β component. The following technique was devised to reduce time wastage in obtaining significant data. Occlusion cuff inflation-deflation sequences are varied between 4 and 8/min. The analogue signal is sampled immediately before occlusion cuff inflation begins and basal tissue volume trend is thereby monitored. Venous occlusion integrates pulsatile flow, and the respiratory and α components are averaged out by using a sufficient number of collections over many α cycles. The monitored basal volume change allows identification of β cycling and the calculation of mean flow is obtained over a small integral number of β fluctuations. This mean result is minimally affected by the naturally occurring volume fluctuations. During on-line data acquisition a 4β mean and standard deviation is calculated and indicates mean flow and dispersion for pulse, respiration and α and β components. It is assumed that the slow γ component does not significantly affect individual 4β means. Verification of the consistency of successive 4β means will give the earliest possible indication of steady state. Drug response and recovery can therefore be more easily identified during the course of an experiment.

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Comparison of atropine and (−)-hyoscyamine on heart rate in man

H. BAGSHAW, D. A. CHAMBERLAIN and P. TURNER, *St. Bartholomew's Hospital, London E.C.*1

(−)-Hyoscyamine is about twice as potent as the racemic mixture atropine when tested on mammalian and human salivary glands, heart rate, and pupil diameter (Cushny, 1920). The two drugs have been compared in five healthy male volunteers aged 22 years pretreated with propranolol. The procedure was based on that described by Chamberlain, Turner & Sneddon (1967), and involved measuring heart rates before and 5 min after propranolol (0·15 mg/kg intravenously). Atropine or (−)-hyoscyamine was then injected intravenously over 1 min. Heart rate was recorded at rest supine for 4 min from the start of injection, again after the subject had stood for 30 s, and subsequently during the last 10 s of consecutive periods of increasingly strenuous exercise on a motor-driven treadmill. Two doses of atropine (1·2 mg and 0·04 mg/kg) and (—)-hyoscyamine (0·6 mg and 0·02 mg/kg) were given to each subject, the drugs being administered on different days in varying order, the smaller before the larger doses.

The heart rate 4 min after injection was significantly increased by both drugs, even in the smaller doses, when compared with propranolol alone. The higher doses produced a significantly greater response than the lower doses, but there was no significant difference between atropine and (—)-hyoscyamine when the effects of corresponding doses were compared (Fig. 1). As vagal tone decreased with increasing levels of exercise the difference between treatments diminished, disappearing at maximum exercise. Comparing their initial parasympathomimetic effects, both

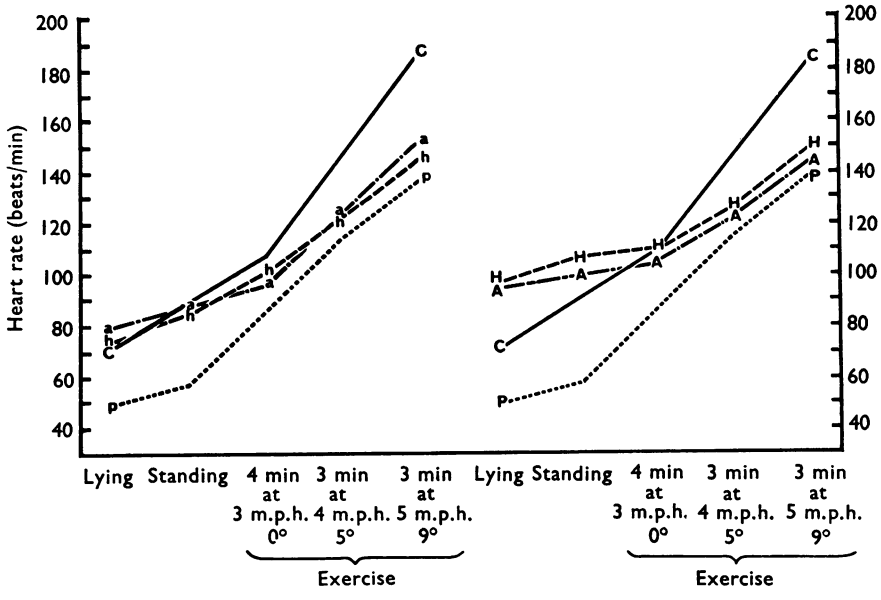

FIG. 1. Mean heart-rates in five volunteers lying, standing and after exercise, without pretreatment (C) and following intravenous administration of propranolol (0·15 mg/kg) alone (P) and with atropine (1·2 mg and 0·04 mg/kg) (*a*, *A*) or (—)-hyoscyamine (0·6 mg and 0·02 mg/kg) (*h*, *H*).

compounds produced a significant fall in heart rate within the first 2 min of injection, but there were no differences between drugs or doses.

The anti-vagal activity of (—)-hyoscyamine is about twice that of atropine on the pharmacologically sympathectomized human heart.

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A class experiment to investigate the side-effects of anti-emetics

R. S. J. CLARKE and J. W. DUNDEE, *Department of Anaesthetics, The Queen's University of Belfast, Northern Ireland*

Opportunity was taken of a practical class in clinical pharmacology to demonstrate and evaluate the side-effects of certain anti-emetic drugs. These are mostly freely available to the public and it seemed worth while to let the students experience their actions because of the high incidence of side-effects, which were on the whole irritating rather than dangerous. Over a 10 year period, four hundred students received some drug (or placebo), and the findings are reported in this demonstration.

The drugs were given intramuscularly on a double-blind basis and included perphenazine (2·5 and 5·0 mg), promethazine (25 mg), propiomazine (20 mg), thiethylperazine (10 mg), cyclizine (25 and 50 mg), hyoscine (0·2 and 0·4 mg), dimenhydrinate (50 mg) and metoclopramide (10 mg). Other students made detailed observations at 10 min intervals for 1 h and the subject noted the effects at 6, 18 and 24 h after injection. Results were later discussed with the whole class.

Contrary to expectations, findings were reasonably consistent in each batch of students and " placebo responses " were infrequent. In the doses given, the cardio-