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# The Hemodynamic Effect of Acute Blood Loss in Normal Man, with Observations on the Effect of the Valsalva Maneuver and Breath Holding

JOHN J. SKILLMAN,* M.D., JOHN E. OLSON,* M.D., JOHN H. LYONS,* M.D., FRANCIS D. MOORE, M.D.

*From the Department of Surgery, Harvard Medical School and Peter Bent Brigham Hospital, Boston, Massachusetts*

IN 1793, Benjamin Rush, writing about the bloodletting treatment (70–80 ounces of blood in 5 days) of patients suffering from yellow fever in the Philadelphia epidemic of that year,[15] stated: ". . . the effects of blood letting on the system were as follow: 1. It raised the pulse when depressed, and quickened it, when it was preternaturely slow, or subject to intermissions 2. It reduced its force and frequency."

More than 150 years later the inconsistency of these two statements was pointed out by Shenkin and co-workers.[17] Shenkin bled 11 human volunteers approximately 500 to 1,000 ml. With the 500-ml. phlebotomies he found a decrease in systolic pressure averaging 13 mm. Hg cuff pressure, but no change in diastolic pressure or pulse rate, and very little change in cardiac output (employing a ballistocardiographic method which gave per cent deviations from average normal values). With larger phlebotomies (approximately 1 liter) he found that blood pressure fell in the majority, pulse rate increased materially in only three subjects, venous pressure either showed a small diminution or no change, and cardiac output fell significantly in almost all.

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* Research Fellow, National Institutes of Health.

Warren and co-workers [23] studied the effect of blood loss (300 to 900 ml.) and application of venous tourniquets on atrial pressure and cardiac output (using the direct Fick principle with 2-minute collections of expired air analyzed for oxygen and $CO_2$ content). He found a decrease in atrial pressure of 20 to 65 mm. $H_2O$ with these maneuvers, but was unable to detect consistent changes in cardiac output.

Ebert, Stead and Gibson [2] studied the effect of acute blood loss in six normal volunteers. They removed 760 to 1,220 ml. of venous blood in 6 to 13 minutes. Circulatory collapse occurred in five of these subjects—developing during the course of phlebotomy in two, and within 1 to 4 minutes in the remaining three. In the four subjects in whom measurements were made there was a slight fall in systolic pressure (mean fall = 11 mm. Hg by arm cuff) just before the onset of circulatory collapse, while diastolic pressure remained unchanged. During this period there was an increased heart rate (14 to 30 beats/min. above control levels). With the onset of collapse, systolic and diastolic pressure fell abruptly and marked bradycardia occurred (36 to 40 beats/min.). For 12 hours after blood loss the subjects would faint when they stood up.

The present study reappraises the hemodynamic effects of blood loss in man. Comparisons in the rate (rapid and slow) and route (venous and arterial) of blood removal were also made to assess the possible differences of these factors on the production of hemodynamic changes. In addition, the effect of the Valsalva maneuver and breath holding were tested, both before and after hemorrhage, to determine whether these circulatory challenges might be useful to uncover hidden volume depletion.

## Materials and Methods

Eleven healthy young male volunteers (ages 21 to 28), two of whom served as controls, were studied during separate hospitalization.* Before the day of hemorrhage each subject had a physical examination, blood count, urinalysis, electrocardiogram, and chest x-ray film.

**Cannulations.** For measurement of central venous pressure (CVP) and for indocyanine green dye injections, a polyethylene catheter (Clay Adams PE 205, length 36″) was inserted into the right brachial vein and passed into the right atrium or superior vena cava.

For measurement of arterial pressure and pulse contour, and for sampling of blood for the cardiac output measurements, a #18 gauge thin-walled Cournand needle was inserted into the right common femoral artery (in subject S. B. the brachial artery was used).

**Pressure monitoring.** Arterial pressure and central venous pressure were monitored by Statham strain gauges (P23AA for arterial and P23BB for venous pressures) connected to a Lexington Instruments dual-channel oscilloscope and a Texas Instruments dual-channel rectilinear writer. A point 5 cm. from the table was taken as the zero reference point for CVP. Hypotension was arbitrarily defined as a systolic blood pressure less than 100 mm. Hg.

**Cardiac output.** Cardiac output (CO) was determined by the dye-dilution method (indocyanine green) using the Gilford densitometer (Model #103-IR) with the Lexington analog cardiac output computer (time constant 0.259). Arterial blood was sampled with a Harvard infusion-withdrawal pump, Model #600-900, aspirating blood at a rate of 24.7 ml. per minute. The densitometer and computer curves were simultaneously recorded on a Texas Instruments dual-channel writer. As many as 30 separate indocyanine green injections were made during the course of a single-patient study.

* The endocrine and urinary composition changes after hemorrhage in these volunteers are reported elsewhere.[19]

*Electrocardiograms* were monitored during the study.

**Calculations.** *Mean arterial pressure (MAP)* was either determined as an electrical mean from the tracings or calculated by the formula:

$$\text{MAP} = \text{diastolic blood pressure} + \tfrac{1}{3} \text{ pulse pressure}$$

These methods of determining MAP agreed within 1 to 3 mm. Hg.

