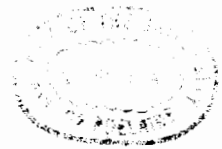


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STUDIES ON SOME CARDIOVASCULAR DRUGS IN MAN.

A THESIS

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of

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by

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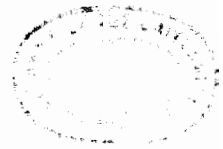
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PREFACE

The present series of studies arose as the result of a clinical trial of a drug for the treatment of hypertension. During this trial it became obvious that tolerance to the drug developed in the majority of patients. Although explanations for the phenomenon of tolerance had been suggested on the basis of animal work, very few investigations on humans had been performed.

The original hypotensive drug and several others were therefore studied on humans in the laboratory not only from the point of view of tolerance, but also to determine their effects on blood vessels of the upper limb. In addition to these acute studies the vascular responses of a number of patients on chronic oral hypotensive drug therapy have been followed, as have those of a patient with pheochromocytoma before and after operation. An investigation of the effects of noradrenaline on the human forearm is included in view of the importance of this subject in the interpretation of blood flow measurements in that segment, since the response of forearm vessels to noradrenaline is frequently used as a measure of vascular sensitivity.

All the studies reported in this thesis have been made on humans. Experiments with human subjects pose a number of special problems, including ethical considerations, technical difficulties with conscious subjects, relatively small numbers, and the small drug dosages that can be employed. In spite of these difficulties and limitations, it is very important that, where possible, a step of what

may be called human pharmacology should be interposed between pharmacological studies on animals and the administration of drugs to patients in clinical trials.