

## CLINICAL PHARMACOLOGY SECTION

### Log dose-response curve to assess the effects of propranolol in angina pectoris

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When propranolol was first used in angina some investigators used small doses (Srivastava, Dewar & Newell, 1964; Keelan, 1965), others larger doses (Gillam & Prichard, 1965), and it was not immediately clear that larger doses were needed for maximum effect.

In the present study a dose-response curve for the effect of propranolol in angina pectoris has been plotted. The dose of propranolol was adjusted in each individual patient; it was increased until resting supine heart rate was 55–60/min or a side effect prevented any further dose increment. This was defined as full dose (average 417 mg/day; range, 80–1,280 mg/day). Full dose, half dose, quarter dose, and one eighth dose, besides placebo were each given for 2 weeks in random order and the cycle of treatment was repeated three times, that is 6 weeks on each dose. There was a straight line relationship from one eighth dose to full dose in terms of the parameters measured, a progressive reduction in angina attacks, a reduction in heart rate supine and standing.

Because even at full dose, as defined above, the dose/response relationship was still linear, it can be concluded that a larger dose would have a still greater effect.

### REFERENCES

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### Hypotensive action from combination of propranolol and other hypotensive drugs

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Propranolol is an effective hypotensive drug when used in adequate doses in man (Prichard & Gillam, 1969), an effect that was not predicted from animal experiments. The antihypertensive action of hydralazine, guanethidine and methyldopa was antagonized by propranolol in renal hypertensive rats (Bein & Brunner, 1966). Grewal & Kaul (1970) have recently discussed the antagonism of the hypotensive action of guanethidine by propranolol that they also observed. Our initial observations suggested that propranolol exerted an additive effect with a variety of hypotensive agents—including bethanidine, guanethidine, methyldopa, hydralazine—and diuretics (Prichard & Gillam, 1969).

Hypertensive patients have been observed over a period of change of treatment from bethanidine, or methyldopa to propranolol. Blood pressures were taken under standard conditions supine after 1 min resting, supine after 3 min (this reading used in assessment), standing after 1 min and after ascending and descending eighteen stairs. Blood pressures were recorded by the London School of Hygiene and Tropical Medicine sphygmomanometer (Rose, Holland & Crowley, 1964), a device that ensures the observer is unaware of the actual pressure when he auscultates. Evidence for