*Cardiac output (CO)* was expressed as *cardiac index (CI)*:

$$\text{CI (L./m.}^2\text{/min.)} = \frac{\text{CO (L/min.)}}{\text{BSA}^{**}}$$

*Stroke volume (SV)*:

$$\text{SV (ml./beat)} = \frac{\text{CO (ml./min.)}}{\text{Pulse Rate}}$$

*Total peripheral resistance (TPR)* was calculated from the standard formula:

$$\text{TPR (dynes}\cdot\text{sec.}\cdot\text{cm.}^{-5}) = \frac{\text{MAP} - \text{CVP} \times 1332 \times 60}{\text{CO (ml./min.)}}$$

**Circulatory challenges: the Valsalva maneuver and breath holding tests.** *The Valsalva maneuver* was performed by each subject before and after hemorrhage to determine its hemodynamic effect and the possible application of this circulatory stress to uncover blood volume deficits. Subjects were instructed to blow forcefully into a rubber tube, one end of which was connected to an aneroid sphygmomanometer gauge. Straining, with airway pressures measuring 40 to 75 mm. Hg (mean = 45 mm. Hg), was continued for 9 to 33 seconds (mean = 19 sec.).

*Breath holding.* Inspiratory breath holding (IBH) and expiratory breath holding (EBH) were maintained for periods up to 45 seconds. Injections of cardiogreen dye for the purpose of cardiac output measurements during breath holding were made within 1 to 3 seconds after the start of the test.

*Blood volume* was measured by the summation method using radiochromate (20 and 40 min. equilibrium times) and Evans Blue (5, 20, and 40 min. equilibrium times). Sampling losses other than the actual hemorrhaged volume were replaced by freshly cross-matched type-specific blood.

*Bleeding procedures.* Blood removal was done by different rates (rapid and slow) and different routes (venous and arterial) to compare its effect on the hemodynamic measurements. The two control subjects underwent exchange transfusion during which the amount of blood removed from one central venous catheter was simultaneously replaced by freshly cross-matched type-specific blood administered by a second intravenous catheter. In an attempt to eliminate statistical errors caused by differences in group size, the mean comparisons of rapid versus slow bleeds and venous versus arterial bleeds throughout this paper are based on the mean values of each individual group.

## Results

Table 1 summarizes the data on rates, routes, volume, and duration of blood removal. The column designated "transient additional hemorrhage" represents an extra sampling which was replaced by freshly cross-matched blood after its hemodynamic effect had been measured. The mean total hemorrhage volume for the nine bled subjects was 764 ml. ± 29 ml. (1 S.D. of the mean). The rapid hemorrhages (both venous and arterial) were approximately five times brisker than the slow hemorrhages (mean rate rapid = 46.2 ml./min.; mean rate slow = 8.9 ml./min.).

**Intra-Arterial Blood Pressure.** Table 2 summarizes the changes in blood pressure. Figure 1 shows typical minute to minute fluctuations of arterial blood pressure in subject C. R. who underwent a 768-ml. slow venous hemorrhage. Almost immedi-

** BSA = body surface area as determined by the standard Dubois nomogram.

TABLE 1. *Summary of Hemorrhages: Route, Rate, Volume, and Duration*

| Subject | Type of Hemorrhage | Hemorrhage | | | | Transient Additional Hemorrhage | |
|---|---|---|---|---|---|---|---|
| | | Volume ml. | % Blood Volume Removed | Duration min. | Rate ml./min. | Volume ml. | Rate ml./min. |
| C. R. | Slow venous | 768 | 13 | 79 | 9.7 | 100 | 25 |
| A. F. | Slow venous | 520 | 10 | 41 | 12.7 | 100 | 10 |
| T. G. | Slow venous | 784 | 15 | 101 | 7.8 | 100 | 10 |
| S. B. | Slow venous | 800 | 16 | 79 | 10.1 | 100 | 20 |
| Mean | | 718 | 13.5 | 75 | 10.1 | 100 | 16 |
| S. K. | Rapid venous | 810 | 19 | 14 | 57.8 | 40 | 80 |
| R. W. | Rapid venous | 780 | 14.7 | 15 | 52.0 | 260 | 43 |
| Mean | | 795 | 16.8 | 14.5 | 54.9 | 150 | 62 |
| P. W. | Slow arterial | 825 | 14.8 | 107 | 7.7 | — | — |
| R. R. | Rapid arterial | 810 | 14.8 | 24 | 33.8 | 290 | 58 |
| S. R. | Rapid arterial | 780 | 16.0 | 19 | 41.0 | 260 | 26 |
| Mean | (Rapid arterial) | 795 | 15.4 | 21.5 | 37.4 | 275 | 42 |
| Mean | (Entire bled group) | 764 | 14.8 | 53 | 25.8 | 139 | 30 |
| Controls | | | | | | | |
| E. D. | Exchange transfusion* | 810 | 14.7 | 93 | 8.7 | 270 (exchange) | 30 |
| T. G. | Exchange transfusion* | 784 | 15.9 | 81 | 9.7 | 260 (exchange) | 12 |
| Mean | | 747 | 15.3 | 87 | 9.2 | 265 | 21 |

* Exchange Transfusion: Simultaneous withdrawal and infusion of blood by two venous catheters resulting in no *net* deficit.

ately after each 250-ml. blood loss there is a rebound increase of blood pressure. However, after the fourth and last blood removal, blood pressure stayed low for 10 minutes, even though replacement was occurring.

