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Haemodynamic effects of indoramin: a non-invasive technique for the cardiovascular evaluation of drugs

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Non-invasive techniques for assessing cardiovascular function have the advantage of safety, simplicity, sensitivity and relatively low costs. They are being increasingly applied to the problems of diagnosis and the relevance of these techniques in the assessment of the cardiovascular effects of pharmacological interventions will be demonstrated.

A non-invasive technique was used in the cardiovascular evaluation of indoramin, a new hypotensive agent with cardio-inhibitory and α -adrenoceptor blocking properties in animals (Alps, Johnson & Wilson, 1970) and the latter in man (Coltart, Lockhart, Royds & Turner, 1971). Five healthy male subjects were studied at the same time of day, semifasting and lying on a bed with a 15° head-up tilt for a period of 2 h after the intravenous administration of indoramin (10 mg); blood pressures were taken with a London School of Hygiene sphygmomanometer (Rose, Holland & Crowley, 1964).

The systolic time intervals of left ventricular systole were obtained at 15 min intervals from simultaneous recordings of the electrocardiogram, phonocardiogram and carotid artery pulse trace, using a multi-channel photographic recorder at a paper speed of 100 mm/second. Left ventricular ejection time (LVET), Q-S₂ and R-R interval were measured and the pre-ejection period (PEP) was derived from Q-2₂ interval less LVET (Weissler, Harris & Schoenfeld, 1968). The ratio PEP/LVET

is a convenient and sensitive expression of changes in systolic intervals without correction for heart rate or sex, varying within narrow limits but related to alterations in cardiac output and stroke volume (Weissler, Harris & Schoenfeld, 1969). Left ventricular end systolic and end diastolic volumes were measured by ultrasonics (Popp, Wolfe, Hirata & Feigenbaum, 1969) and stroke volume, cardiac output and the ejection fraction (EF) derived. EF and PEP/LVET have been shown to closely correlate with direct measurements of myocardial function.

Indoramin produced a statistically significant decrease in blood pressure with little change in R-R interval but PEP, LVET, PEP/LVET, EF and cardiac output were not significantly altered.

Indoramin, therefore, produces a hypotensive effect in man with no measurable change in the functional state of the myocardium. This contrasts with its cardio-inhibitory properties in animal studies.

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Peripheral blood scintillometry in psychophysiological research

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Venous occlusion plethysmography has several disadvantages (Landowne & Katz, 1942; Whitney, 1953; Brown, Giddon & Dean, 1965; Greenfield, Whitney & Mowbray, 1963), some of which may be overcome by the technique of peripheral blood scintillometry.

An intravenous injection of 200 μ Ci of 113m indium remains within the bloodstream and after equilibrium is attained within a few minutes, can be used to reflect the blood volume present in the part under investigation in a given interval of time.

The 113m indium in the forearm circulation, is detected by using two opposed sodium iodide scintillation counters mounted coaxially with the forearm resting on the lower counter. The system is adjusted so that only the 390 KeV photopeak gamma rays from the 113m indium are counted. The outputs from each counter are summed and displayed on a scaler so that the counts for any selected time interval can be recorded. They are also recorded on a ratemeter, from which a pen-recorder trace gives a graphical display of the count rate as a function of time. A facility also exists which enables the counts in any set time interval to be printed on punched tape so that the correction for radioactive decay of 113m indium can be made automatically with the aid of a computer.