# PULSE AND BLOOD PRESSURE

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STUDIES IN HEALTHY patients indicate that cardiac output and tissue perfusion are maintained at normal or above normal levels during surgical anaesthesia with isoflurane.[11] In vitro myocardial performance as judged by contractility studies of isolated papillary heart muscle[12] is depressed in a dose related way comparable to the effects of halothane. On the other hand, in vivo studies in elderly patients[13] or patients with coronary artery disease[4] do not show any significant depression. Further, in healthy young patients myocardial function remains stable at 1 and 2 MAC with isoflurane.[11]

Typically in healthy patients stroke volume is reduced about 20 per cent below awake values at 1.5 MAC while heart rates increased by about the same amount, resulting in no change or very little change in cardiac output.[11] Arterial blood pressure is reduced about 35 per cent below awake levels, but because peripheral resistance is also reduced by about 30 per cent, overall muscle and skin perfusion increases.[11] The use of spontaneous ventilation during isoflurane anaesthesia increases heart rate and cardiac output but not arterial pressure compared to patients in whom ventilation is controlled.[15]

Most of the above studies were conducted on limited numbers of patients or healthy volunteers. Only limited information has been available on the effect of age and body size, coexisting disease and drugs, procedure site and anaesthetic drugs, including muscle relaxants, on the cardiovascular response to isoflurane.

## METHODS

The raw data which were collected on pulse (P) and blood pressure (BP) included highest (HP, HBP), lowest (LP, LBP), and typical (TP, TBP) values during the induction period (first 10 minutes) classified as period 2 and during maintenance (after first 10 minutes) classified as period 3. The values immediately before induction were classified as period 1.

The derived values included change in pulse and blood pressure for periods 2 and 3 with respect to period 1 and for period 3 with respect to period 2. In addition the lability of pulse and pressure (difference between highest and lowest values) was calculated. Each of the raw and derived values was examined by multiple regression analysis and analysis of variance against demographic, patient and anaesthetic factors to determine predictive values for various subgroups of patients. Only those relationships which were statistically significant or clinically relevant are discussed below. To facilitate description of this complex analysis the abbreviated form of each variable will be used throughout. A definition of each is given in Table 18. The level of statistical significance was set at $P \leq 0.001$. Correlation coefficients which are significant at this level are of a lower numeric value than is commonly experienced because of the very large degrees of freedom. Thus for more than 1,000 cases a correlation coefficient equal to or greater than 0.250 is significant at $P \leq 0.0001$.

## SUMMARY OF MEAN VALUES

The overall mean ($\pm 1$ SEM) values for 6,798 patients are given in Table 19 for each period of study. Pulse increased on average 5.3 b/min at induction and 2.2 b/min during maintenance compared to preinduction values, whereas blood pressure decreased 1.24 kPa (9.3 mmHg) at induction and 1.96 kPa (14.7 mmHg) during maintenance. Note that the average isoflurane concentrations used during these periods were 1.69 and 1.20 per cent respectively. Change in pulse and blood pressure was related to average concentration of isoflurane during maintenance ($aF_3$) (Table 25). The lability of pulse and blood pressure was generally not different between induction and maintenance, thus (m $\pm$ 1 SEM) H-$LP_2$ equalled 18.7 $\pm$ 0.17, H-$LP_3$ equalled 20.14 $\pm$ 0.17, H-$LBP_2$ equalled 3.62 $\pm$ 0.03 kPa (27.22 $\pm$ 0.25 mmHg) and H-$LBP_3$ equalled 3.82 $\pm$ 0.03 kPa (28.72 $\pm$ 0.26

TABLE 18

| | Pulse | Blood pressure |
|---|---|---|
| Preinduction | $P_1$ | $BP_1$ |
| Induction | | |
| highest | $HP_2$ | $HBP_2$ |
| lowest | $LP_2$ | $LBP_2$ |
| typical | $TP_2$ | $TBP_2$ |
| change | $P_1$–$HP_2$, $P_1$–$LP_2$, $P_1$–$TP_2$ | $BP_1$–$HBP_2$, $BP_1$–$LBP_2$, $BP_1$–$TBP_2$ |
| lability | H–$LP_2$ | H–$LBP_2$ |
| Maintenance | | |
| highest | $HP_3$ | $HBP_3$ |
| lowest | $LP_3$ | $LBP_3$ |
| typical | $TP_3$ | $TBP_3$ |
| change 1 | $P_1$–$HP_3$, $P_1$–$LP_3$, $P_1$–$TP_3$ | $BP_1$–$HBP_3$, $BP_1$–$LBP_3$, $BP_1$–$TBP_3$ |
| change 2 | $HP_2$–$HP_3$, $LP_2$–$LP_3$, $TP_2$–$TP_3$ | $HBP_2$–$HBP_3$, $LBP_2$–$LBP_3$, $TBP_2$–$TBP_3$ |
| lability | H–$LP_3$ | H–$LBP_3$ |

TABLE 19

| | Pulse (b/min) | Blood pressure kPa(mmHg) |
|---|---|---|
| Preinduction | $P_1$ = 87.71 ± 0.27 | $BP_1$ = 16.82 ± 0.04 (126.50 ± 0.27) |
| Induction | $TP_2$ = 93.12 ± 0.27 | $TBP_2$ = 15.58 ± 0.03 (117.18 ± 0.25) |
| | $HP_2$ = 104.17 ± 0.30 | $HBP_2$ = 17.71 ± 0.04 (133.13 ± 0.32) |
| | $LP_2$ = 85.47 ± 0.26 | $LBP_2$ = 14.09 ± 0.03 (105.92 ± 0.25) |
| Maintenance | $TP_3$ = 89.99 ± 0.27 | $TBP_3$ = 14.86 ± 0.03 (111.76 ± 0.21) |
| | $HP_3$ = 101.81 ± 0.29 | $HBP_3$ = 16.94 ± 0.04 (127.36 ± 0.29) |
| | $LP_3$ = 81.66 ± 0.26 | $LBP_3$ = 13.12 ± 0.03 ( 98.64 ± 0.21) |

Mean pulse and blood pressure values ±1 SEM for each period.

mmHg). Only lability of pressure was related to preoperative values (see Table 24).

### Influence of Age and Body Size

Significant correlations were found for virtually all pulse and pressure variables against age and body size factors such as weight, height, and surface area. Calculated differences between preinduction values and those under isoflurane anaesthesia usually eliminated these correlations. In general terms, pulse decreased with age and blood pressure increased. The mean values ±1 SEM for the most important variables are given in Table 20. It can be seen that over the age of 20 years there is little change in any of the pulse variables with age. The difference between the preinduction value and typical value during induction diminished with age and averaged about 5 beats/min, while the difference with the typical maintenance value was around 1.5 beats/min. The lability of pulse (difference between highest and lowest values) at both induction and maintenance decreased with age, whereas lability of blood pressure increased with age. There were significant linear relationships for pulse (inverse) and for blood pressure (direct) against age with pulse showing an overall increase with induction compared to a decrease in blood pressure. The principle linear regression equations against age, weight, height, and surface area are given in Table 21. Note the exceptional decrease in pulse rate in the group under one year old. At age 20 years there was a mean eight per cent increase in pulse and five per cent decrease in blood pressure, while at age 60 years pulse increased by about four per cent and blood pressure decreased about eight per cent. Similar trends were found for height, body weight, and surface area for each pulse and pressure variable (Table 21).