Comparison of rapid with slow hemorrhages shows that with the latter, the mean blood pressure was lowered by 12%, while with slow hemorrhages the mean blood pressure was lowered by only 5% (rapid group—mean control BP = 99 mm. Hg, mean hemorrhage BP = 87 mm. Hg; slow group—mean control BP = 95 mm. Hg, mean hemorrhage BP = 90 mm. Hg). In three of the four rapidly bled subjects hemorrhage produced precipitous drops in blood pressure, whereas a similar drop in blood pressure occurred in only one of the five slowly bled subjects (subject A. F., who had a "vasovagal" reaction with an abrupt transient slowing of the pulse and a fall in blood pressure to 80/30 mm. Hg).

Comparison of venous with arterial hemorrhages shows that with venous hemorrhages the mean blood pressure was lowered by 16%, while with arterial hemorrhages the mean blood pressure was lowered by only 3% (venous group—control BP = 94 mm. Hg, mean hemorrhage

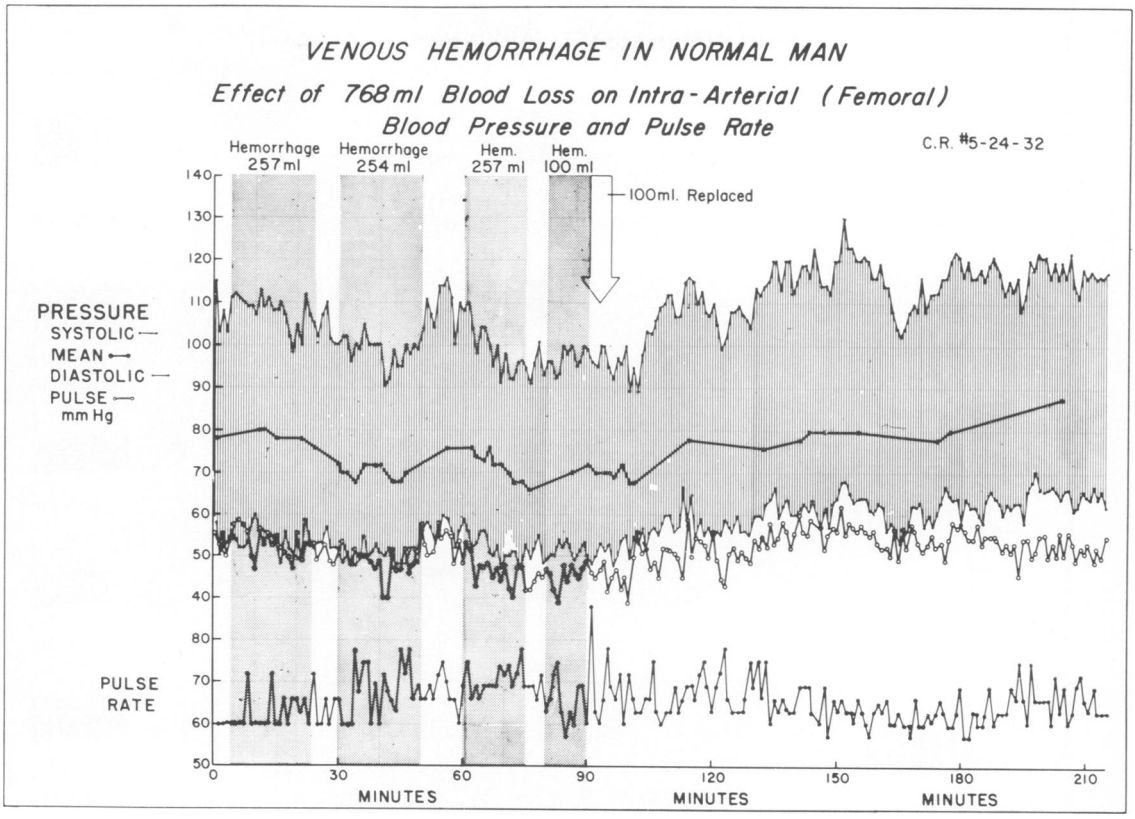



FIG. 1. Minute-to-minute fluctuations in pulse rate and in systolic, diastolic, mean, and pulse pressure during and after a slow 768 ml. venous bleed are plotted. A rebound increase of blood pressure is seen after each 250 ml. of blood loss. This rebound was slower to occur after the last 100 ml. hemorrhage (see text).

BP = 79 mm. Hg; arterial group—mean control BP = 100 mm. Hg, mean hemorrhage BP = 97 mm. Hg).

The rate and route of hemorrhage produced significant differences in the duration of hypotension. The duration of hypotension was longer after slow bleeds than after rapid bleeds (slow: mean duration of hypotension = 15 min.; rapid: mean duration of hypotension = 9 min.). With venous hemorrhages hypotension lasted 22 minutes compared to only 1 minute when blood was removed from the arterial side.

In the recovery period (up to 3½ hours after hemorrhage) the slow-hemorrhage group maintained a lower mean pressure (80 mm. Hg) than the rapid hemorrhage group (89 mm. Hg). Fluctuations in arterial pressure normally produced by respiration and changes in position of the subject were often exaggerated after hemorrhage (Fig. 2). Nonrespiratory oscillations of the arterial pressure are seen in the inspiratory breath holding tracing of subject R. W. before hemorrhage (Fig. 8). These oscillations show a natural frequency of about 0.05 cycles per second. After hemorrhage these waves are not as prominent (Fig 9).

