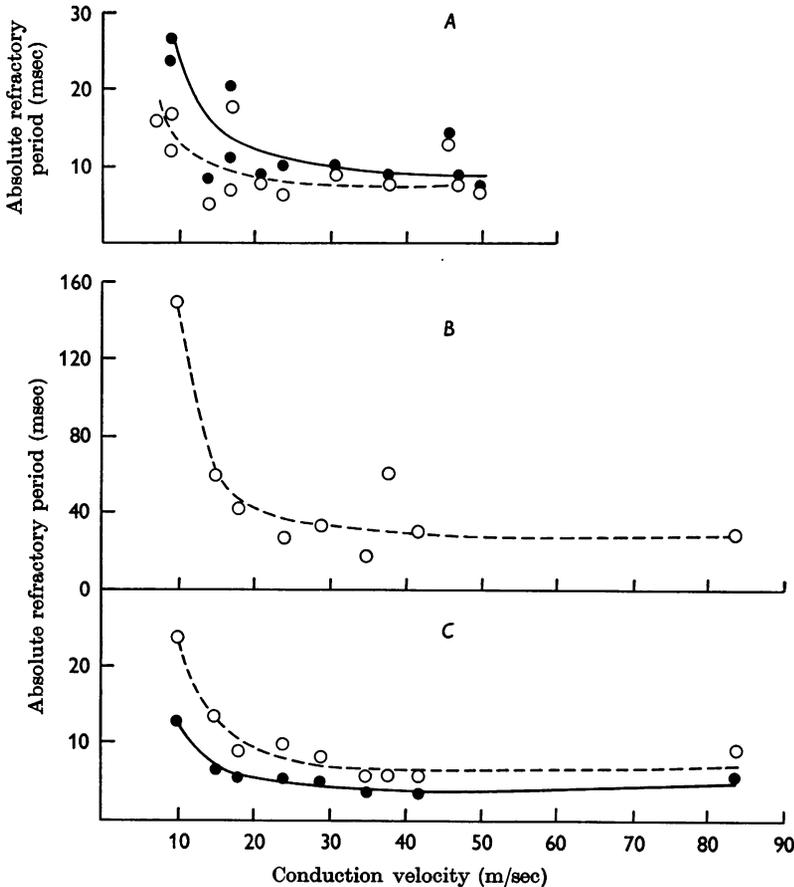


Fig. 8. Relation of absolute refractory period to conduction velocity of vagal nerve fibres at different temperatures. The points in *A* were all obtained from one experiment by recording the absolute refractory period between 16 and 17.7° C and correcting to 17° C assuming a Q_{10} of 3.5; length of cooled nerve, 13 mm. The points in *B* and *C* belong to nine vagal nerve fibres (mostly sensory but normally silent) with blocking temperatures between 6.2 and 8.2° C. These points were read off from graphs such as those shown in Figs. 6 and 7 in each case. Apart from the greater scatter in *A*, the graphs pertaining to the open circles in *A* and *C* (at 16° C) are similar; the initially greater slope in *C* is attributable to greater than usual absolute refractory period in one sensory fibre with a normal conduction velocity of 10 m/sec. Filled circles in *A*, absolute refractory period after the second impulse. *A*, 17°; *B*, 10°; *C*, open circles, 16°, filled circles, 20°.

the two are similar but the scatter is greater in Fig. 8A. This could be due to variations in the blocking temperatures of the fibres which were not determined. Thus it is conceivable that the blocking temperature of the fibre with a conduction velocity of 46 m/sec may have been appreciably higher than that of the other fibres, and that of the fibre with a conduction velocity of 14 m/sec may have been lower. The curve in Fig. 8C is a little steeper than that in Fig. 8A, possibly because the absolute refractory period in the sensory fibre with a conduction velocity of 10 m/sec may have been unusually high.

The temperature coefficient averaged 3.6 in the range 18–28° C, and 3.2 in the range 27–37° C (Table 1). These figures are similar to the values reported by others (Amberson, 1930; Schoepfle & Erlanger, 1941; Tasaki & Fujita, 1948; Tasaki, 1949). However, in the range of 8–18° C the Q_{10} was much higher (mean, 12.2). This was due to the greater increase in the absolute refractory period near the blocking temperature of the fibres and may therefore represent a real difference between the actual refractory period and the 'non-conducting phase' as suggested by Tasaki (1959).

Absolute refractory period after second impulse. In fifteen out of eighteen fibres it was found that the absolute refractory period after the second impulse was greater than that after the first (Fig. 6A and D and 12C); in the remaining three fibres it was the same. The difference between the two was much more marked in the more slowly conducting fibres (Fig. 8A) and at lower temperatures (Fig. 6D). The observations in Fig. 6D were not extended to 37° C owing to possible errors arising at the recording electrodes.

It is clear from Fig. 8A that the absolute refractory period after the second impulse also varies inversely with the conduction velocity of fibres. As shown below, the reciprocal of this interval determines the peak frequency of a train of impulses in a stretch of cooled nerve, irrespective of its length.