### Influence of Preinduction Values

The linear regression analysis which was done for pulse and blood pressure against preinduction values resulted in highly significant linear correlations for each of five age groups as well as for all patients. These are given in Table 22. In general, up to the age of 40 years there was an

TABLE 20

MEAN ± 1SD PULSE AND BLOOD PRESSURE

| Age grp. | No. of Cases | $P_1$ | $TP_2$ | $TP_3$ | $H–LP_2$ | $BP_1$ | $TBP_2$ | $TBP_3$ | $H–LBP_2$ |
|---|---|---|---|---|---|---|---|---|---|
| < 1 | 135 | 155.9 | 150.0 | 149.9 | 28.9 | 94.1 | 88.5 | 84.4 | 18.7 |
| | | 24.2 | 21.7 | 19.5 | 21.5 | 20.8 | 18.0 | 17.6 | 12.1 |
| 1–10 | 639 | 116.9 | 127.2 | 125.7 | 27.9 | 105.0 | 103.3 | 100.3 | 17.4 |
| | | 23.9 | 22.7 | 20.1 | 20.7 | 15.5 | 16.0 | 13.8 | 13.5 |
| 11–20 | 558 | 86.9 | 93.9 | 90.7 | 20.0 | 119.8 | 111.4 | 108.7 | 20.9 |
| | | 17.6 | 18.0 | 17.8 | 14.7 | 16.5 | 16.5 | 14.9 | 15.3 |
| 21–30 | 1218 | 83.6 | 90.8 | 87.9 | 18.9 | 121.4 | 113.9 | 110.0 | 22.3 |
| | | 15.8 | 16.4 | 16.1 | 13.6 | 16.1 | 15.9 | 13.9 | 15.5 |
| 31–40 | 1081 | 84.4 | 90.8 | 87.2 | 18.7 | 122.6 | 115.7 | 111.7 | 24.5 |
| | | 16.2 | 15.6 | 15.0 | 13.5 | 17.5 | 16.0 | 14.8 | 17.5 |
| 41–50 | 874 | 83.9 | 88.5 | 84.5 | 17.2 | 127.7 | 118.7 | 112.0 | 26.8 |
| | | 15.6 | 15.6 | 15.0 | 12.1 | 18.6 | 18.6 | 15.3 | 19.2 |
| 51–60 | 1009 | 81.7 | 85.3 | 82.0 | 16.5 | 134.8 | 122.6 | 114.8 | 33.8 |
| | | 15.2 | 15.5 | 14.7 | 11.8 | 21.7 | 21.1 | 17.5 | 23.4 |
| 61–70 | 746 | 81.1 | 83.8 | 80.1 | 16.4 | 140.9 | 126.4 | 117.8 | 36.4 |
| | | 16.6 | 15.5 | 14.5 | 11.4 | 22.8 | 21.7 | 18.3 | 25.0 |
| 71–80 | 413 | 79.6 | 82.8 | 79.7 | 15.2 | 144.1 | 130.1 | 120.7 | 36.8 |
| | | 14.2 | 13.8 | 13.6 | 10.8 | 24.0 | 22.6 | 17.6 | 24.7 |
| 81–90 | 108 | 80.4 | 82.8 | 80.0 | 14.4 | 150.4 | 133.0 | 126.0 | 38.0 |
| | | 14.7 | 14.5 | 15.1 | 9.6 | 25.9 | 22.7 | 19.1 | 27.0 |
| 91–100+ | 16 | 83.0 | 82.3 | 77.7 | 9.9 | 145.2 | 135.0 | 120.0 | 29.8 |
| | | 14.5 | 14.7 | 10.4 | 8.2 | 17.4 | 25.2 | 22.1 | 26.2 |

Period 1 = preinduction; 2 = induction; 3 = maintenance.
P = pulse; BP = blood pressure; T = typical value; H–L = Difference between highest and lowest values.

increase in preoperative blood pressure as well as slope of the relationship against change in blood pressure for periods 2 and 3. Above this age there was a further increase in slope but little change in preoperative values. On the other hand, the slope of change in pulse against the preoperative value decreased with age, as did the preoperative value. The predictiveness of these relationships is extremely high and shows little variability around the mean values for each preoperative value. Thus for a patient less than 10 years of age with a mean preoperative pulse of 127 b/min and blood pressure of 13.7 kPa (103 mmHg), pulse can be expected to increase during maintenance by 6.1 b/min and blood pressure to decrease by 0.76 kPa (5.7 mmHg), compared to a patient over 60 years old with mean preoperative pulse and blood pressure of 81 b/min and 19.02 kPa (143 mmHg) in whom pulse will decrease by 1 b/min, and blood pressure will decrease by 3.19 kPa (24 mmHg).

Figure 2 shows the typical blood pressure and pulse values during maintenance for the range of preoperative values in the oldest and youngest age groups, as well as for all patients. Clearly this shows that while blood pressure decreased to a greater extent with increasing age, the resulting pressure is only slightly different than that found for all ages. Note that the neutral values for blood pressure and pulse (zero changes) for all patients are 13.3 kPa (100 mmHg) and 96 b/min respectively and that, where preoperative values are less than these, both pulse and blood pressure increased during the maintenance period. This is especially so for the younger age group. The hatched line on Figure 2 indicates the line of no change. Although pulse rate decreased with age and blood pressure increased, the predictive value of the relationships on Figure 2 using the preoperative values is of great clinical significance. Even within one age group, where various conditions were present to either increase or decrease the preoperative pulse and blood pressure about the mean value for that age group, the responses during isoflurane anaesthesia can be predicted with a high degree of accuracy. The mean value for each group is indicated in Figure 2.

TABLE 21

AGE, WEIGHT, HEIGHT, AND BODY SURFACE AREA LINEAR REGRESSIONS (Y = aX + b)

| Y | aX | b | r = correl. coeff. |
|---|---|---|---|
| $P_1$ | −0.024 A | +97.21 | −0.310 |
| | −0.433 W | +114.81 | −0.457 |
| | −0.516 H | +169.66 | −0.579 |
| | −29.220 S | +135.59 | −0.541 |
| $BP_1$ | 0.041 A | +107.15 | 0.466 |
| | 0.378 W | +102.21 | 0.380 |
| | 0.315 H | +76.14 | 0.336 |
| | 21.639 S | +90.56 | 0.381 |
| $TP_2$ | −0.032 A | +106.98 | −0.406 |
| | −0.443 W | +120.82 | −0.468 |
| | −0.493 H | +171.19 | −0.559 |
| | −28.605 S | +139.80 | −0.536 |
| $TP_3$ | −0.034 A | +104.39 | −0.430 |
| | −0.474 W | +119.62 | −0.505 |
| | −0.518 H | +172.01 | −0.595 |
| | −30.366 S | +139.53 | −0.576 |
| $TBP_2$ | 0.028 A | +104.17 | 0.351 |
| | 0.299 W | +98.02 | 0.333 |
| | 0.243 H | +78.35 | 0.288 |
| | 16.863 S | +89.25 | 0.329 |
| $TPB_3$ | 0.019 A | +102.93 | 0.285 |
| | 0.236 W | +96.57 | 0.311 |
| | 0.205 H | +78.85 | 0.287 |
| | 13.611 S | +89.10 | 0.314 |

All listed correlations are significant at $P < 0.0001$.