The blood pressure changes in the hemorrhaged subjects contrast strikingly with the absence of changes in the two control subjects who underwent exchange transfusion. These two subjects E. D. and T. G., showed a slight increase in mean blood pressure with the exchange procedure

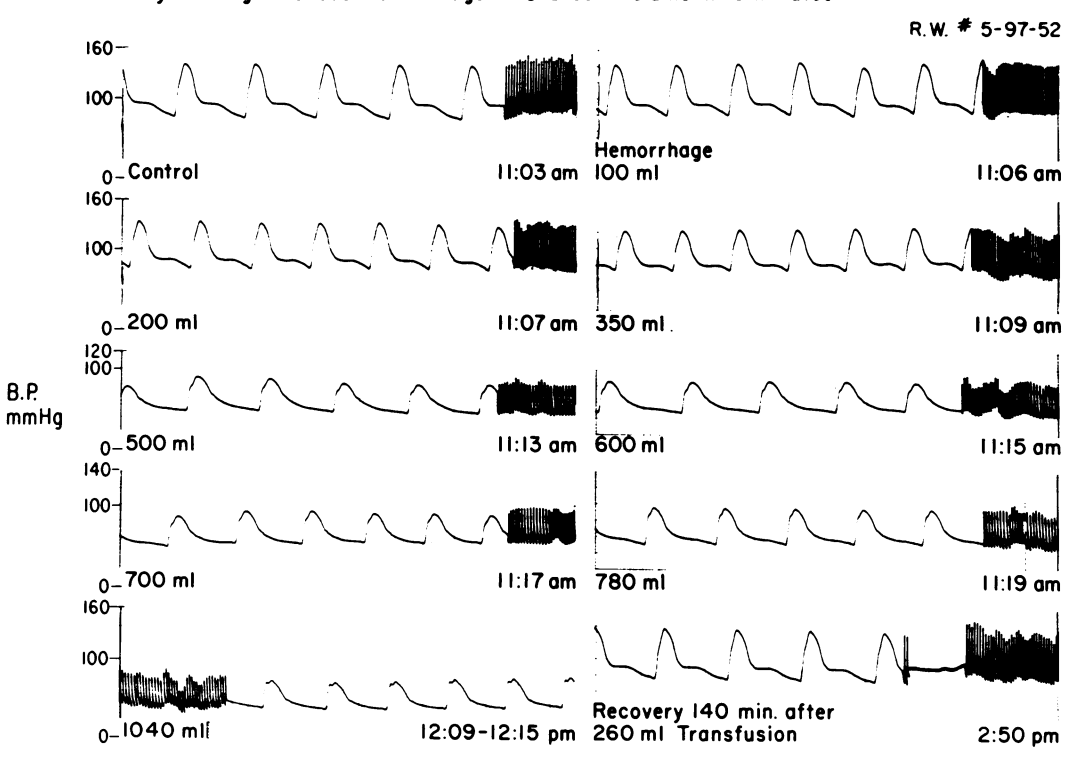



FIG. 2. A diminishing area under the arterial pressure pulse contour curve occurs during this rapid venous hemorrhage. This decrease in area is proportional to the decrease in stroke volume.

(mean control BP = 95 mm. Hg; mean exchange period BP = 101 mm. Hg) and, therefore, give significance to the interpretation that the observed hemodynamic changes in the bled group are due to the effects of volume depletion.

**Arterial Pressure Pulse Contours.** Figure 2 shows the arterial pressure pulse contours in subject R. W. who underwent a rapid venous hemorrhage of 15% blood volume. The shrinking area under the arterial curve seen in this subject is typical of bled subjects, particularly when the blood loss is rapid. This shrinking area suggests a reduction in stroke volume which is confirmed by the calculations of stroke volume based on the cardiac output and pulse rate measurements (subject R. W.: control SV = 71 ml./beat; SV 30 seconds after 780 ml. rapid venous hemorrhage = 48 ml./beat). In contrast to these pulse pressure contours are those of control subject E. D. (Fig. 3) who, during his exchange transfusion, shows no change in the area or in stroke volume (control SV = 81 ml./beat; SV after 810 ml. exchange transfusion = 81 ml./beat).

**Pulse Rate.** Hemorrhage increased the pulse rate in eight of the nine subjects (Table 5). The mean control pulse rate for the nine subjects was 72 beats per minute. During the period of hemorrhage the mean pulse rate increased to 81 beats per minute, a significant rise ($p < 0.025$). During recovery this increased rate was maintained (mean = 80 beats/min. [$p < 0.05$]).