Least interval between first and second impulses. It is generally accepted that the peak frequency of discharge that can be generated in myelinated fibres is about 2500/sec (Evans, 1956). This information is derived from studies in which the impulses are recorded close to the stimulating electrodes (Gasser & Grundfest, 1936; Erlanger & Gasser, 1937). However, when these impulses are conducted over a certain distance the picture becomes quite different, owing to the increasing lag of the second impulse due to the reduced conduction velocity of the latter. Thus, even when the conduction distance is only 60 mm as in Fig. 9A, the peak frequency of discharge (i.e. 1/least interval between first and second impulses) is found to be lower in fibres with lower conduction velocities, the relation between conduction velocity and peak frequency of discharge being almost linear

between 10 and 60 m/sec. Such results are to be expected not only because recovery of conduction velocity of the second impulse is slower in the more slowly conducting fibres (Fig. 5A), but also because the actual conduction velocity itself is lower.

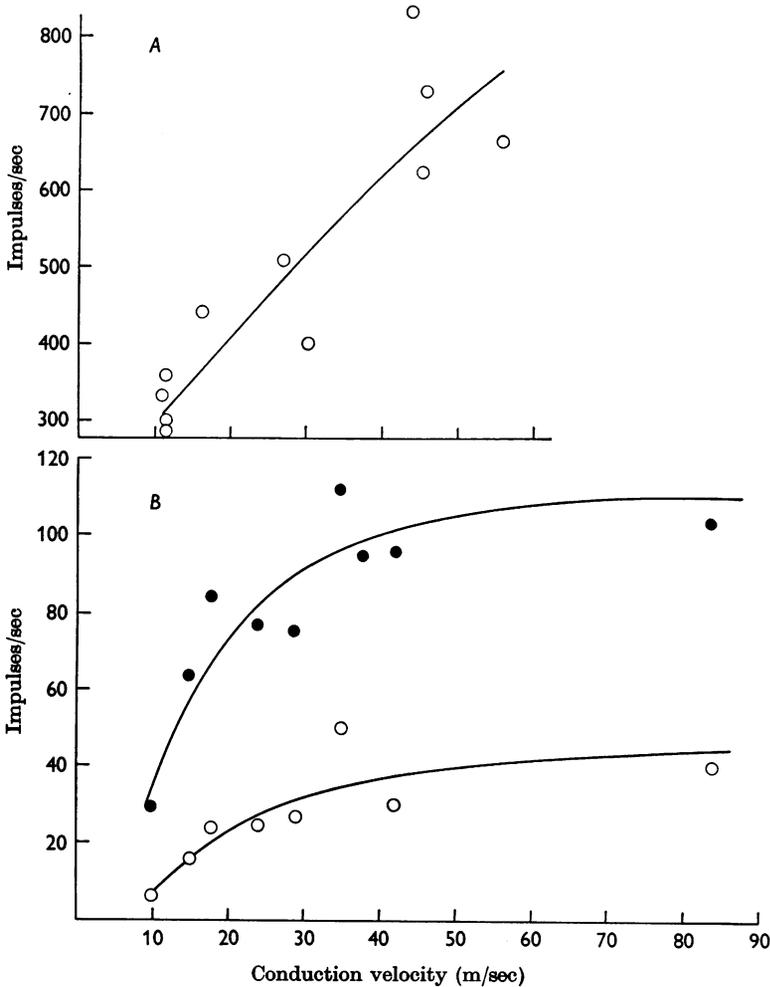


Fig. 9. Relation of peak frequency of discharge (i.e. reciprocal of smallest interval between first two impulses) at different temperatures to conduction velocity of vagal nerve fibres. The data in *A* at 37° C, were obtained from one experiment in which there was no pool and the vagus was in contact with the tissues; the conduction distance was 60 mm. The data in *B* (filled circles, 16°; open circles, 10°) refer to nine fibres with blocking temperatures between 6.2 and 8.2° C (same fibres as in Fig. 8 *B* and *C*); these points in each case were obtained from graphs such as those shown in Fig. 10 *A*. All values in *B* have been scaled to correspond to a conduction distance of 12 mm in the cold pool.

On lowering the temperature the difference between the fast and slow fibres became more pronounced even though the conduction distance in the present experiments was small, i.e. about 12 mm. This difference was unequivocally demonstrated in slow and fast fibres with the same blocking temperature. In fact Fig. 10*A* shows that even though the blocking temperature of a fast fibre was higher than that of the slower one, still the peak frequency in the former was higher at different temperatures.