A is age in months; W is weight in kg; H is height in cm; S is surface area in $m^2$, blood pressure is in mmHg.

### VARIATION WITH SEX AND AGE

The differences between male and female for three age groups (infant = <1 year, youth = 1–20 years, and adult = >20 years) for induction pulse and blood pressure and for the difference during induction and maintenance, are shown in Table 23. The difference between sexes was significant only in the adult group for preinduction pulse (higher in females) and blood pressure (higher in males) and for the pressure difference during induction and maintenance (higher in both cases in males). These differences are significant at $P < 0.001$.

### LABILITY OF PULSE AND PRESSURE

The difference between the highest and lowest values recorded during induction and maintenance is a measure of lability of these parameters. Linear regression analysis for each against preinduction values was done and is shown in Table 24. Only the differences for blood pressure were statistically significant. Thus lability of blood pressure increased as preinduction blood pressure increased. Since age is also associated with an increase in preinduction blood pressure it is to be expected that lability increased with age, as it did also with weight, height and body surface area.

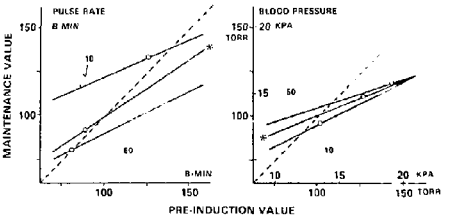


FIGURE 2 Linear regressions for typical maintenance values for pulse rate (beats/min) and blood pressure (torr and KPA) against the pre-induction value. The linear regressions for all patients (asterisk) and those under 10 years and over 60 years are shown in each case. The hatched line shows the line of unity (no change). Complete linear regression for all age groups are given in Table 22.

### VARIATIONS WITH ISOFLURANE CONCENTRATION

Multiple linear regression analysis was done for each pulse and blood pressure variable against the highest (HF) and average (aF) isoflurane concentration used during induction and maintenance. The variables tested included highest, lowest and typical pulse and blood pressure in each period, the differences between preinduction values and the two anaesthetic periods. The most important linear regressions are summarized in Table 25 with the correlation coefficient shown in each case. Those correlations which are significant at $P < 0.001$ are indicated. The typical pulse during induction was significantly increased as average or highest isoflurane concentration increased. On the other hand, the difference between preinduction and induction pulse (negative value = increased pulse) was significantly related to average isoflurane used during induction, and increased with increased isoflurane. None of the blood pressure variables during induction was significantly related to isoflurane concentrations.

During maintenance, the typical pulse and the difference with pre-induction values were significantly related to average isoflurane concentra-

TABLE 22

LINEAR REGRESSION EQUATIONS OF CHANGE IN PULSE AND BLOOD PRESSURE WITH AGE

| | Y = aX + b | | r = correl. coeff. |
|---|---|---|---|
| Less than 10 yrs. | $P_1$–$TP_2$ = 0.502 | $P_1$ − 71.07 | 0.588 |
| | $P_1$–$TP_3$ = 0.571 | $P_1$ − 78.60 | 0.657 |
| | $BP_1$–$TBP_2$ = 0.351 | $BP_1$ − 33.67 | 0.425 |
| | $BP_1$–$TBP_3$ = 0.487 | $BP_1$ − 44.46 | 0.521 |
| 10–20 yrs. | $P_1$–$TP_2$ = 0.418 | $P_1$ − 44.27 | 0.453 |
| | $P_1$–$TP_3$ = 0.522 | $P_1$ − 50.57 | 0.523 |
| | $BP_1$–$TBP_2$ = 0.325 | $BP_1$ − 31.11 | 0.385 |
| | $BP_1$–$TBP_3$ = 0.528 | $BP_1$ − 52.48 | 0.545 |
| 40–60 yrs. | $P_1$–$TP_2$ = 0.336 | P1 − 31.97 | 0.400 |
| | $P_1$–$TP_3$ = 0.530 | $P_1$ − 44.38 | 0.542 |
| | $BP_1$–$TPB_2$ = 0.371 | $BP_1$ − 38.12 | 0.441 |
| | $BP_1$–$TBP_3$ = 0.610 | $BP_1$ − 62.58 | 0.657 |
| More than 60 yrs. | $P_1$–$TP_2$ = 0.323 | $P_1$ − 28.44 | 0.419 |
| | $P_1$–$TP_3$ = 0.508 | $P_1$ − 40.16 | 0.554 |
| | $BP_1$–$TBP_2$ = 0.475 | $BP_1$ − 52.77 | 0.515 |
| | $BP_1$–$TBP_3$ = 0.677 | $BP_1$ − 73.27 | 0.690 |
| All patients | $P_1$–$TP_2$ = 0.244 | $P_1$ − 26.71 | 0.341 |
| | $P_1$–$TP_3$ = 0.323 | $P_1$ − 30.53 | 0.404 |
| | $BP_1$–$TBP_2$ = 0.385 | $BP_1$ − 39.37 | 0.499 |
| | $BP_1$–$TBP_3$ = 0.583 | $BP_1$ − 58.99 | 0.671 |

Note: Blood pressure is in mmHg.

TABLE 23

PULSE AND BLOOD PRESSURE VS AGE GROUP VS SEX

| | Infant (<1 yr) | | Youth (1–20 yr) | | Adult (>20 yr) | |
|---|---|---|---|---|---|---|
| n | Female (34) | Male (101) | Female (533) | Male (664) | Female (3099) | Male (2366) |
| $P_1$ | 158.0 | 153.0 | 99.1 | 100.0 | 84.6 | 80.4* |
| $BP_1$ | 12.87 (96.8) | 12.71 (95.6) | 14.84 (111.6) | 15.32 (115.2) | 16.89 (127.0) | 17.82* (134.0)* |
| $P_1$–$TP_2$ | 3.8 | 6.8 | −7.9 | −8.7 | −4.8 | −5.2 |
| $P_1$–$TP_3$ | 7.1 | 5.4 | −6.5 | −5.6 | −1.6 | −1.4 |
| $BP_1$–$TBP_2$ | 1.02 (7.7) | 0.86 (6.5) | 0.77 (5.8) | 0.70 (5.3) | 1.22 (9.2) | 1.49* (11.2)* |
| $BP_1$–$TBP_3$ | 1.69 (12.7) | 1.32 (9.9) | 1.00 (7.5) | 1.20 (9.0) | 1.93 (14.5) | 2.47* (18.6)* |

*Statistically significant at 0.1% level. Blood pressures are in kPa (mmHg).

tion used. While the typical blood pressure was not significantly related to average or highest isoflurane during maintenance, the difference from preinduction blood pressure was significantly related. Thus the change in blood pressure increased as isoflurane concentration increased and reflects a consistent decrease in blood pressure compared to preinduction values.