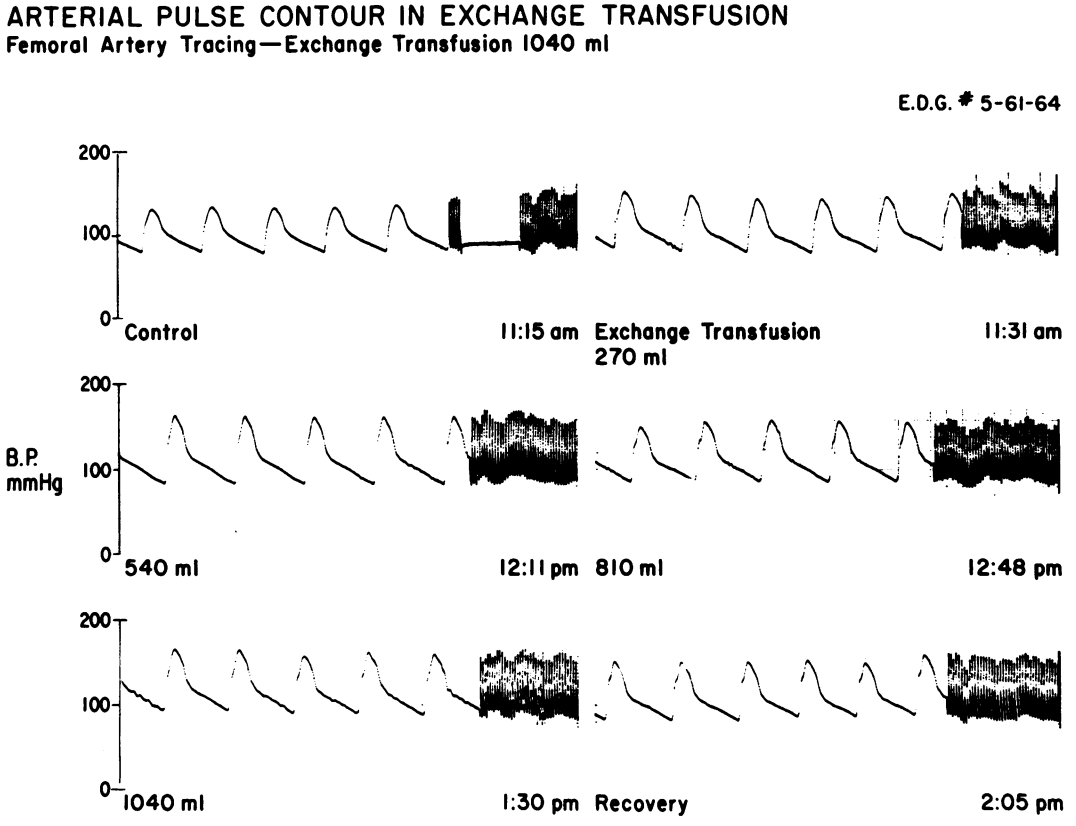



FIG. 3. No change in the arterial pressure pulse contour area is seen in this control exchange transfusion. Stroke volume is constant throughout the period of exchange transfusion.

In contrast, exchange transfusion increased the pulse rate from a mean control value of 73 beats per minute to 74 beats per minute during the exchange period and then to 78 beats per minute in the recovery period. (Control subject T. G. showed no increase in pulse rate during his exchange period.)

Comparisons of the mean increase of pulse rate in rapid, slow, venous, and arterial hemorrhages showed no appreciable differences (mean increase in pulse rate: rapid = 7 beats/min.; slow = 11 beats/min., arterial = 11 beats/min.; venous = 8 beats/min.).

**Cardiax Index (CI) and Stroke Volume (SV).** Tables 3 and 4 summarize the data on cardiac index and stroke volume. The mean control CI for the seven bled subjects in which it was measured was 2.8 L./m.$^2$/min. $\pm$ 0.3 (1 S.D. of the mean). The mean CI immediately after hemorrhage was 2.5 L./m.$^2$/min. $\pm$ 0.3. This difference is not statistically significant ($0.1 > p > 0.05$). The CI fell after hemorrhage in all except subjects S. K. (Fig. 11) and T. G. (Fig. 10). Figure4 shows sequential cardiac output changes with hemorrhage in subject R. R. and demonstrates the decrease in CI that occurs after blood loss. There were no significant differences in the drop of CI immediately after hemorrhage between the rapid and slow rates of blood removal or the venous and arterial routes of blood removal. After exchange transfusion CI remained the same or increased slightly.

All of the bled subjects showed a decrease in stroke volume after blood loss

TABLE 2. *Intra-arterial Blood Pressure Measurements with Hemorrhage*

| | | Intra-arterial Blood Pressure (mm.Hg) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Control Period | Hemorrhage Period | | | | | Recovery Period |
| Subject | Type of Hemorrhage | Mean Sys/Dias (Mean BP) | Mean Sys/Dias (Mean BP) | % Decrease Mean BP | Duration Hypotension* (min) | Lowest Recorded BP | Comments | Mean Sys/Dias (Mean BP) |
| C. R. | Slow venous | 107/53 (71) | 104/54 (71) | 0 (.01) | 40 | 88/53 | Sys: Gradual fall Dias: No change | 111/58 (76) |
| A. F.** | Slow venous | 117/69 (85) | 106/54 (71) | 16.5 | 5 | 80/30 | Sys: Precipitous fall Dias: Precipitous fall | 130/63 (85) |
| T. G. | Slow venous | 116/72 (87) | 101/65 (77) | 11.5 | 55 | 95/70 | Sys: Gradual fall Dias: Gradual fall | 103/67 (79) |
| S. B. | Slow venous | 121/77 (92) | 112/73 (86) | 6.5 | 15 | 95/70 | Sys: Gradual fall Dias: Gradual fall | 112/74 (87) |
| Mean | | 115/68 (84) | 106/62 (76) | 8.6 | 29 | 90/56 | | 114/66 (82) |
| S. K. | Rapid venous | 133/73 (93) | 116/71 (86) | 7.5 | 17 | 80/46 | Sys: Precipitous fall Dias: Precipitous fall | 124/68 (87) |
| R. W. | Rapid venous | 154/91 (112) | 111/61 (78) | 30.4 | 13 | 80/40 | Sys: Precipitous fall Dias: Precipitous fall | 116/64 (81) |
| Mean | | 144/82 (103) | 114/66 (82) | 19.0 | 15 | 80/43 | | 120/66 (84) |