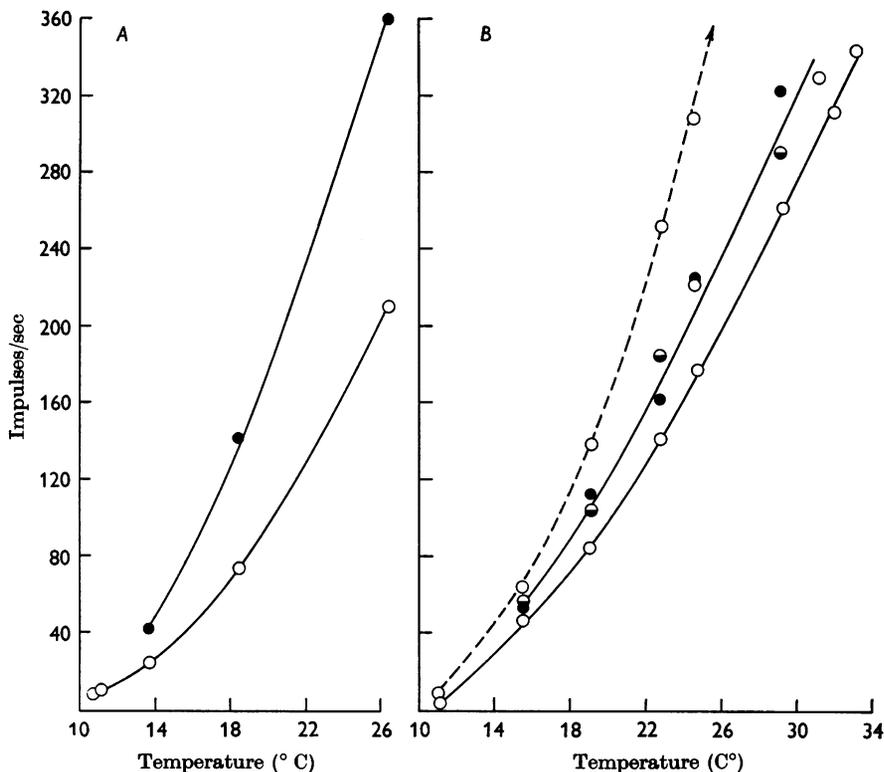


Fig. 10. Frequency of discharge in nerve fibres at different temperatures. In *A*, filled circles, 63 m/sec; open circles, 20 m/sec. The ordinate for *A* represents the reciprocal of the smallest interval between first and second impulses; this also applies to the open circles in *B* with continuous curve obtained from another fibre with conduction velocity of 12 m/sec. The open circles with interrupted curve in *B* represent the frequency of discharge that would result if they were calculated from the reciprocal of the absolute refractory period; arrow is directed towards a point at 555/sec and 29.3° C. The difference between these two curves is due to the slowing of the second impulse in the cooled region. The filled circles in *B* represent the reciprocal of the interval between the second and third impulses; half-filled circles represent the frequency of discharge as calculated from the reciprocal of the absolute refractory period after the second impulse; note the correspondence between the two. Length of cooled nerve in *B*, 11.5 mm; in *A*, 11.0 mm.

The relation between the temperature of the cooled portion of the fibre and the peak frequency of discharge in three fibres is shown in Fig. 10. The initial slope, i.e. between 37 and 30° C (not shown in Fig. 10) varied in different fibres; in some it was reduced. On further lowering the temperature the slope increased in most cases and at still lower temperatures the slope fell in most fibres (Fig. 10). In some fibres the relation between temperature and the peak frequency of discharge was practically linear.

Since the frequency of discharge will depend on the length of cooled nerve, it was necessary to make an allowance for this. The results in Fig. 9*B* were therefore plotted after scaling them to correspond to a conduction distance of 12 mm which was the conduction distance in most of the fibres. These results show the relation between the conduction velocity of the fibres, and the peak frequency of discharge that can pass through at 16 and 10° C in nine fibres with almost similar blocking temperatures ranging between 6.2 and 8.2° C. It is clear that the slower fibres conduct a lower frequency of discharge. Also the curves tend to flatten out at the higher conduction velocities, so that one can assume that above 30 or 40 m/sec the frequency will be nearly the same for all fibres. This information is of importance in the interpretation of the effects of cold block on the vagus on various reflexes produced by repetitive stimulation. The curve of Fig. 9*A* at 37° C is different from the others because here the conduction distance was much greater (60 mm).

At first it would appear that the curves of the peak frequency of discharge are the reciprocal of those of the absolute refractory period. This is not so, because, as shown in Fig. 10*B*, plotting the frequency as the reciprocal of the absolute refractory period of the fibre yields a different curve, i.e. displaced to the left. This difference in these two curves of Fig. 10*B* is due to the increased interval between the first and second impulses caused by the reduction in the conduction velocity of the second impulse. This reduction is most marked at temperatures of about 12–26° C (Fig. 5*C* and *D*) when the conduction velocity of the second impulse is about 16–47% of the first impulse. At the lowest temperatures the actual peak frequency corresponds more closely to that computed from the absolute refractory period because, at the lowest temperatures, the conduction velocity of the second impulse approaches that of the first.

Relation of interval between two stimuli to interval between the corresponding impulses. Figure 11 shows the interval between the first and second impulses plotted against the interval between the first and second stimuli at 36° C and at 12° C; in the latter case the interval between the stimuli is actually the interval between the two impulses before they enter the cooled region. At 36° C the interval between impulses is the same as the interval between the stimuli when the latter is greater than 5 msec (Fig.

