Occurrence of intimal thickening of the peripheral arteries in response to local vibration

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ABSTRACT Experiments were performed to elucidate a possible mechanism for the peripheral circulatory disturbance caused by vibration. Rats were exposed to local vibration (60 Hz, 5 G) on their hind legs for four hours a day for 30 days or 90 days. With exposure for 30 days the small arteries at the exposed site did not change. With exposure for 90 days, however, disruption of the internal elastic lamina was observed in the small arteries. This disruption was followed by focal cell proliferation with regenerative formation of collagen and elastic fibres. The fibrocellular thickening of the intima was further augmented, and in addition a complete stenosis of the lumen of the small arteries was observed. Electron micrography showed that the fibrocellular thickening of the intima consisted of a proliferation of arterial smooth muscle cells and numerous collagen and elastic fibres. These alterations were not observed in the arteries of the controls. The thickness of the media did not differ between the control and exposed groups or in animals with different durations of exposure. Concerning plasma total cholesterol, HDL-cholesterol, and lipoperoxide, there were no significant differences between the control and exposed groups after either 30 or 90 days, but the whole blood viscosity was significantly increased by day 90. This finding may be related to the intimal thickening.

To clarify the mechanism of the occurrence of Raynaud's phenomenon, which is a characteristic symptom of the vibration syndrome, it is important to study the effects of hand arm transmitted vibration. Some researchers have reported histological changes in the peripheral arteries in workers with Raynaud's phenomenon using vibrating tools. It is necessary, however, to ascertain experimentally whether or not these changes are specific to exposure to local vibration.

Recently, we have succeeded in demonstrating the occurrence of intimal thickening in the peripheral arteries of the rat after long term exposure to local vibration. The purpose of the present study was to evaluate the relation between the histological changes in the peripheral arteries and the mechanism of the occurrence of Raynaud's phenomenon in response to vibration.

Materials and methods

Materials
Twenty male Wistar rats, initially weighing 230–250 g, were used in groups of five.

Exposure to vibration
The apparatus used to induce vibration comprised an electromagnetic shaker (EMIC 513-A) with a shaking power of 7.5 kg (vibration frequency range 5–5000 Hz) coupled to an amplifier (TACHIKAWA TA-100), a function oscillator (TORIO AG202), and a vibration meter (EMIC 505-D).

The animals were placed prone in individual mesh cages. The hind legs were outside the cage and the plantar surfaces were horizontally fixed to the vibrating plate by means of double sided adhesive tape, so that the vibration would be transmitted only to the hind legs. The part of the cage containing the rest of the animal was fixed on a non-vibrating plate separated from the shaker. The hind legs of the rat were exposed to vertical sinusoidal vibration with a frequency of 60 Hz under a constant acceleration of 5 G. The duration of exposure was for four hours a day for either 30 or 90 days.

Before the experiments, the rats were trained for one week to ride on the vibrating platform.

The control animals for each experiments were also placed in wire mesh cages, which were placed near to the electromagnetic shaker during the exposure experiment so that any noise produced would be experienced but not the vibration.

The temperature in the laboratory room was
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The statistical analysis of the results was tested with Student's t test.

Results

Effects of local vibration exposure on the intima of the arteries

After 30 days exposure, the small arteries at the exposed site did not change histologically. In three of the five rats exposed for 90 days, however, there were some histological changes in the small arteries at the exposed site; alterations in the arteries of the control group were not observed. Figure 1 shows the histological changes in the small artery of the rat's hind leg after exposure to local vibration for 90 days; disruption of the internal elastic lamina may be observed in the artery. This disruption was followed by focal cell proliferation with regenerative formation of collagen and elastic fibres. Figure 2 shows a fresh fibrin thrombus in the lumen of the small artery observed at the exposed site in one of the five rats exposed for 90 days and in figure 3 mild fibrocellular thickening of the intima may be seen. Further thickening of the intima was followed by complete stenosis of the lumen observed (figure 4). Figure 5 shows that the fibrocellular thickening of the intima results from the proliferation of arterial smooth muscle cells from the media associated with the formation of collagen and elastic fibres.

Discussion

Both Pellegrini and Richard have suggested the possibility that there is some relation between organic changes in the artery and the occurrence of Raynaud's phenomenon after exposure to vibration. In the present study we found that intimal thickening of the small arteries in the rat was induced by repetitive...
Fig 1  **Small artery of rat hind leg after exposure to local vibration for four hours a day for 90 days.** Disruption of internal elastic lamina and focal cell proliferation with formation of collagen and elastic fibres are shown. (Elastica-Van Gieson stain, × 330.)

Fig 2  **Small artery of rat hind leg after exposure to local vibration for four hours a day for 90 days.** A fresh fibrin thrombus is shown in lumen of small artery. (Haematoxylin-eosin stain, × 330.)
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Fig 3  Small artery in rat hind leg after exposure to local vibration for four hours a day for 90 days. Mild fibrocellular thickening of intima is shown. (Elastica-Van Gieson stain, × 330.)