TABLE 2. (*Continued*)

| | | Intra-arterial Blood Pressure (mm.Hg) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Control Period | Hemorrhage Period | | | | | Recovery Period |
| Subject | Type of Hemorrhage | Mean Sys/Dias (Mean BP) | Mean Sys/Dias (Mean BP) | % Decrease Mean BP | Duration Hypotension* (min) | Lowest Recorded BP | Comments | Mean Sys/Dias (Mean BP) |
| P. Q. | Slow arterial | 153/83 (106) | 146/82 (103) | 2.8 | 0 | 120/60 | Practically no change | 143/85 (77) |
| R. R. | Rapid arterial | 129/65 (86) | 123/70 (88) | 0 | 0 | 110/72 | Practically no change | 126/71 (89) |
| S. R. | Rapid arterial | 144/81 (102) | 121/79 (93) | 8.8 | 4 | 82/50 | Sys: Precipitous fall<br>Dias: Precipitous fall | 129/81 (97) |
| Mean | | 137/73 (94) | 122/75 (91) | 4.4 | 2 | 96/61 | | 128/76 (93) |
| Control*** | | | | | | | | |
| E. D. | Exchange transfusion | 141/85 (104) | 153/86 (108) | 0 | 0 | 148/80 | No change | 156/86 (109) |
| T. G. | Exchange transfusion | 119/70 (86) | 130/76 (94) | 0 | 0 | 120/72 | No change | 126/74 (91) |
| Mean | | 130/78 (95) | 142/81 (101) | 0 | 0 | 134/76 | | 141/80 (100) |

* Hypotension: Arbitrarily defined as a systolic blood pressure <100 mm.Hg.
** Subject A. F. had blood pressures recorded by aneroid cuff.
*** Exchange transfusion: Simultaneous withdrawal and infusion of blood by two venous catheters resulting in no *net* deficit.

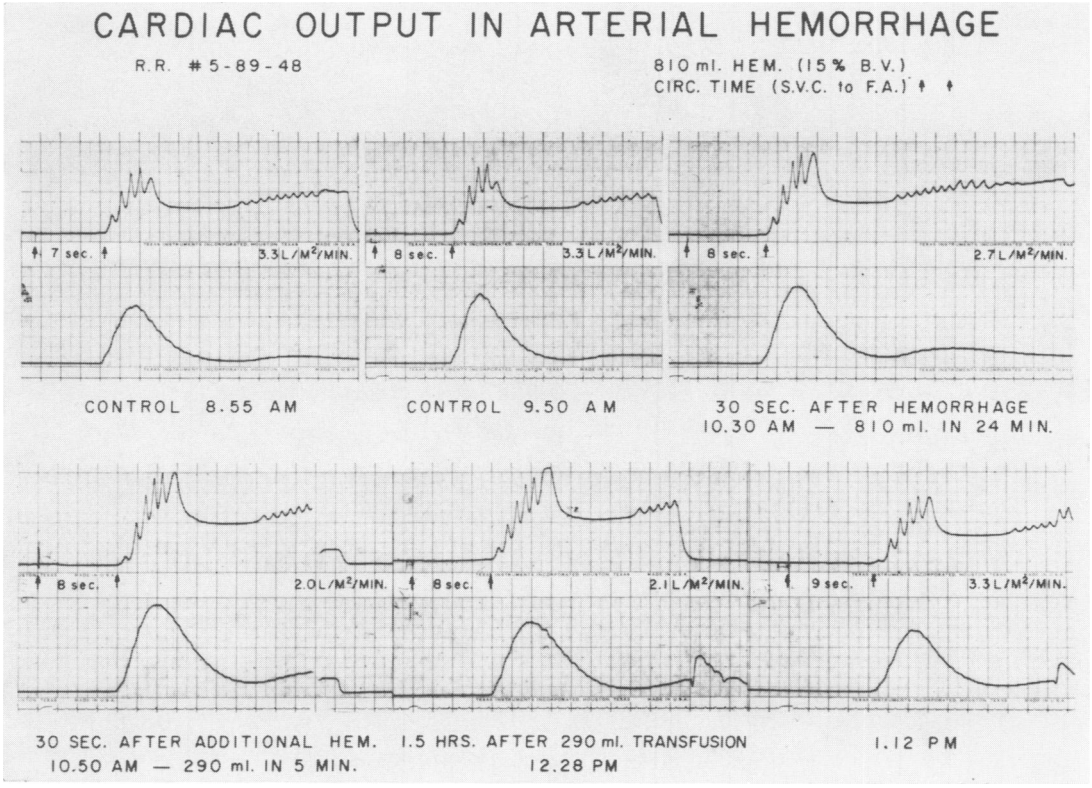



FIG. 4. The lower curve in each section represents dye dilution as sampled from the femoral artery (FA) after indocyanine green injection into the superior vena cava (SVC). Circ. time is the appearance time of dye from the injection site to the sampling site. The upper curve represents the analog computer interpretation of the lower curve. The straight line portion of the computer curve represents the exponential decay of the dye-dilution curve. A gradually decreasing cardiac output occurs with increasing blood loss.