11). On further reducing the inter-stimulus interval, the interval between the impulses does not keep in step owing to the greater and greater reduction in the conduction velocity of the second impulse when the second stimulus is brought closer to the first, and the curve therefore tends to flatten out. This feature is greatly exaggerated at lower temperature. As shown in Fig. 11, at 12°C (8.5°C above blocking temperature of this fibre), owing to the conduction velocity of the second impulse being less than that of the first even when the former enters the cooled region 70 msec

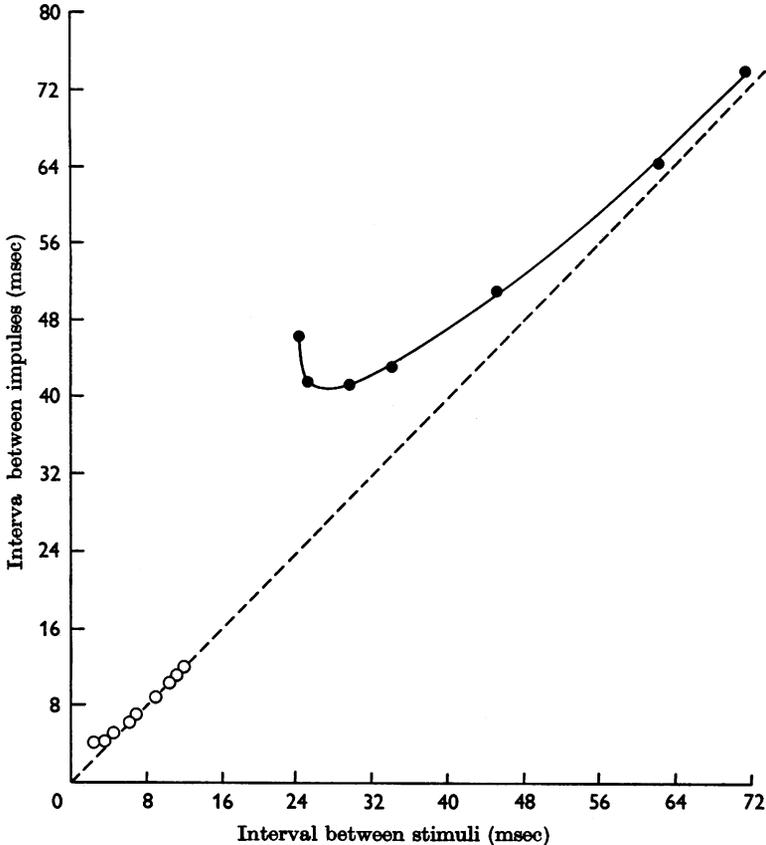


Fig. 11. Graphs showing the relation of interval between two stimuli to the interval between the two corresponding impulses at 36°C (open circles) and 12°C (closed circles). Length of cooled nerve, 16 mm.

after the first, the interval between the two impulses after they emerge from the cooled region is increased. This deviation becomes more marked as the interval between the entering impulses is reduced still further, till the interval is reduced to about 30 msec when the curve flattens out. On further reducing this interval, the interval between the emerging impulses

actually increases. Such behaviour was seen in several fibres between 10 and 20° C.

It is, therefore, clear that there is a certain interval (between stimuli or between impulses before they enter a cooled stretch of nerve) which will yield the smallest interval between impulses at their destination. In the case of the fibre shown in Fig. 11 it was about 30 msec at 12° C. This interval depends on the length of nerve cooled and the rate of recovery of the second impulse at different temperatures (Fig. 5).

As indicated in Table 1, the Q_{10} for the peak frequency (reciprocal of least interval between first two impulses) is the same as that for the absolute refractory period. No values have been given for the range 27–37° C because there were no measured values at 37° C with the same conduction distance as that used for determining the peak frequency at 27° C.

Least interval between second and third impulses. Two new findings concerning this interval observed in eighteen fibres are noteworthy. First, that it is less than the least interval between first and second impulses at various temperatures (Fig. 10*B*). Secondly, that it appears to be identical with the absolute refractory period after the second impulse (Fig. 10*B*). This is because the conduction velocity of the third impulse immediately after the absolute refractory period of the second impulse is the same as the conduction velocity of the second impulse immediately after the absolute refractory period of the first (cf. above). This also applies to other impulses of a train. These important results, therefore, indicate that the peak frequency of a train of impulses that can pass through will be independent of the length of cooled nerve, because it will be determined almost entirely by the absolute refractory period after the second impulse, which itself is independent of the length of nerve cooled.

The amount of disparity between the first and second inter-impulse intervals depends on the conduction distance; the larger the distance, the greater the disparity. From the results it is estimated that when the conduction distance of a cooled nerve is about 8–10 mm, then there will be no difference between the two inter-impulse intervals, because, at this conduction distance and at a temperature of 12–30° C, the lag in the second impulse will be compensated by the increased absolute refractory period after the second impulse.

Conduction of a train of impulses through cooled region of nerve. Since cold block is frequently used for blocking trains of impulses, it was important to study the manner in which trains of impulses of different frequencies are conducted through a length of nerve cooled to various temperatures. This was done on five vagal nerve fibres and one saphenous nerve fibre by applying trains of stimuli at different frequencies (Figs. 12 and 13).

