Vascular changes during acute inflammatory responses in rat hindpaws

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In acute inflammatory responses, increased blood flow and vascular permeability are important events which largely determine the extent of tissue swelling. Although the vascular changes which follow the administration of many substances thought to be mediators of inflammation have been widely studied, simultaneous measurement of changes in blood flow and vascular permeability, and their relationship to the inflammatory response within discreet regions has not been clearly established.

A method has recently been developed in our laboratories to measure these vascular changes precisely and determine their relationship to swelling in rat hindpaws.

METHODS

Studies have been made in male rats, body weight 250 g. The measurements of swelling (increase in weight relative to the control paw), local blood flow (using radioactive microspheres, 25 μm diameter) and extravasation of albumin (using [125I]human serum albumin) were made as described previously. Inflammatory mediators were injected into the plantar surface of one hindpaw in a volume of 0.1 ml. The same volume of saline was injected into the other hindpaw to serve as control. Thermal injuries were elicited by immersion of the paw in water (for temperature see Results) for 30 s duration.

Animals were sacrificed 15 min after injection of the inflammatory mediators.

RESULTS

In uninjured rat hindpaws, mean blood flow was 0.4 ± 0.06% of cardiac output; albumin content was 0.05 ± 0.01 ml. Injection of saline, 0.1 ml, had no
effect on blood flow, 0.38 ± 0.05% of cardiac output, but significantly increased albumin content to 0.17 ± 0.03 ml. Swelling in one paw did not change blood flow or albumin content of the other paw.

The injury-induced changes in paw blood flow are shown in Figure 45.1 and changes in extravasation of albumin are shown in Figure 45.2.

Thermal injury at 53 °C, 57 °C, 60 °C and 65 °C caused temperature dependent swelling, and increases in paw blood flow and extravasation of albumin.

5-hydroxytryptamine, 8 μg per paw, increased paw weight and caused marked extravasation of albumin with no significant change in local blood flow. In contrast, PGE₂, 25 and 50 ng caused large dose-dependent increases in blood flow to the paw although neither dose caused significant paw swelling.

48/80, 2.5 μg, caused substantial paw swelling with increases in both local blood flow and extravasation of albumin. Bradykinin, 2.5 μg, increased extravasation of albumin more effectively than blood flow. Histamine, 2.5 μg, caused small increases in paw weight, paw blood flow and extravasation of albumin.

Figure 45.1 Swelling and changes in blood flow to rat hindpaws caused by inflammatory stimuli. Blood flow in untreated or saline injected paws was 0.4% of cardiac output (represented by histogram in lower right hand corner). Responses to various inflammatory stimuli are indicated as follows: Thermal injury (●), PGE₂ (■), 48/80 (○), histamine (▼, H), bradykinin (◆, B) and 5-hydroxytryptamine (▲ 5-HT)