## ANAESTHETIC DRUGS – INFLUENCE ON PULSE AND BLOOD PRESSURE

The anaesthetic drugs recorded are shown in Table 26. The 'other' category comprises further combinations of drugs listed in Table 26 but, because of the extremely low incidence, these have been excluded from comparison with those

TABLE 24

LABILITY OF PULSE, BLOOD PRESSURE: LINEAR REGRESSIONS (Y = aX + b)

| Y | aX | b | r = correl. coeff. |
|---|---|---|---|
| $H-LP_2$ | $0.08\ P_1$ | +11.5 | 0.124* |
| $H-LP_3$ | $0.03\ P_1$ | +17.1 | 0.053 |
| $H-LBP_2$ | $0.35\ BP_1$ | −17.8 | 0.382* |
| $H-LBP_3$ | $0.33\ BP_1$ | −12.6 | 0.342* |

*Significant at $P < 0.001$.
H–L = Difference between highest and lowest values.
2 = Induction.
3 = Maintenance.
Blood pressures are in mmHg.

TABLE 25

ISOFLURANE: LINEAR REGRESSIONS (Y = aX + b)

| Y | aX | b | r = correl. coeff. |
|---|---|---|---|
| $TP_2$ | $1.76\ HF_2$ | +88.2 | 0.137 |
| | $2.01\ AF_2$ | +87.0 | 0.145 |
| $TP_3$ | $8.77\ AF_3$ | +78.6 | 0.242 |
| $P_1-TP_2$ | $-1.95\ AF_2$ | −2.0 | −0.130 |
| $P_1-TP_3$ | $-6.32\ AF_3$ | +5.5 | −0.214 |
| $BP_1-TBP_3$ | $-4.36\ AF_3$ | +20.1 | −0.130 |

All correlations listed are significant at $P < 0.001$.
Highest isoflurane (HF) and average isoflurane (AF) are indicated for induction (2) and maintenance (3).
Blood pressures are in mmHg.

listed. Inhalation induction without the use of any other drugs was done in 16.9 per cent of cases. Comparison of this group with all other combinations of anaesthetic drugs revealed multiple significant differences, but few differences between drug groups with the exception of pulse and blood pressure after alfathesin and the anticholinergic combinations. These latter have been detailed in Table 27 for typical pulse and blood pressure and difference from preinduction values during the induction period. Comparison between the no drug group, anticholinergic plus other drug or drug combinations (A) and the other drug groups (B) was done as a three-sided analysis. The P values are indicated. Pulse variables differed between the no drug group and A and B groups and also between the A and B groups. On the other hand, pressure variables differed only between the B group and A and no drug groups. Generally, the use of anticholinergics increased pulse rate and decreased blood pressure.

## INFLUENCE OF PREMEDICATION

The summary values for pulse and blood pressure and most frequent premedicant drugs and combinations are given in Table 28. The most common premedication was the combination of anticholinergic plus tranquilizer plus narcotic (21.5 per cent of all patients having premedication). Note that 20.3 per cent of all patients did not have premedication. The next most commonly prescribed premedication was anticholinergic plus narcotic in 19.7 per cent of all premedicated patients. Anticholinergics were used in 57.5 per cent of all premedicated patients. Generally, these patients given premedication without anticholinergic showed smaller increased heart rates and overall lower values but little difference in blood pressure. The addition of anticholinergic generally increased pulse rates but reduced the differences from preinduction values. No significant differences in blood pressure occurred in the anticholinergic groups but there was a general trend to lower values.

The influence of narcotic on pulse and blood pressure is shown in Table 29 for four combinations; (a) barbiturate ± narcotic, (b) tranquilizer ± narcotic, (c) anticholinergic ± narcotic, (d) anticholinergic plus tranquilizer ± narcotic. Those variables which differed significantly ($P < 0.001$) are indicated and include preinduction pulse for T ± N compared to T, for A + N compared to A and change in pulse for A + T + N compared to A + T and preinduction blood pressure for A + N compared to A. Addition of narcotic generally decreased pulse and increased pressure with the exception of A + T + N where there was a non-significant decrease.

## INFLUENCE OF MUSCLE RELAXANTS

Succinylcholine alone or in combination with other relaxants was used in 4,358 cases (64.1 per cent), tubocurarine in 2,236 cases (32.9 per cent), and pancuronium in 1,937 cases (28.5 per cent). In the latter two instances, the use of small doses to prevent fasciculation with succinylcholine was taken into consideration by setting a lower limit per kg body weight for the purpose of calculating means, carrying out analysis of variance and regressions. Of the numerous cross correlations and regressions examined, only those found to be significant at $P < 0.001$ are shown in Table 30.

TABLE 26

ANAESTHETIC DRUGS AT INDUCTION (6,798 CASES)

| | No. of Cases | % | $P_1$ | $TP_2$ | (%) | $BP_1$ | $TPB_2$ | (%) |
|---|---|---|---|---|---|---|---|---|
| None | 1149 | 16.9 | 88.2 | 101.1 | (+14.6) | 15.16 (114.0) | 14.14 (106.3) | (−6.8) |
| Barb. (B) | 4072 | 59.9 | 83.5 | 89.3 | (+6.9) | 16.16 (121.5) | 14.96 (112.4) | (−7.5) |
| Narc. (N) | 116 | 1.7 | 83.1 | 85.6 | (+3.0) | 16.16 (121.5) | 14.47 (108.8) | (−10.5) |
| N + B | 537 | 7.9 | 83.8 | 86.3 | (+3.0) | 16.09 (121.0) | 14.34 (107.8) | (−11.0) |
| Tranq. (T) | 61 | 0.9 | 77.6 | 83.8 | (+8.0) | 16.49 (124.0) | 15.47 (116.3) | (−6.2) |
| T + B | 129 | 1.9 | 87.6 | 92.7 | (+5.8) | 16.16 (121.5) | 14.63 (110.0) | (−9.5) |
| T + N | 75 | 1.1 | 84.8 | 85.0 | (+0.2) | 15.83 (119.0) | 14.04 (105.6) | (−11.3) |
| T + N + B | 211 | 3.1 | 85.7 | 86.9 | (+1.4) | 16.43 (123.5) | 14.58 (109.6) | (−11.3) |
| Alfathesin. | 20 | 0.3 | 84.4 | 101.4 | (+20.1) | 16.47 (123.8) | 16.23 (122.0) | (−1.5) |
| Antichol. (A) | 88 | 1.3 | 110.8 | 113.7 | (+2.6) | 14.30 (107.5) | 13.03 ( 98.0) | (−8.8) |
| A + B | 251 | 3.7 | 94.4 | 115.1 | (+21.9) | 14.99 (112.7) | 14.44 (108.6) | (−3.6) |
| A + N + B | 41 | 0.6 | 83.3 | 87.1 | (+4.6) | 16.04 (120.6) | 14.55 (109.4) | (−9.3) |
| A + T + B | 14 | 0.2 | 79.6 | 85.6 | (+7.5) | 16.57 (124.6) | 15.18 (114.1) | (−8.4) |
| A + T + B + N | 20 | 0.3 | 86.7 | 95.3 | (+9.9) | 17.38 (130.7) | 16.44 (123.6) | (−5.4) |
| (Other | 13 | 0.2) | | | | | | |

Blood pressures are in kPa(mmHg).