(mean control SV = 77 ml./beat; mean SV after hemorrhage = 52 ml./beat)—a significant decrease ($p < 0.005$). After rapid hemorrhage the mean SV was 65% of control compared to 72% of control after slow hemorrhage. After arterial hemorrhage the mean SV was 61% of control compared to 82% of control when blood was removed by the venous route. Stroke volume decreased further after the transient additional hemorrhage in four of the five subjects in whom it was measured.

With exchange transfusion mean SV changes were minimal, varying above and below the mean control value by 6 to 9 ml. per beat.

**Total Peripheral Resistance (TPR).** The total peripheral resistance decreased slightly after hemorrhage in five of the seven subjects in whom the cardiac output was measured (Table 3), but these decreases were not significant. The two subjects whose TPR increased after hemorrhage were the only two who had rapid arterial hemorrhages (subjects R. R. and S. R.). The mean TPR for the entire bled group in the initial control period was 1,434 dynes·sec.·cm.$^{-5}$. This group mean figure was 1,361 dynes·sec.·cm.$^{-5}$ in the control period immediately before hemorrhage and 1,356 dynes·sec.·cm.$^{-5}$ at 3–10 minutes afterwards, an insignificant change.

Rapid hemorrhages produced the greatest changes in TPR. At 30 seconds after

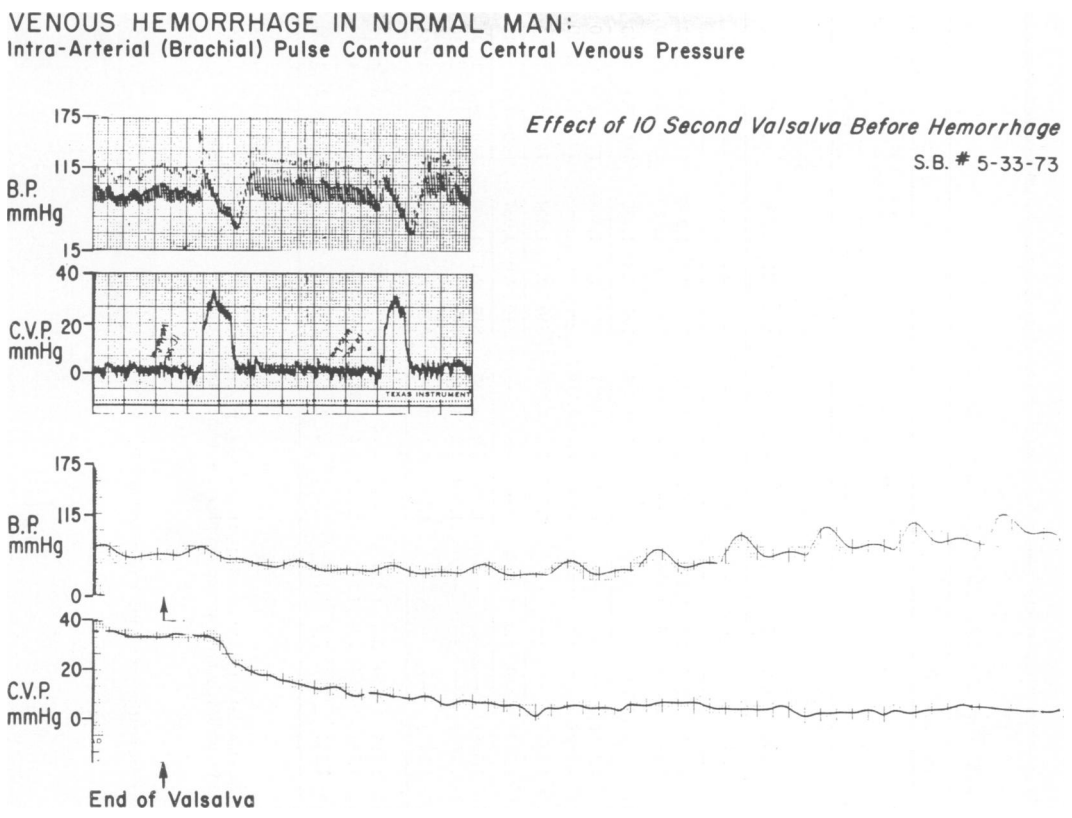



FIG. 5. Paper speed on the two left upper tracings = 1 mm. per second; on the two lower tracings = 25 mm. per second. The flattened tracing after hemorrhage indicates the absence of effective cardiac output at the end of the Valsalva.

rapid arterial hemorrhage, mean TPR had risen 31.9 per cent over its immediate prehemorrhage control value, falling back to 23.0% over control by 5–10 minutes afterward. At 30 seconds after rapid venous hemorrhage, mean TPR had dropped to 27.3% below its immediate prehemorrhage value, rising back to 17.7% below control by 5 to 10 minutes afterward. Slow venous and slow arterial hemorrhages, as well as exchange transfusion, produced smaller decreases in TPR.

**Central Venous Pressure (CVP).** In every hemorrhaged subject CVP dropped during the hemorrhage period or in the immediate recovery period (Table 5). With slow hemorrhage mean CVP decreased 1 mm. Hg in the recovery period. With rapid hemorrhage CVP always dropped during the hemorrhage period itself. There did not seem to be a difference in CVP drop between venous and arterial hemorrhages.

