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MECHANISM OF EXCITATION OF TYPE J RECEPTORS

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Abstract. The type J receptors are stimulated during pulmonary congestion produced by occluding the aorta or left a-v junction which causes the left atrial pressure to rise with consequent rise in pulmonary artery pressure. Such acute congestion can be maintained only for brief periods (1–2 min). Longer lasting congestion leading eventually to pulmonary oedema is produced by injecting alloxan into the right atrium or right ventricle. A marked rise in pulmonary artery pressure follows the injection and after a lag there follows intense excitation of the type J receptors. It was concluded that this excitation was due to a rise in pulmonary capillary pressure and increase in permeability of the capillary membrane. Recent experiments have revealed that a considerable increase in activity can also be produced by injecting plastic microemboli (diameter $50 \mp 10\mu m$, i.v.). This increase occurs a few minutes after the rise in pulmonary artery pressure and is not due to a direct action of the microemboli on the endings nor can it be due to increased capillary permeability. Here, there can be no doubt that the increase in activity is a consequence of the rise in pulmonary artery pressure leading to a rise in pulmonary capillary pressure. This causes increase in interstitial volume leading to excitation of the endings. It was postulated that the endings were located in collagen tissue which acts like a sponge. Recently electronmicroscopic evidence has been obtained showing the presence of non-medullated sensory fibres in this collagen tissue but the precise structure of the endings (presumably type J) and their physical relation to the collagen tissue still remains to be established.

The recent electronmicroscopic observations of Meyrick and Reid (1971*ab*) on the alveolar endings in the rats lung have provided substantial support for the suggestion that the type J receptors are located in the interstitial tissue between the endothelium on one side and the alveolar epithelium on the other (Paintal 1969, 1970). Indeed Meyrick and Reid (1971*b*) have not only found non-medullated afferent nerve fibres in the

predicted location, i.e. the collagen tissue but they seem to have found some evidence for the presence of structures highly suggestive of afferent endings. Although on the basis of these findings one could speculate on possible ways in which the ending could be stimulated mechanically, it would be more helpful in the long run if information on the electron-microscopic structure of the endings of the cat could first be obtained — it is only in the cat that there is some quantitative information about excitation of the endings by substances either injected into the blood stream or insufflated into the lungs (Paintal 1955, 1957, 1969). Further there is information about the responses to increase in pulmonary capillary pressure produced by occluding the aorta (Paintal 1969).

Occluding the aorta or left atrio-ventricular junction stimulates most of these endings. Excitation starts a few seconds after the start of the occlusion which produces a rise in pulmonary venous capillary and arterial pressures and also oedema of the lung. The records reveal that there is always a lag between the rise in the pulmonary artery pressure and the excitation of the endings. Similarly when the occlusion is released there is a lag between the fall in pulmonary artery pressure and the reduction in activity. There is, as a rule, no cardiac rhythm to the receptor discharge, the latter being typically irregular. It is important to note that even though the average frequency of discharge may be of the order of 2 or 3 impulses/sec, such activity must be regarded as significant because this is the order of activity that occurs in endings with non-medullated fibres (Paintal 1970) under moderate stimulation. For example in chemoreceptors under intense stimulation the average frequency of discharge is about 8 impulses/sec (Paintal 1967).

Another method of stimulating the ending is by injecting alloxan intravenously and creating pulmonary oedema. The pulmonary arterial pressure rises, but there is no information on the pulmonary capillary pressure. There is certainly an increase in pulmonary capillary permeability (Aviado 1965, Staub et al. 1967, Goetzman and Visscher 1969). Alloxan causes increased fluid movement into the interestitial tissue and this may be the cause of the marked excitation of type J receptors. It is noteworthy that there is a delay not only between the injection of alloxan into the right ventricle and the excitation, but also between the rise in pulmonary artery pressure and excitation of the ending. If lung interstitial oedema is the cause of the receptor excitation, then this delay may be due to the time needed for the movement of a sufficient amount of fluid into the interstitial space.

It has been known for some time that starch embolism stimulates type J receptors (Paintal 1955). Recently Guz and Trenchard (1971) have found that injection of 50 μm emboli causes tychypnoea which is not abolished

by blocking the modullated fibres using a d-c block technique described by Mendell and Wall (1964). Guz and Trenchard (1971) therefore concluded that the tachypnoea was mediated by non-medullated fibres and that the microemboli stimulated the type J endings mechanically by distorting the arterioles and the adjacent alveolar walls. Experiments were therefore conducted to find out if this was so. These experiments will be reported in full elsewhere. Briefly, after isolating a type J fibre (identified by three essential criteria) (Paintal 1969) viz. stimulation within 2.5 sec following injection of phenyl diguanide into the right ventricle, no stimulation following a similar injection into the ascending aorta and marked sudden stimulation within 0.3 sec of insufflation of halothane into the lungs about 600–800 mg of 50 μm emboli (3M Co. Ltd.) were injected into a saphenous vein. In none of the 8 injections (2 of which were sudden injections) was there any immediate stimulation of the eight endings. In three cats there first appeared a rise in pulmonary artery pressure (as indicated by the systolic right ventricular pressure recorded simultaneously) and after a lag of 1–12 min excitation of the ending started and developed in intensity. It lasted for a few minutes. In one cat there was no obvious increase in pulmonary artery pressure and in this case the type J receptor was not stimulated either. In the other four cats, a rise in pulmonary artery pressure occurred without excitation of the single fibre from which recordings were being taken.

It is unlikely that excitation of the endings resulted from mechanical stimulation by the emboli themselves. The reasons for this conclusion are:

1. That there was never any immediate stimulation of the endings.
2. The pattern of stimulation was quite unlike that seen on stimulating the endings mechanically by inflation or deflation of the lungs or by application of local mechanical stimuli (*see* Fig. 8, 9, 10 and 11 in Paintal 1969).
3. If the emboli had in fact impacted in the capilary close to the ending, then one would have expected that the blood flow in this channel would be reduced if not blocked. This did not happen because the type J receptors continued to be stimulated by injections of phenyl diguanide into the right ventricle without any increase in latency. On the other hand in two instances the latency was reduced and in all cases the degree of excitation was obviously increased. This is probably due to the increased blood flow in the channels that were open and so the type J receptors located in their vicinity received a greater fraction of the injected phenyl diguanide than they did before embolization.

Finally the statistical probability of stimulating the endings by the

about 12×16^6. From measurements made on sections of the lung it was found that on the average about a fourth of the alveoli lay in proximity to the emboli. However, an embolus was in actual contact with less than 10% of the alveolar wall of such alveoli. Thus at the most only 3% of the alveolar surface was involved and since there are at the most 4,000 non-medullated fibres destined for each lung (Paintal 1963) it is clear that the possibility of an embolus directly stimulating an ending is very small.

The pattern of excitation was similar to that seen on rising pulmonary capillary pressure following occlusion of the aorta or left a-v junction. There were periods of irregular activity, unrelated to respiration, interspersed by periods of relative silence. This pattern is also seen when pulmonary oedema results from the administration of alloxan. It is therefore likely that in pulmonary microembolism the excitation is due to an increase in interstitial fluid resulting from an alteration in capillary haemodynamics consequent upon the obstruction. The emboli used were biologically inert (Guz and Trenchard 1971).

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