TABLE 27

ANAESTHETIC DRUGS m ± SEM
COMPARISON BETWEEN NONE, ANTICHOLINERGIC AT INDUCTION, OTHER DRUGS

| | None | P | Antichol. and other | P | Other | P | None |
|---|---|---|---|---|---|---|---|
| No. of cases | 1149 | | 423 | | 5225 | | |
| $TP_2$ | 101.1<br>0.9 | 0.0001 | 110.1<br>1.7 | 0.0001 | 88.9<br>0.3 | 0.0001 | |
| $P_1-TP_2$ | −2.9<br>0.5 | 0.0001 | −14.4<br>1.2 | 0.0001 | −5.1<br>0.2 | 0.0001 | |
| $TBP_2$ | 14.95<br>0.09 | | 14.84<br>0.13 | | 15.81<br>0.04 | | |
| | (112.4)<br>(0.0) | 0.501 | (111.6)<br>(1.0) | 0.0001 | (118.9)<br>(0.3) | 0.0001 | |
| $BP_1-TBP_2$ | 1.02<br>0.07 | | 0.84<br>0.13 | | 1.32<br>0.04 | | |
| | (7.7)<br>0.5 | 0.222 | (6.3)<br>1.0 | 0.0001 | (9.9)<br>0.3 | 0.0001 | |

Blood pressures are in kPa(mmHg).

Succinylcholine reduced pulse rate during maintenance, did not change typical pressure but reduced highest pressure and increased lowest pressure, thus reducing the level of pressure lability when expressed per kg body weight per minute of anaesthesia.

Tubocurarine as a total dose or total dose per kg body weight was linearly related to the change in pulse rate during maintenance (a positive correlation here means an inverse relationship when pulse is expressed as percent control value). Thus the higher the dose/kg of tubocurarine, the lower the increase in pulse rate.

Pancuronium total dose was linearly related to typical and highest blood pressure during maintenance and the latter was also linearly related to the total dose per kg body weight.

Specifically no significant relationship was found between change in pulse rate with pancuronium or change in blood pressure with tubocurarine.

TABLE 28

PREMEDICATION

| | No. of Cases | $P_1$ | $TP_2$ | $TP_3$ | $BP_1$ | $TBP_2$ | $TBP_3$ |
|---|---|---|---|---|---|---|---|
| None | 1380 | 93.8 | 101.0 | 97.1 | 123.5 | 116.0 | 109.9 |
| Barb. (B) | 55 | 84.8 | 95.7 | 89.4 | 124.7 | 114.5 | 108.0 |
| Narc. (N) | 477 | 81.3 | 84.0 | 81.1 | 129.7 | 118.8 | 113.0 |
| N + B | 90 | 81.4 | 85.0 | 80.8 | 127.0 | 114.2 | 110.3 |
| Tranq. (T) | 721 | 83.2 | 89.8 | 86.6 | 127.3 | 118.8 | 112.8 |
| T + B | 20 | 93.7 | 103.1 | 97.9 | 131.6 | 124.7 | 115.6 |
| T + N | 905 | 79.7 | 83.3 | 80.5 | 129.1 | 117.4 | 111.7 |
| T + N + B | 29 | 77.7 | 82.6 | 80.0 | 123.7 | 119.3 | 112.7 |
| Antichol. (A) | 228 | 108.6 | 113.4 | 112.0 | 117.6 | 110.9 | 105.3 |
| A + B | 104 | 90.9 | 102.3 | 99.1 | 122.3 | 112.8 | 110.9 |
| A + N | 1069 | 86.1 | 89.8 | 86.3 | 127.9 | 117.9 | 112.8 |
| A + N + B | 177 | 90.2 | 93.1 | 90.6 | 121.8 | 111.2 | 108.7 |
| A + T | 269 | 85.2 | 94.3 | 92.2 | 130.5 | 123.0 | 116.1 |
| A + T + B | 52 | 81.4 | 86.3 | 91.2 | 128.4 | 117.9 | 113.0 |
| A + T + N | 1167 | 85.8 | 91.1 | 87.7 | 127.4 | 117.8 | 112.6 |
| A + T + N + B | 27 | 83.0 | 87.4 | 82.2 | 131.6 | 128.6 | 116.7 |

Blood pressure is in mmHg.

TABLE 29

PREMEDICATION ± NARCOTIC (m ± 1 SEM)

| | Barb. | Barb. and Narc. | Tranq. | Tranq. and Narc. | Antichol. | Antichol. and Narc. | A + T | A + T + N |
|---|---|---|---|---|---|---|---|---|
| No. of cases | 55 | 90 | 721 | 905 | 228 | 106 | 296 | 1167 |
| $P_1$ | 84.8 | 81.4 | 83.2 | 79.7* | 108.6 | 86.1* | 85.2 | 85.9 |
| | 2.9 | 1.8 | 0.6 | 0.6 | 2.6 | 0.7 | 1.1 | 0.6 |
| $P_1$–$TP_3$ | −4.6 | 0.6 | −3.4 | −0.9 | −3.3 | −0.3 | −7.0 | −1.9* |
| | 2.8 | 1.7 | 0.7 | 0.6 | 1.4 | 0.6 | 1.1 | 0.5 |
| $BP_1$ | 124.7 | 126.9 | 127.3 | 129.1 | 117.6 | 127.9* | 103.5 | 127.4 |
| | 3.0 | 2.5 | 0.9 | 0.8 | 1.8 | 0.7 | 1.4 | 0.7 |
| $BP_1$–$TBP_3$ | 16.5 | 16.6 | 14.5 | 17.3 | 12.0 | 15.1 | 14.3 | 14.8 |
| | 2.7 | 2.9 | 0.8 | 0.7 | 1.3 | 0.6 | 1.4 | 0.6 |

*Statistically significant at $P < 0.0001$ comparing drug plus narcotic with drug alone.
Blood pressures are in mmHg.