As is to be expected from the foregoing results, all impulses of a train

were conducted through the cooled nerve when their inter-impulse interval was a little greater than the absolute refractory period after the second impulse. Below this peak frequency, the first inter-impulse interval was greater than any other inter-impulse interval (Fig. 12*B* and *E*) and the

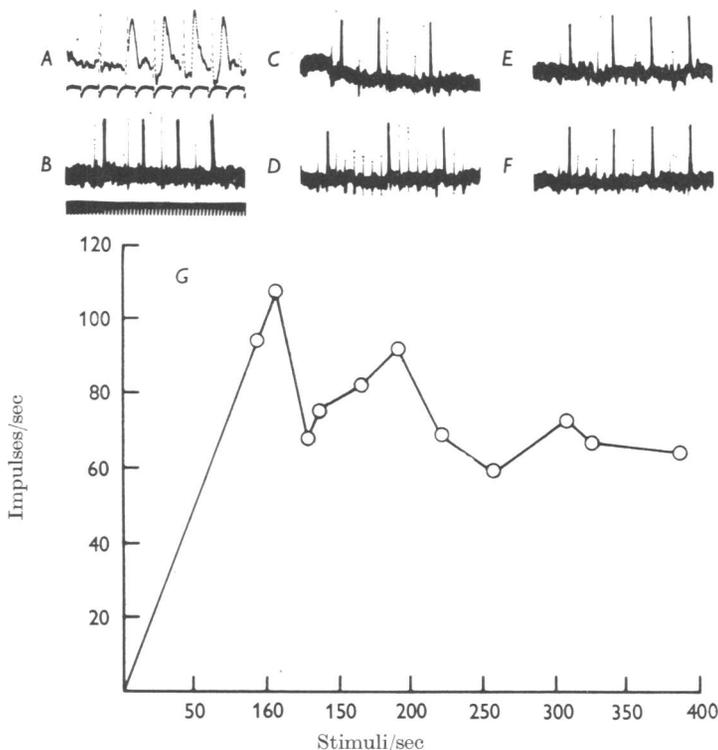


Fig. 12. Transmission of trains of impulses through a vagal nerve fibre with a normal conduction velocity of 42 m/sec, cooled to 15° C. *A* shows that a high frequency discharge of 660/sec generated at the stimulating electrodes could pass through the fibre at 35° C. Sweeps *B* to *F* were recorded after cooling the nerve to 15° C. Frequency of stimulation in *B*, 107/sec; *C*, 129/sec; *D*, 391/sec; *E*, 96/sec and *F*, 192/sec. *B* shows the maximum frequency of discharge that could pass through the cooled nerve fibre and *C*, *D* and *F* show that the cooled fibre conducted only some of the incoming impulses. *G* shows the results plotted from records such as those shown above; note that the second peak occurs at about twice the frequency of stimulation required to produce the first peak in the curve. Millisecond time marks in *B* apply to all sweeps except *A* which has its own time marks. Length of cooled nerve, 10.5 mm.

latter was identical with the interval between stimuli (frequency of stimulation, abscissa in Fig. 12*G*). On further increasing the frequency of the train of impulses entering the cooled region (represented by the stimulus artifacts) the frequency that emerged fell sharply (Fig. 12*G*) because now only every second impulse could get through (Fig. 12*F* and *G*). The

emerging frequency then increased on further increasing the frequency of the entering train till a second peak was attained (Fig. 12*G*). This peak occurred when the entering frequency of discharge was approximately twice that required to produce the first peak. For example, in Fig. 12*G*, the first peak occurring at 107 impulses/sec was produced when the entering frequency was 107 impulses/sec. The next peak of 92 impulses/sec occurred when the entering frequency was 192/sec. It is possible that it may have occurred at a higher frequency (e.g. 214/sec) if such testing frequency had been applied. After the second peak the response was variable in different fibres. In some the emerging frequency was reduced, but not greatly (Fig. 12*G*). In others it was reduced greatly with increasing frequency of stimulation. The actual behaviour differed at different temperatures.

Frequently, at low temperatures, complete block of the entering impulses occurred if their frequency was suitable. Thus at 11° C, Figs. 13*A* and *B* show that except for the first, all of a train of impulses were blocked when their frequency was between 10 and 27 impulses/sec. Above this frequency occasional impulses passed through the cooled nerve. When the temperature of the nerve was raised to 14° C, the same fibre (large-spiked) passed a higher frequency of discharge of about 19 impulses/sec; this was a critical frequency because occasional impulses were blocked at this frequency (Fig. 13*C*). On further increasing the entering frequency to 26/sec there was total block except for the first impulse, and when the frequency was raised to 33–358/sec some impulses again emerged through the cooled nerve. Their frequency was variable but, under suitable conditions (e.g. at 61/sec in Fig. 13*D*), a regular discharge could be produced. Similarly, in the case of the small-spiked faster fibre, block of occasional impulses occurred when the frequency was 39/sec and complete block at all frequencies above 49 impulses/sec. The records in Fig. 13*C* and *D* show clearly that the faster conducting fibre could conduct a higher frequency of discharge than the slower fibre, even though its blocking temperature was higher than that of the lower one.

The above results therefore show that the frequency of impulses emerging through a cooled region depends on the conduction velocity of the fibre and on the entering frequency of impulses, and that complete block of a train of impulses can occur if the frequency is appropriate. Apart from exceptional cases (e.g. small-spiked fibre in Fig. 13*D*), total block is not produced by increasing the frequency of stimulation, because some impulses get through the cooled region under these conditions. The possible mechanisms concerned which probably lie in the transition zone will be discussed below.

