

This Week's Citation Classic

de la Lande I S & Rand M J. A simple isolated nerve-blood vessel preparation. *Aust. J. Exp. Biol. Med. Sci.* 43:639-56, 1965.
[Dept. Human Physiol. and Pharmacol., Univ. Adelaide, Adelaide, South Australia]

The isolated perfused rabbit ear artery responded by vasoconstriction to noradrenaline and to periarterial stimulation of intramural sympathetic nerves. Acetylcholine caused dilatation, but only when the tone was raised by sympathetic nerve stimulation; 5-hydroxytryptamine had only weak vasoconstrictor activity, but markedly potentiated the effects of noradrenaline. [The SCI® indicates that this paper has been cited over 145 times since 1965.]

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"The paper described the pharmacology of an isolated perfused artery which responded rapidly and reproducibly to sympathetic nerve stimulation. As a result, the preparation has come into widespread use for the study of adrenergic transmission in arteries and of the modification of transmission by drugs, in particular nowadays, drugs acting via pre-synaptic receptors.

"The preparation was essentially a 'spin-off' from a collaborative study on sympathetic neurotransmitter release in the perfused rabbit ear carried out in 1963 while I was on 12 months' study leave from the department of human physiology and pharmacology. University of Adelaide, in WDM. Paton's laboratory at Oxford. Bill Paton, Barbara Waud, and I spent much of the year being baffled by the tiny amounts of transmitter released during seemingly massive vasoconstrictor responses to periarterial sympathetic nerve stimulation. We finally investigated the possibility that much of the response may have been localized to the region of the artery immediately distal to the site of stimulation. Small segments of the artery when perfused in identical fashion to the whole ear did indeed prove to be highly

responsive. As my leave had expired, we concluded the study at that stage, but I arranged to explore further the potential of the isolated segment preparation on my return to Adelaide.

"Progress in 1964 was slow and went little beyond defining the optimal conditions for perfusing the vessel; however, the situation changed dramatically when Michael Rand, a former colleague from PhD student days, spent a short period in our department towards the end of 1964. His extensive experience in the area of adrenergic pharmacology was just what was needed to get the pharmacological characterization of the isolated rabbit ear artery 'off the ground,' and there followed several weeks of intensive activity during which most of the basic pharmacology described in the paper was defined. Indeed, my recollection is that the only 'recreation' Michael enjoyed during that time in Adelaide was to assist in the removal of a large orange tree from my garden in near-century heat! Predictably, in addition to providing a simple model for studying established vascular phenomena, the study gave us tantalizing glimpses of hitherto unsuspected phenomena. The mechanism of one of these —cholinergic inhibition of the response to sympathetic transmission —subsequently has been explained in terms of pre-synaptic receptors; however, another (serotonin-induced sensitization of other vasoactive agents) still awaits explanation after 15 years!

"I believe that two messages emerge from the history of the research which led to this publication. One is that it is yet another reminder of the way a new and useful technique can emerge as an unexpected bonus from a purely basic research project, in this instance, the study at Oxford. The other is that it illustrates the importance of collaboration between individuals who can bring quite different points of view and expertise into the solution of a problem of common interest, as was the case with Rand and myself."