### INFLUENCE OF BLOOD LOSS AND FLUIDS ADMINISTERED

Multiple linear regression analysis was done for the numerous pulse and blood pressure variables against blood loss and fluids administered in absolute values, per minute of anaesthesia time, per minute of anaesthesia per $m^2$ body surface and against the net fluid balance (fluids minus blood loss) in absolute terms, per minute anaesthesia and per minute anaesthesia per $m^2$ body surface. Only significant linear correlations ($P < 0.001$) are given in Table 31. Generally as fluids increased pulse rate fell and blood pressure increased, especially during induction. On the other hand, reduction of the net fluid balance was also inversely related to pulse during induction and maintenance and change in pressure during maintenance. (Note that, in correlations of differences between preinduction and post-induction values, a negative correlation coefficient means an increase in the variable). This might suggest that, as fluids were given, a normal baroreceptor response prevailed. The pulse rate changes corrected for fluids administered suggest that this response was already stimulated. However caution should be exercised in making such an interpretation. It is equally possible that

TABLE 30

MUSCLE RELAXANTS: LINEAR REGRESSIONS (Y = aX + b)

| Y | aX | b | r = correl. coeff. |
|---|---|---|---|
| $TP_3$ | −0.040 ST | +92.3 | −0.145 |
| | 193.78 (S/kg/M) | +84.4 | 0.227 |
| $TBP_3$ | 0.58 PT | +111.8 | 0.128 |
| $P_1$–$TP_3$ | 0.23 TT | −2.3 | 0.122 |
| | 14.45 (TT/kg) | −2.3 | 0.122 |
| $BP_1$–$TBP_3$ | 142.89 (S/kg/M) | +18.0 | 0.170 |

All listed correlations significant at $P < 0.001$.
S = dose of succinylcholine during anaesthesia.
ST = total succinylcholine dose.
TT = total tubocurarine dose.
PT = pancuronium dose.
kg = body weight.
M = minutes of anaesthesia.
Blood pressures are in mmHg.

TABLE 31

BLOOD LOSS (B) AND FLUIDS (F): LINEAR REGRESSION (Y = aX + b)

| Y | aX | b | r = correl. coeff. |
|---|---|---|---|
| $TP_2$ | −0.002 F | +95.4 | −0.165 |
| | −0.531 F/M | +98.0 | −0.208 |
| | −0.530 F/M/S | +95.3 | −0.122 |
| | −0.003 (F–B) | +95.7 | −0.171 |
| | −0.592 (F–B)/M | +97.7 | −0.208 |
| $TP_3$ | −0.002 F | +91.9 | −0.155 |
| | −0.501 F/M | +94.5 | −0.198 |
| | −0.003 (F–B) | +92.4 | −0.170 |
| | −0.572 (F–B)/M | +94.3 | −0.202 |
| $HBP_2$ | 0.003 F | +129.4 | 0.170 |
| | 0.004 (F–B) | +129.3 | 0.166 |
| $BP_1$–$TBP_3$ | 0.002 F | +12.5 | 0.134 |
| | 0.002 (F–B) | +12.4 | 0.135 |

All listed correlations are significant at $P < 0.001$.
M is minutes of anaesthesia.
S in $m^2$ is body surface area.
F–B in ml is net fluid balance.
Blood pressures are in mmHg.

this indicates a simple volume effect which could occur in the absence of normal baroreception.

### INFLUENCE OF SYSTEM DISEASE

The typical pulse and blood pressure values as means ±1 SEM are given for each category of system disease in Table 32. Those parameters which differ significantly ($P < 0.0001$) from the control group (no disease, no drugs) are indicated. Virtually without exception blood pressure was significantly higher in all disease groups. Preoperative pulse was significantly lower in the circulatory and orthopedic disease group, while in most disease groups pulse rate under isoflurane was consistently lower compared to controls. Figures 3 and 4 show the mean values for pulse and blood pressure respectively for controls and patients with respiratory or circulatory disease alone.

### INFLUENCE OF CURRENT MEDICATION

The influence of current medications on preoperative pulse rate and blood pressure and the

TABLE 32

DISEASE AREAS VS CONTROL (NO DISEASE, NO DRUGS) $\bar{m} \pm$ SEM

| | Control | Resp. | Hepatic | Circ. | CNS | Renal | Endoc. | GI | Gyn. | Ortho. |
|---|---|---|---|---|---|---|---|---|---|---|
| No. | 1645 | 799 | 221 | 1513 | 396 | 445 | 410 | 712 | 857 | 806 |
| $P_1$ | 87.8 | 88.9 | 86.1 | 82.0* | 86.6 | 86.8* | 86.5 | 88.8 | 85.9 | 84.4* |
| | 0.6 | 0.9 | 1.5 | 0.5 | 1.0 | 1.0 | 1.0 | 0.9 | 0.6 | 0.7 |
| $TP_2$ | 95.4 | 92.7 | 92.1 | 84.6* | 90.6* | 88.9* | 90.3* | 93.7 | 91.1* | 89.5* |
| | 0.7 | 0.8 | 1.5 | 0.5 | 1.0 | 1.0 | 1.0 | 0.8 | 0.6 | 0.7 |
| $TP_3$ | 92.1 | 89.2 | 89.2 | 81.8* | 86.6* | 86.0* | 87.7* | 91.4 | 88.4 | 84.9* |
| | 0.7 | 0.8 | 1.4 | 0.5 | 1.0 | 1.0 | 0.9 | 0.8 | 0.6 | 0.7 |
| $BP_1$ | 119.1 | 131.3* | 131.1* | 141.5* | 131.1* | 139.8* | 138.5* | 129.8* | 122.6* | 130.2* |
| | 0.5 | 0.9 | 1.5 | 0.7 | 1.3 | 1.5 | 1.3 | 1.0 | 0.7 | 0.8 |
| $TBP_2$ | 112.2 | 120.5* | 122.5* | 126.8* | 120.3* | 123.7* | 125.4* | 119.2* | 114.7 | 119.8* |
| | 0.5 | 0.9 | 1.6 | 0.7 | 1.2 | 1.3 | 1.3 | 1.0 | 0.6 | 0.8 |
| $TBP_3$ | 108.3 | 113.6 | 114.6* | 118.5* | 112.1* | 115.3* | 116.7* | 113.7* | 111.5* | 113.6* |
| | 0.4 | 0.7 | 1.2 | 0.5 | 1.0 | 1.0 | 1.0 | 0.8 | 0.5 | 0.7 |

*Significantly different from control value at $P < 0.0001$.
Blood pressures are in mmHg.

TABLE 33

CURRENT MEDICATIONS VS CONTROL GROUP (NO DISEASE, NO DRUGS) m $\pm$ SEM

| | Control | Digitalis | Beta block | Diuretic | Nitrate | Bronchodil |
|---|---|---|---|---|---|---|
| No. of cases | 1647 | 204 | 355 | 667 | 214 | 114 |
| $P_1$ | 87.8 | 81.9 | 77.4* | 85.3 | 80.4 | 88.1 |
| | 0.6 | 2.4 | 1.8 | 0.9 | 3.1 | 2.3 |
| $P_1$–$TP_3$ | 4.2 | −3.2 | −0.9 | 2.7* | −1.7 | 0.1 |
| | 0.5 | 1.9 | 1.5 | 0.8 | 3.3 | 2.3 |
| $BP_1$ | 119.1 | 137.9* | 141.6* | 143.0* | 147.6* | 127.3* |
| | 0.5 | 3.4 | 2.5 | 1.3 | 5.8 | 2.2 |
| $BP_1$–$TBP_3$ | 10.7 | 19.0 | 23.9* | 23.5* | 28.2 | 15.9 |
| | 0.5 | 2.9 | 2.7 | 1.3 | 5.7 | 2.4 |

*Significantly different from ($P < 0.001$) control.
Blood pressures are in mmHg.

change in those variables during maintenance was examined by multiple analysis of variance and is summarized in Table 33. In the control group, pulse typically increased by about four beats per minute and blood pressure decreased by about 1.46 kPa (11 mmHg).