The mechanism for the block of a train of impulses cannot be in the

cooled region itself, because it is to be expected that if an impulse arrives at the cooled region when the fibre is in the absolute refractory state, it should not have any effect. This has been confirmed in several experiments. For example, Fig. 12C shows that the impulse after the third stimulus did not get through the cooled region as it must have arrived there during the

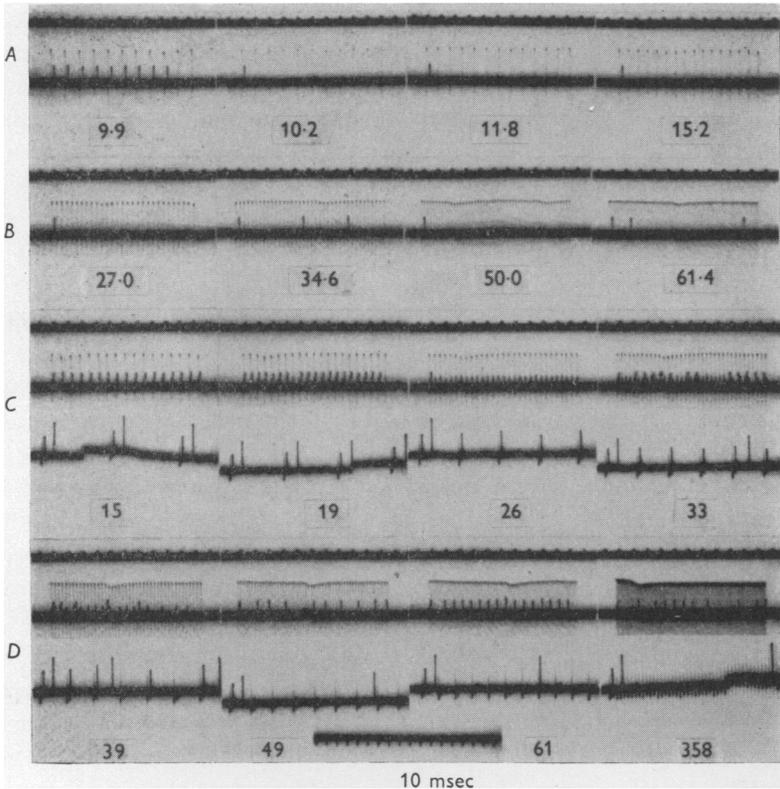


Fig. 13. Transmission of trains of impulses in two saphenous nerve fibres with normal conduction velocities of 20 m/sec (large spike) and 63 m/sec (small spike). At 11° C, in series A and B, only the large-spiked fibre (blocking temperature 9° C) is active, the faster fibre having been blocked at 13° C. A and B show that apart from the first impulse there is complete block of all other impulses when the entering frequency of impulses is about 10 to 27/sec. At 14° C, in C and D, there is block of the train at 26/sec in the large-spiked fibre. D shows that complete block (apart from the first impulse) in the small-spiked faster fibre was produced when the frequency was raised to 49/sec and above, and that it transmitted every impulse up to 33/sec. In C and D there are sweeps of the initial 0.23 sec of the segments of continuous record at each frequency. Time marks of 10 msec at the bottom apply to all these sweeps. The amplification for the sweeps at 19, 33 and 49/sec was slightly lower than that of the others. The numbers indicate the frequency of stimulation, i.e. the frequency of impulses arriving at the cooled region. Upper trace in each record 0.1 sec time marks. Length of cooled nerve, 11.0 mm.

absolute refractory period following the second impulse. Figure 12*C* also shows that the interval between the fourth stimulus and its corresponding impulse is less than that following the second stimulus; this therefore suggests that the third impulse that must have arrived at the cooled region (during the absolute refractory period following the second impulse) had no depressant effect. Also, in Fig. 12*F* the frequency of stimulation is exactly double that in Fig. 12*E*, but the number and timing of the impulses is almost identical in both, thus showing that every alternate impulse arriving at the cooled region in Fig. 12*F* not only failed to get through, but it left no depressant effect either. Similarly, Fig. 6*B* shows that the third stimulus, which was applied such that its impulse arrived at the cooled region during the absolute refractory period following the second impulse, yielded only one response. The appearance of this single response is due to the absence of a response to the second stimulus in one of the superimposed sweeps. Since the impulse following this second stimulus must have arrived at the cooled region, this sweep therefore shows that a blocked non-propagating impulse has no measurable depressant effect, because the latency for the third impulse is what one would expect in the absence of the second impulse.

From the above observations it can therefore be concluded that the block of a train of impulses does not occur at the cooled region itself. The only other region where this block can occur is in the transition zone. This will be discussed below.

DISCUSSION

It was shown in the first paper (Paintal, 1965) that conduction in slow and fast myelinated nerve fibres was blocked at about the same temperature. In agreement with this is the present observation that the degree of temperature dependence of the conduction velocity of the fibres also bears no relation to their normal conduction velocities, the Q_{10} being nearly the same for fibres of different conduction velocities (Figs. 2, 3 and 4). Also the minimum conduction velocity (% of normal) before block of conduction is the same in different fibres; this is also true of the conduction velocity of the second impulse immediately after the absolute refractory period of the first impulse.

