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# MODULATION OF ARTERIOLAR DIAMETER BY ENDOTHELIUM-DERIVED RELAXING FACTOR (EDRF) RELEASED FROM ITS PAIRED VENULE

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Submitted to the faculty of the Graduate School
in partial fulfillment of the requirements
of the degree
Doctor of Philosophy
in the Department of Physiology and Biophysics
Indiana University

December, 1988

Accepted by the Graduate Faculty, Department of Physiology and Biophysics, Indiana University, in partial fulfillment of the requirements of the degree of Doctor of Philosophy.

December 20, 1988

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**Announcing the**
**Final Examination of**
**Jeffrey C. Falcone**
**for the**
**Degree of**
**Doctor of Philosophy in Physiology and Biophysics**
**Tuesday, December 20, 1988; 10:00 A.M.**
**Indiana University School of Medicine**
**Medical Sciences Building, Room 309**
**Indianapolis, Indiana**

Dissertation: Modulation of arteriolar diameter by endothelium-derived relaxing factor (EDRF) released from its paired venule.

Arterioles, with an inner diameter > 30um, are closely paired with venules in most microvascular beds. The distance between these vessels varies from 0-200um. If EDRF were released from these venules it might diffuse to and initiate dilation of its companion arteriole. In the microvasculatures of the rat small intestine (n=8) and rat spinotrapezius muscle (n=7), continuous micro-iontophoretic application of acetylcholine (Ach) (0.1M) was used to stimulate the release of EDRF. Ach was applied directly to the arteriolar wall at currents of 25 and 50nA. These direct ejections caused intestinal arterioles to dilate 30% and 40%, respectively and spinotrapezius arterioles to dilate 55% and 90%, respectively. Ach was next ejected onto the venular wall farthest from the nearest paired arteriolar wall at currents of 40 - 80nA. Arteriolar response to the venular application of Ach took place within 15 seconds with a maximum response occurring within one minute. The venular Ach applications caused an 18% arteriolar dilation in the intestine and a 20% - 50% arteriolar dilation in the spinotrapezius. The response could be sustained for at least five minutes. Ach applied at 70 and 90nA in the tissue at a distance equal to that used above but on the opposite side of the arteriole from the venule did not cause arteriolar dilation and rules out the diffusion of Ach from the venule to the arteriole. Blockers of the EDRF effect methylene blue (100uM) and dithiothreitol (50uM) when suffused over the tissue significantly attenuated (>80%) the arteriolar dilation during Ach application to both vessels. Indomethacin (10uM) suffused over the tissue had no effect on the arteriolar dilations observed during any of the Ach applications; indicating that prostaglandins were not significantly involved. The observations indirectly indicate that EDRF released during application of Ach onto the venular wall can cause arteriolar dilation. Therefore, blood and interstitial conditions both in and around the large venules which stimulate the release of EDRF may influence the regulation of arteriolar diameter in both the rat small intestine and spinotrapezius muscle microvasculatures.

<u>Outline of Study</u>
Major: Physiology
Minor: Life Science

<u>Educational Career</u>
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Any member of the Graduate Faculty may attend. As a courtesy, please notify the Committee Chairman in advance.

ABSTRACT

Arterioles, with an inner diameter > 30um, are closely paired with venules in most microvascular beds. The distance between these vessels varies from 0-200um. If EDRF were released from these venules it might diffuse to and initiate dilation of its companion arteriole. In the microvasculatures of the rat small intestine (n=8) and rat spinotrapezius muscle (n=7), continuous micro-iontophoretic application of acetylcholine (Ach) (0.1M) was used to stimulate the release of EDRF. Ach was applied directly to the arteriolar wall at currents of 25 and 50nA. These direct ejections caused intestinal arterioles to dilate 30% and 40%, respectively and spinotrapezius arterioles to dilate 55% and 90%, respectively. Ach was next ejected onto the venular wall farthest from the nearest paired arteriolar wall at currents of 40 - 80nA. Arteriolar response to the venular application of Ach took place within 15 seconds with a maximum response occurring within one minute. The venular Ach applications caused an 18% arteriolar dilation in the intestine and a 20% - 50% arteriolar dilation in the spinotrapezius. The response could be sustained for at least five minutes. Ach applied at 70 and 90nA in the tissue at a distance equal to that used above but on the opposite side of the arteriole from the venule did not cause arteriolar dilation and rules out the diffusion of Ach from the venule to the arteriole. Blockers of the EDRF effect methylene blue (100uM) and dithiothreitol (50uM)

when suffused over the tissue significantly attenuated (>80%) the arteriolar dilation during Ach application to both vessels. Indomethacin (10uM) suffused over the tissue had no effect on the arteriolar dilations observed during any of the Ach applications; indicating that prostaglandins were not significantly involved. The observations indirectly indicate that EDRF released during application of Ach onto the venular wall can cause arteriolar dilation. Therefore, blood and interstitial conditions both in and around the large venules which stimulate the release of EDRF may influence the regulation of arteriolar diameter in both the rat small intestine and spinotrapezius muscle microvasculatures.

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