The use of beta blockers was associated with significantly lower preinduction pulse rates and higher blood pressures. While all other drugs resulted in similar increased preinduction blood pressures, none of these drugs significantly decreased preoperative pulse rate although all mean values were lower than control.

Only beta blockers and diuretics were associated with significantly greater decreases in blood pressure of more than twice the decrease in control values during maintenance.

## COMPARISON OF PATIENTS WITH AND WITHOUT HYPOTENSION

Patients in whom there was a drop in blood pressure greater than 2.66 kPa (20 mmHg) compared with preinduction values and in those where hypotension was recorded as a complication, were examined separately and compared to those without hypotension. The significant characteristics of these hypotensive groups are summarized in Table 34. Most patients (70.9 per cent) had a change in blood pressure less than 2.66 kPa (20 mmHg) (control group). Where hypotension occurred, the mean age was higher than the control group and this was particularly so where hypotension was judged a complication. In this latter group, respiratory disease was

TABLE 34

BLOOD PRESSURE CHANGES DURING MAINTENANCE

| | Control ($BP_1$–$TBP_3$ < 20 mmHg) | Hypotension ($BP_1$–$TBP_3$ > 20 mmHg) | Hypotension as a compl. |
|---|---|---|---|
| No. of cases | 4818 (70.9%) | 1922 (28.3%) | 187 (2.8%) |
| Mean age yr. (±1 SEM) | 36.3 ± 0.3 | 47.4 ± 0.5 | 53.1 ± 1.4 |
| Disease (%) | | | |
| Resp. | 11.1 | 13.6 | 19.8 |
| Circ. | 17.1 | 35.2 | 51.3 |
| Renal | 4.4 | 9.5 | 9.6 |
| Drugs | | | |
| Digitalis | 2.3 | 4.7 | 4.3 |
| Beta Block | 4.1 | 8.1 | 13.9 |
| Diuretic | 7.3 | 16.3 | 21.4 |
| Nitrate | 2.5 | 4.8 | 7.5 |
| Bronch. Dil. | 1.6 | 1.8 | 3.2 |
| $BP_1$ (±1 SEM) | 119.0 ± 0.3 | 145.2 ± 0.5 | 134.8 ± 1.8 |
| $TBP_2$ (±1 SEM) | 114.9 ± 0.3 | 122.9 ± 0.5 | 120.4 ± 1.9 |
| $TBP_3$ (±1 SEM) | 113.7 ± 0.2 | 106.9 ± 0.4 | 106.1 ± 1.4 |
| Blood Loss (±1 SEM) ml | 231 ± 7 | 301 ± 12 | 666 ± 77 |
| Av. Isoflurane % (±1 SEM) | 1.24 ± 0.01 | 1.11 ± 0.01 | 0.91 ± 0.04 |
| Highest Isoflurane % (±1 SEM) | 1.73 ± 0.01 | 1.67 ± 0.02 | 1.59 ± 0.06 |

Blood pressures are in mmHg. Control group is no hypotension.

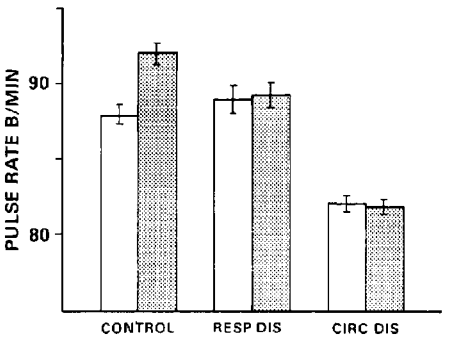


FIGURE 3 Mean ±1 SD values for pulse rate during pre-induction (open bars) and maintenance periods (hatched bars) for controls (no disease, no current drugs), a group with respiratory disease alone ± bronchodilator therapy and a group with circulatory disease alone ± any of the listed cardiac drugs.

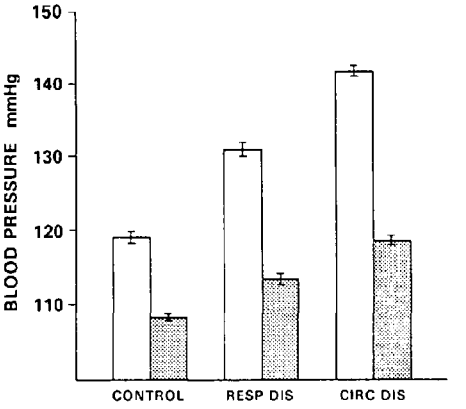


FIGURE 4 Mean ±1 SD values for blood pressure during pre-induction (open bars) and maintenance periods (hatched bars). The groups are identical to those shown on Figure 3.

twice as common, circulatory disease was three times as common, and renal disease twice as common as in the control group. Similar increases in the hypotensive groups were found for the listed cardiorespiratory drugs. The preoperative pressure was significantly higher ($P < 0.001$) in the group who were hypotensive during maintenance. The mean pressures of 14.11 and 14.22 kPa (106.1 and 106.9 mmHg) during maintenance in the two hypotensive groups were not statistically different from the control group value of 15.12 kPa (113.7 mmHg).

Blood loss was almost three times greater (666 ml) in the hypotensive complication group. Notably average isoflurane as a percentage was lower in the hypotensive groups compared to

control. Linear regression analysis of change in blood pressure ($BP_1$–$TBP_2$, $BP_1$–$TBP_3$) for each period against average isoflurane concentration did not result in any significant correlation (correlation coefficients were −0.096 and −0.130 respectively). The mean values (±1 SEM) for $BP_1$–$TBP_2$ and $BP_1$–$TBP_3$ in the hypotensive group were 2.97 ± 0.05 kPa (22.3 ± 0.4 mmHg) and 5.09 + 0.04 kPa (38.3 ± 0.3 mmHg) and in the hypotensive complication group were 1.90 ± 0.21 kPa (14.3 ± 1.6) and 3.79 ± 0.23 kPa (28.5 ± 1.7) respectively. These compare to values for $BP_1$–$TBP_2$ and $BP_1$–$TBP_3$ obtained from the highly significant relationships mentioned in Table 22 for different age groups against $BP_1$, of 1.58 and 3.46 kPa (15.8 and 26.0 mmHg) respectively where $BP_1$ = 19.31 kPa (145.2 mmHg) as it was in the hypotensive group. Similarly, when $BP_1$ = 17.93 kPa (134.8 mmHg), this yields values for $BP_1$–$TBP_2$ = 1.58 kPa (11.9 mmHg) and for $BP_1$–$TBP_3$ = 2.62 kPa (19.7 mmHg) compared to those above for the hypotension complication group. Although the changes in pressure for both periods are greater in each hypotensive group than those predicted from the relationship which was obtained overall for each age group against $BP_1$, this difference is not statistically significant. Thus the definition of hypotension is somewhat arbitrary, as is its classification as a complication in this context. The actual mean pressures in each hypotensive group at induction and maintenance were not statistically different from the control (non-hypotensive group).

