enced the marked increase in output from 1·91 to 6·79 l./min. No arterial oxygen tension value fell below normal during the study and no significant changes were noted in pH nor in the arterial carbon dioxide tension.

In three patients the onset of nodal rhythm was associated with an immediate increase in right atrial pressure from 3 to 5 cm H_2O together with a slight but definite fall in arterial blood pressure. The return of sinus rhythm restored these variables to their previous values.

Practolol in the management of cardiac dysrhythmias in patients anaesthetized with halothane

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Disturbances of rate and rhythm were studied in twenty-one patients (average age 62 years, range 35 to 81) anaesthetized with halothane after premedication with pentobarbitone (200 mg intramuscularly) for a variety of surgical procedures. Induction was with 5% thiopentone (250–400 mg intravenously); when intubation was necessary suxamethonium (40–100 mg intravenously) was used, thereafter the patients breathed spontaneously. Cardiac rhythm was followed by a single non-conventional e.c.g. lead displayed on a suitable oscilloscope and charted on a Mingograph 81 recorder. Blood pressure was measured intermittently in seven patients with a Von Recklinghausen oscillotonometer and continuously in fourteen from a catheter inserted percutaneously into a radial artery. Arterial blood samples were withdrawn before and after treatment with practolol for the measurement of oxygen and carbon dioxide tensions.

The development of sinus tachycardia (four patients), nodal rhythm (four), pulsus bigeminus (five) and multifocal ventricular extrasystoles (eight) was treated with practolol (4 mg intravenously); almost invariably normal rate and rhythm was restored but in three patients a second injection was required; the mean recovery time was 39 s (range 8 to 65). The heart rate was slowed significantly ($P<0.0005$) from a mean of 108 to 85 beats/min but the blood pressure was unchanged. At the onset of the dysrhythmia no arterial oxygen tension was below normal (mean $\pm$ S.E.M. $Pa_{O_2}=227\pm83$ mmHg, range 95 to 370/mmHg) but most carbon dioxide tensions were high ($Pa_{CO_2}=62\pm15$ mmHg, range 41 to 89 mmHg). In eighteen of the twenty-one patients the onset of the cardiac disturbances was preceded by the injection of atropine (0·6 mg intravenously). In the remaining three patients not given atropine a significant fall in blood pressure ($P<0.0005$) associated with a marked reduction in heart rate followed the administration of practolol. In one patient the heart rate dropped markedly from 108 to 36 beats/min and the blood pressure fell from 115/80 to 65/40 mmHg; atropine (0·6 mg intravenously) abolished the bradycardia and restored the blood pressure.

In seven patients from whom consent for the investigation had previously been obtained, the effect of practolol on cardiac output and on the right atrial pressure was studied. No significant change in cardiac output could be detected but a 15% increase in the appearance time of the dye was noted. In no patient did the stroke volume fall and in five it improved (mean increase 26·7%). The right atrial pressure was unchanged.

Thus practolol (4 mg intravenously) appears to abolish certain ventricular dysrhythmias occurring during anaesthesia without depressing cardiac action.

Blood levels of practolol following intravenous administration

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Blood concentrations of the cardioselective β-adrenoceptor blocking agent practolol (I.C.I. 50172, Eraldin) have been studied in normal volunteers following oral administration. Concentrations in blood were correlated with the percentage inhibition of exercise tachycardia. The peak concentration in blood occurred 1·5–3 h after the oral administration and decayed thereafter with a half life of 10 ± 2 h (Fitzgerald & Scales, 1968).

In the present study intravenous practolol was administered to six volunteer hypertensive patients. The decay curve can only be explained by the use of a three compartmental mathematical model. The initial short half-life of 5 min is due to a rapid tissue equilibration and the later long half-life component of 12 h may be the result of entero-hepatic recirculation. These results are supported by results in animals (Scales & Cosgrove, 1970).

The blood levels required to produce over 30% inhibition of isoprenaline tachycardia (4 μg/min) are greater than 0·5 μg/ml, exercise tachycardia (100 W, 2 min) are over 1 μg/ml. Levels of 1 μg/ml can only be maintained by the administration of 20 mg intravenously at 10 min intervals. A single injection of 20 mg only gives levels above 1 μg/ml for about 5 min.

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Vascular actions of clonidine in man

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Clonidine, an imidazoline derivative, has been recently introduced for the treatment of hypertension. Animal studies indicate an action on sympathetic centres. Surprisingly, the peripheral action on blood vessels is constrictor, probably the result of stimulation of α-adrenoceptors. The drug has been given to man intravenously, but little information is available on the direct effects on human blood vessels.

Clonidine (250–500 ng/min) was infused into a brachial artery of each of twelve normal volunteers, and the effects on hand or forearm blood flow were recorded. There was a prompt dose-related vasoconstriction lasting for the period of the infusion (in one instance for 30 min). This constriction was abolished completely by α-adrenoceptor blocking agents and occurred in the skin vessels rather than the