So far the only known aspect of conduction that varies with normal conduction velocity of the fibres is the rate of recovery of conduction velocity after an impulse, this being slower in the fibres with lower normal conduction velocities (Figs. 5, 7 and 8). Accordingly, the absolute refractory period is longer in the slower fibres (Fig. 8). Another consequence of slower recovery in normally slowly conducting fibres is that the peak frequency of discharge that can pass through them is less than that which

can pass through faster conducting fibres (Fig. 9*B*). This applies to both the first and subsequent impulse intervals but, unlike the other intervals, the first impulse interval depends on the conduction distance. The slope of the curves showing the time course of recovery of conduction velocity (Fig. 5) will also depend on the length of nerve cooled, because the conduction velocity of the second impulse in the initial part of the total conduction distance is less than that in the latter part (Tasaki, 1953, p. 86). It follows that the minimum conduction velocity of the second impulse (Fig. 4) must also depend on the length of cooled nerve.

Some of the properties that are independent of length of nerve cooled are: (1) absolute refractory period of the first or subsequent impulses since this will be determined by the coldest node; (2) the conduction velocity of the first impulse at different temperatures; (3) the blocking temperature of the fibres provided the length of nerve cooled is large enough to prevent jumping of the impulse (cf. Douglas & Malcolm, 1955) and (4), the peak frequency of a train of impulses since this is determined by the absolute refractory period after the second or subsequent impulses, the conduction velocities of all of which (except the first) are the same.

The results have shown unequivocally that the absolute refractory period after the first or subsequent impulses varies with the normal conduction velocities of the fibres (Fig. 8). This was mentioned by Erlanger & Gasser (1937, p. 48) (cf. data obtained earlier by Blair & Erlanger (1933), but they were cautious in their statement, perhaps partly because of the large individual variations, and also because of some anomalous results (produced by strong electrical stimuli) concerning the relative durations of absolute and relative refractory periods; this led Shoepfle & Erlanger (1941) finally to regard these results as an artifact. In another paper on mammalian nerve fibres, Gasser & Grundfest (1939) again observed that the absolute refractory period was greater in the more slowly conducting fibres, but they did not give due importance to this observation as they could not reconcile it with the constancy of spike duration with which they seemed much impressed. Because of this uncertain state of affairs Rushton (1951) also could not adopt a firm position.

Assuming that the spike duration of the fibres at 37° C is about 0.5 msec (Gasser & Grundfest, 1939), and the Q_{10} for spike duration for mammalian fibres is 3.5 (Inman & Peruzzi, 1961) it follows that the spike duration at 16° C will be about 7 msec. In view of the established fact that the absolute refractory period lasts as long as the spike (Adrian, 1921; Tasaki, 1949), it is to be expected that the absolute refractory period at 16° C should be about 7 msec. Figure 8*C* shows this is precisely what has been found in fibres with conduction velocities greater than 30 m/sec, but this is not true for fibres with conduction velocities less than 30 m/sec. The

present findings concerning the faster fibres are, therefore, in full agreement with what is already known about the spike duration and absolute refractory periods of myelinated fibres.

According to conventional methods (Adrian, 1921; Amberson, 1930; Gasser, 1931; Shoepfle & Erlanger, 1941), the ability of the second impulse to be conducted is implicit in measurements of the absolute refractory period. The present measurements are, therefore, in accordance with the classical concept of absolute refractory period and with what Tasaki terms as the 'non-conducting phase' (Tasaki, 1949) or the 'least (critical) interval' (Tasaki, 1959). According to Tasaki (1949) the absolute refractory period should be regarded as being coincident with the end of the spike even though the next impulse generated at this time may be abortive. In the present experiments, as far as the faster conducting fibres are concerned, the absolute refractory period corresponds to that predicted from the known properties of spike duration, even at a temperature of about 16° C. It is, therefore, very likely that above this temperature the absolute refractory period (according to Tasaki) and the 'non-conducting phase' are identical. However, at the lowest temperatures and especially in the more slowly conducting fibres (say below 20 m/sec) it appears that there might be a marked difference between the two, because the absolute refractory periods recorded are very long, e.g. 100 msec (Figs. 6-8). Alternatively, the spike durations may be very long, but it is difficult to imagine that spikes that last normally only about 0.6 msec will have a duration of 100 msec or more at low temperatures. On the other hand, it is possible that Tasaki's non-conducting phase may be a feature of local conditions leading to the production of abortive spikes (cf. Fig. 5 in Tasaki, 1949). In the present experiments the nerve fibres were inside their sheath which had a normal blood supply, and the stimuli used for testing refractoriness were the natural impulses in the fibre itself.

Since the absolute refractory period is now known to vary with conduction velocity, it follows that spike duration must vary with conduction velocity and it should, therefore, be longer in the slower fibres. This is contrary to the generally accepted belief that originated with Gasser & Grundfest (1939), that spike duration is dependent on the conduction velocity of the fibres. Gasser & Grundfest based this conclusion largely upon observations concerning the extrapolated compound action potential, but also from observations of spikes of ten single fibres obtained from a variety of sources which are shown in Fig. 3 of their paper, and which showed no consistent relation of spike duration to conduction velocity. Recent experiments (to be published) have shown that there is indeed an even wider scatter than that observed by them, but these also show definitely that spike duration varies with the normal conduction velocity

of the fibres, the relation between the two being very similar to the relation between conduction velocity and the absolute refractory period (Fig. 8).