Indeed, during induction the absolute values were higher than in the control group. As previously indicated, the very high degree of predictability of changes in blood presssure and pulse (Table 22) based on preinduction values is of considerable importance clinically. When those patients classified as having hypotension during anaesthesia are examined by using those predictions, the differences with actual pressures and pulse rates were relatively small. The fact that isoflurane concentrations were lower in the hypotensive groups could be interpreted as evidence for a lack of a dose-response relationship. However, change in pulse at induction and change in blood pressure during maintenance were significantly related to average concentration of isoflurane in those periods (Table 25). It seems likely then that those patients in whom hypotension was judged to have occurred were given smaller concentrations of isoflurane for other reasons, such as higher ASA status rating, prevalence of disease, older age, and more major procedures. Detailed examination of all of the various demographic and patient subgroups in terms of the pulse and blood pressure changes during isoflurane anaesthesia in this large series of 6,798 patients clearly indicates that isoflurane, given alone or in combination with other anaesthetic drugs, has a wide margin of safety and cardiovascular stability.

## Discussion

In healthy subjects the average change in pulse rate with isoflurane at 1.5 MAC has been reported as an increase of about 20 per cent above awake values[11] while blood pressure showed a decrease of about 35 per cent. This contrasts with the present study of 6,798 patients where pulse rate increased 6.2 per cent at induction and 2.6 per cent during maintenance and blood pressure decreased 7.4 per cent and 11.7 per cent during each of these periods respectively. The average isoflurane concentrations were 1.69 and 1.20 per cent, equivalent to 3.2 MAC on induction and 2.3 MAC during maintenance. These lesser changes in both pulse rate and blood pressure were related to several factors including premedicant drugs, adjuvant anaesthetic drugs and, most important, certain patient characteristics. These latter deserve special mention, since they clearly demonstrate the predictive accuracy of the haemodynamic response under isoflurane anaesthesia.

Knowledge of the relationships between age and body size and resting pulse and blood pressure has hitherto been limited. One large study[16] of 9,865 children (6 to 9 years) found linear regressions with slope coefficients of 0.266 for height in cm and 0.94 for body mass index in kg/m$^2$, compared to 0.315 and 0.792 respectively in the present study for patients of all ages. It is clear however, from previous reports, that considerable variability exists within each age group and that some form of multiple index is necessary to increase the accuracy of the linear relationship.[17] This was confirmed in the present study. On the other hand, the highly significant relationships between preoperative pulse rates and blood pressures and those during operation showed considerably less variability within each age group. The clinical usefulness of an accurate prediction of the pulse and blood pressure change under isoflurane from knowledge of the preoperative values is obvious. In each age group the intercept of the linear correlations for pulse and blood pressure change with the neutral line for no change is important

and occurs at intermediate preoperative values. Thus in children, when preoperative pulse is 137 b/min or more or when blood pressure is 12 kPa (90 mmHg) or less, the response under isoflurane was a decrease in pulse and an increase in pressure. Similarly, in patients over 60 years of age, when preoperative pulse was 80 b/min or over pulse decreased and when pressure was 14 kPa (105 mmHg) or less pressure increased under isoflurane. This contrasts with the overall change of increased pulse rate and decreased pressure previously mentioned, which showed a trend similar to previous reports.[11,13,15]

The explanation of this unexpected finding is difficult and somewhat speculative. It is clear that for each age group there is some neutral pulse rate and blood pressure value and that these decrease and increase respectively with age. Under isoflurane anaesthesia the response is a shift toward the neutral value, resulting in either a decrease or an increase in each variable, depending on whether the preoperative value was above or below the neutral value. This suggests that cardiovascular homeostasis under anaesthesia with isoflurane is a protective mechanism tending to the ideal or neutral value. However further studies are necessary to confirm this hypothesis. Whatever the explanation of this response, the reliability of the result is clear. In clinical terms, isoflurane offers a perhaps unique advantage over other agents in that the patient whose preoperative blood pressure is below the expected neutral value or whose pulse is higher can be expected to show a moderate increase in blood pressure and decrease in pulse rate under isoflurane anaesthesia. Caution should be exercised in drawing any conclusions for the individual patient. It is not possible from our data to predict accurately the changes in cardiac output associated with these changes in the pulse rate and blood pressure, although previous studies found no change or an increase in cardiac output.[11,14] Calculation of the pulse pressure product as an index of output was for the most part unchanged or slightly decreased in each age group around the mean values, but tended to increase when preoperative values were lower than the expected neutral value and to decrease when preoperative values were higher than the expected neutral value.

The relationships with concentration of isoflurane during maintenance indicate that pulse rate increases and blood pressure decreases as isoflurane concentration increases. This confirms previous findings for blood pressure,[11] although absolute values of change in each variable were somewhat less in the present study. The findings for the effects of premedicant and anaesthetic drugs on pulse rate and blood pressure changes under isoflurane anaesthesia are consistent with the overall depressant effects of these drugs, with the exception of anticholinergics, where pulse increased over controls while blood pressure was no different to controls. The use of narcotic was not associated with significant change in blood pressure but did decrease the magnitude of change of pulse rate. Somewhat unexpectedly muscle relaxants had little effect on blood pressure or pulse. The question of whether this represents suppression by isoflurane of the inotropic effects of pancuronium, histaminic effects of tubocurarine, or muscarinic effects of succinylcholine must await further study.

A finding of particular interest is that patients taking beta blocking drugs showed no significant change in pulse rate under isoflurane anaesthesia and, although blood pressure decreased to a greater extent from significantly higher preoperative values, the result under isoflurane was not different from controls. This contrasts with studies in dogs, where propranolol pretreatment did not alter the cardiovascular response to isoflurane.[18] In those patients where hypotension (change greater than 2.66 kPa (20 mmHg)) occurred under isoflurane anaesthesia, the actual values during maintenance were again not different from controls.

In summary, isoflurane was found to be compatible with all premedicant and adjuvant anaesthetic drugs normally used in clinical practice. Further, the use of cardiovascular and respiratory drugs or the presence of disease in those systems did not present any evidence that isoflurane was contraindicated. On the contrary, the bulk of evidence suggests that isoflurane offers a considerable margin of safety and caridovascular stability in patients of all ages with or without disease and having all types of surgical procedures. Therefore its use in high risk patients having major operations may be viewed as a positive advantage in much the same way as in those patients without serious risk having routine or uncomplicated procedures. The predictability of the pulse and blood pressure response under isoflurane anaesthesia from knowledge of preoperative values, offers the anaesthetist an important degree of control in modulating cardiovascular homeostasis in individual patients.