Fig 4  Small artery in rat hind leg after exposure to local vibration for four hours a day for 90 days. Severe intimal thickening and complete stenosis of lumen are shown. (Elastica-Van Gieson stain, × 330.)
and long term exposure to local vibration (figs 1–5). Recently, Ross et al proposed a new hypothesis for the pathogenesis of atherosclerosis. According to this hypothesis, the lesions result from some form of injury to the arterial endothelium that results in endothelial desquamation. This is followed by adherence, aggregation, and release of platelets at the focal site of injury. During the process of release, a mitogenic factor is secreted from the platelets which gains entry into the arterial wall, resulting in focal intimal proliferation of the smooth muscle cells. If the injury is a single event the lesions may heal and regress, leaving a slightly thickened intima. If the injury to the endothelium is repeated or chronic, however, the lesions may become complete, resulting in the production of pronounced intimal thickening. In the present experi-

![Electron micrograph of small artery of rat hind leg after exposure to local vibration for four hours a day for 90 days. Proliferation of arterial smooth muscle cells from media associated with formation of collagen and elastic fibres is shown (×4500).](image)

**Fig 5** Electron micrograph of small artery of rat hind leg after exposure to local vibration for four hours a day for 90 days. Proliferation of arterial smooth muscle cells from media associated with formation of collagen and elastic fibres is shown (×4500).

**Fig 6** Changes in medial thickness (represented as $D/R$) of arteries caused by local vibration.

**Fig 7** Effects of local vibration on whole blood viscosity measured at shear rates of 115 and 230 $s^{-1}$.
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Effects of local vibration exposure on plasma lipids

<table>
<thead>
<tr>
<th>Exposure for 30 days</th>
<th>Total cholesterol (mg/dl)</th>
<th>HDL-cholesterol (mg/dl)</th>
<th>Lipoperoxide (nmol/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>66.3 ± 3.4</td>
<td>22.3 ± 0.9</td>
<td>3.65 ± 0.21</td>
</tr>
<tr>
<td>Vibration exposed</td>
<td>69.2 ± 3.1</td>
<td>23.0 ± 1.8</td>
<td>3.46 ± 0.29</td>
</tr>
<tr>
<td>Exposure for 90 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>47.0 ± 2.5</td>
<td>19.8 ± 1.8</td>
<td>2.42 ± 0.15</td>
</tr>
<tr>
<td>Vibration exposed</td>
<td>45.4 ± 2.9</td>
<td>19.0 ± 1.6</td>
<td>2.78 ± 0.38</td>
</tr>
</tbody>
</table>

Each value represents the mean ± SE.

ment a fresh fibrin thrombus was observed in the small artery after 90 days exposure (fig 2). Therefore, it is considered that vibration induces intimal thickening through the processes described by Ross.7

Azuma et al reported that, after vibratory stimulation, the responsiveness of arterial smooth muscle to noradrenaline was greatly increased and that the vasoconstrictive activity of noradrenaline was also greatly raised.8 Kobori observed that endothelial injury may be caused to the mesenteric artery by the injection of methoxamine HCl, which is a vasoconstrictive agent.9 Therefore it is considered that the sensitivity of arterial vessels to noradrenaline increases after exposure to vibration and that the artery constricts or goes into spasm, thus causing injury to the endothelium. Moreover, it may be supposed that if repeated or chronic endothelial injury was caused by local vibration, pronounced intimal thickening of the artery would appear at the exposed site. In the present experiment histological changes were observed in the small arteries at the exposed site after 90 days exposure but not after 30 days. This also suggests that repetitive injury to the endothelium is important in producing severe intimal thickening.

Ashe and Williams reported that the clinical condition of workers using vibrating tools whose skin biopsy showed intimal thickening of the artery was more severe than those without.1 The data from the present study suggested that there is some relation between the intimal thickening in the small arteries and the attacks of Raynaud’s phenomenon. Our results support the theory that intimal thickening is related to the severity of the attack.

In general, vibration induced medial thickening of the artery is given greater attention than intimal thickening.2 Therefore we examined whether vibration can induce changes in the thickness of the media of the artery but found this was not the case. Furuyama reported significant correlations between the medial thickness of the mesenteric and femoral arteries and the systemic blood pressure.3 Therefore, the results of skin biopsy of workers using vibrating tools should be interpreted with due consideration to their blood pressure.

Changes in blood lipids induced by local vibration were not observed in this experiment; plasma TCH, HDL-C, and LPO concentrations which are considered to be related to atherosclerosis10 were not significantly different between the control and the exposed groups for any duration of exposure. Nevertheless, the whole blood viscosity was significantly increased after 90 days exposure and not 30 days. Fujinaga reported that in workers with Raynaud’s phenomenon using vibrating tools the whole body viscosity was significantly higher than in normal workers. Therefore, there may be some relation between the increase in whole blood viscosity and the intimal thickening seen in the small arteries at the exposed site and, in addition, whole blood viscosity may be useful in diagnosing the hand-arm vibration syndrome.

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