As shown in Table 1, the Q_{10} for absolute refractory period varies with the range of temperature over which it is examined, being much larger in the lower range of temperature (Fig. 6). This is also true of other aspects of nerve conduction, except for the conduction velocity of the second impulse immediately after the absolute refractory period of the first impulse (Fig. 4) which bears a logarithmic relation to temperature. Large values of Q_{10} at low temperatures are a feature of several biological processes (Fuhrman & Fuhrman, 1961) and are to be expected if a physiological process varies linearly (e.g. conduction velocity), or hyperbolically (e.g. absolute refractory period (Figs. 6 and 7), with temperature.

No explanation can at present be provided for the increased absolute refractory period after the second impulse (Figs. 6*B* and 8*A*) which is observed at all temperatures (Fig. 6*D*), but it does lead to the conclusion that either the duration of the second spike is greater than that of the first spike, or that the absolute refractory period outlasts the second impulse. This needs to be investigated as there is no available information concerning it in the literature.

The results of the first paper (Fig. 3, Paintal, 1965) have shown that complete block of a natural train of impulses can occur at reduced temperatures if the conditions are appropriate. As shown in the present results the mechanism for this block cannot be in the cooled region itself but in the transition zone. In this transition zone, i.e. between the nerve at 37° C and the cooled nerve, there will be a temperature gradient and different nodes will be at different temperatures and they will therefore have different absolute refractory periods and will be in a varied state of recovery after an impulse. Under these conditions the impulses of a gradually increasing frequency of discharge will get blocked further and further distal to the cooled region with the arrival of each additional impulse. Thus, in the case of a fibre with a conduction velocity of about 18 m/sec (3 μ in diameter), the internodal length will be about 0.3 mm (cf. Fig. 2 in Rushton, 1951, drawn from data given by Hursh, 1939) and if the transition zone is assumed to be about 5 mm, there will be about fifteen nodes at different temperatures, and therefore, with different absolute refractory periods. Such a situation can prevent the passage of a train of impulses with gradually increasing frequency. A similar mechanism will explain how a discharge of constant frequency can be blocked (Fig. 13). According to this scheme it is, therefore, possible to understand how trains of impulses of different frequencies, all of which are much higher than the frequency that can actually pass through the cooled region, can be blocked (Fig. 13).

The maximum frequency of a train of impulses that can pass through the cooled region will be determined by the absolute refractory period after the second impulse (which is the same as the absolute refractory period after subsequent impulses). This frequency will be unaffected by the length of cooled nerve (cf. results) or by the transition zones if the discharge is of this or lower frequency. However, if the entering frequency is higher than this, then the emerging discharge will depend, not only upon the temperature of the nerve, but on the frequency of discharge entering the cooled nerve, and also on the length of the transition zone; a longer transition zone will presumably block a greater range of frequencies.

In the light of these results, it is now necessary to reinterpret the observations concerning the many reflex changes that are brought about by cooling the vagus to various temperatures.

SUMMARY

1. The effects of variation of temperature on the conduction velocity of the myelinated vagal and saphenous nerve fibres of cats was studied systematically in the same series of experiments described in the first paper (Paintal, 1965). Reduction of temperature affected slow and fast fibres in the same way. The Q_{10} which was unrelated to normal conduction velocity averaged 1.6 between 18 and 37° C; between 8 and 18° C the mean was 4.8. The minimum conduction velocity just before block averaged 2.5% of normal. This was much increased in saphenous nerve fibres with abnormally high blocking temperatures.

2. The conduction velocity of the second impulse just after the absolute refractory period of the first impulse fell logarithmically with fall in temperature, the Q_{10} being about 2.7 and 3.4 between 8 and 37° C. This was not related to the normal conduction velocity of the fibres.

3. The rate of recovery of conduction velocity after an impulse which falls markedly with fall in temperature is related to the normal conduction velocity of the fibres, being lower in the slowly conducting fibres. Accordingly, the absolute refractory period which increases with fall of temperature (the Q_{10} being about 3.4 between 18 and 37° C) varies inversely with the normal conduction velocity of the fibres.

4. The absolute refractory period after the second impulse is greater than that after the first, especially at low temperatures and in the more slowly conducting fibres. In spite of this, the least interval between the first and second impulses (which depends on the conduction distance) is greater than any other inter-impulse interval. This is due to the reduced conduction velocity of the second impulse, which is the same as that of subsequent impulses of a train of uniform frequency.

5. The peak frequency of discharge of a train of impulses that can pass through a cooled region depends on the absolute refractory period after the second impulse, and it is, therefore, independent of the length of cooled nerve. If the entering frequency is greater than this peak frequency, then the emerging frequency of discharge is reduced; the reduction depends on the entering frequency. Complete block of a train of impulses of appropriate frequency can be produced at suitable temperatures. It is suggested that this block occurs at the transition zone between the stimulating electrodes at the cooled region of the nerve.

6. The results predict that spike duration must vary with the normal conduction velocity of the fibres.

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