Exchange transfusion produced a mean drop in CVP of 1 mm. Hg in subject E. D., while subject T. G. showed no change in mean CVP during the exchange or recovery periods.

**Valsalva Maneuver.** Typical responses to the Valsalva maneuver before and after hemorrhage can be observed in subject S. B. (Fig. 5) and subject R. W. (Fig. 8, 9). Before hemorrhage the Valsalva maneuver produces the typical changes which have been well described previously by Gorlin, Knowles, and Storey.[4] As airway pressure rises there is an abrupt increase in CVP and arterial pressure, which is fol-

TABLE 3. *Relationship Between Cardiac Index and Total Peripheral Resistance: Effect of Increasing Blood Loss*

| | | Control Period | | | | | | Hemorrhage Period | | | | | | | | | | | | Recovery Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Initial Mean | | | Immediate Pre-Hem. Mean | | | 1 | | | 2 | | | 3 | | | Transient Additional Hemorrhage | | | Time After Last Hemorrhage: 16–110 min. (Mean = 70) | | | Time After Last Hemorrhage: 55–215 min. (Mean = 131) | | |
| Subject | Type of Hem. | Hem. Vol. ml. | CI | TPR | Cum. Hem. Vol. ml. | CI | TPR | Cum. Hem. Vol. ml. | CI | TPR | Cum. Hem. Vol. ml. | CI | TPR | Cum. Hem. Vol. ml. | CI | TPR | Cum. Hem. Vol. ml. | CI | TPR | Cum. Hem. Vol. ml. | CI | TPR | Cum. Hem. Vol. ml. | CI | TPR |
| C. R. | SV | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| A. F. | SV | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |
| T. G. | SV | 0 | 2.7 | 1,372 | 0 | 2.7 | 1,285 | 266 | 2.8 | 1,227 | 521 | 2.8 | 1,243 | 787 | 2.7 | 1,233# | 887 | 2.3 | 1,446 | 787 | 2.9 | 1,254 | 787 | 3.4 | 947 |
| S. B. | SV | 0 | 2.9 | 1,369 | — | — | — | 260 | 2.8 | 1,321 | 530 | 3.2 | 1,129 | 800 | 2.4 | 1,336# | — | — | — | 800 | 2.6 | 1,419 | 800 | 3.2 | 1,179 |
| Mean | | 0 | 2.8 | 1,371 | — | 2.7 | 1,285 | 263 | 2.8 | 1,274 | 526 | 3.0 | 1,186 | 794 | 2.6 | 1,335# | 887 | 2.3 | 1,446 | 794 | 2.8 | 1,337 | 794 | 3.3 | 1,063 |
| S. K. | RV | 0 | 2.3 | 1,737 | 0 | 2.2 | 1,679 | 810* | 2.8* | 806* | 810† | 2.7† | 1,161† | — | — | — | 1,050 | 2.4 | 1,057 | 810 | 2.3 | 1,604 | 810 | 2.7 | 1,370 |
| R. W. | RV | 0 | 2.7 | 1,758 | 0 | 2.7 | 1,569 | 780* | 2.0* | 1,553* | 780† | 2.2† | 1,513† | — | — | — | 1,040 | 2.7 | 1,170 | — | — | — | 780 | 2.9 | 1,360 |
| Mean | | 0 | 2.5 | 1,748 | 0 | 2.5 | 1,624 | 795* | 2.4* | 1,180* | 795† | 2.5† | 1,337† | — | — | — | 1,045 | 2.6 | 1,114 | 810 | 2.3 | 1,604 | 795 | 2.8 | 1,365 |
| P. Q. | SA | 0 | 3.2 | 1,342 | 0 | 3.2 | 1,346 | 270 | 3.2 | 1,283 | 540 | 3.1 | 1,355 | 810 | 3.0 | 1,333# | — | — | — | 810 | 4.0 | 1,057 | 810 | 4.6 | 942 |
| R. R. | RA | 0 | 3.2 | 1,079 | 0 | 3.3 | 1,076 | 810* | 2.7* | 1,325* | 810† | 2.7† | 1,325† | — | — | — | 1,100 | 2.0 | 1,750 | 810 | 2.1 | 1,660 | 810 | 3.2 | 1,191 |
| S. R. | RA | 0 | 2.7 | 1,468 | 0 | 3.0 | 1,305 | 780* | 1.8* | 2,170* | 780† | 2.2† | 1,768† | — | — | — | 1,040 | 2.2 | 1,931 | 780 | 2.3 | 1,688 | 780 | 2.2 | 2,130 |
| Mean | | 0 | 3.0 | 1,274 | 0 | 3.2 | 1,191 | 795* | 2.3* | 1,748* | 795† | 2.5† | 1,547† | — | — | — | 1,090 | 2.1 | 1,841 | 795 | 2.2 | 1,674 | 795 | 2.7 | 1,661 |
| Control E. D. | Ex. Tr. | 0 | 3.3 | 1,330 | — | — | — | 270 | 3.4 | 1,260 | 540 | 3.5 | 1,315 | 810 | 3.6 | 1,231 | — | — | — | 810 | 3.6 | 1,253 | 810 | 3.6 | 1,219 |
| T. G. | Ex. Tr. | 0 | 2.6 | 1,600 | 0 | 2.1 | 1,881 | 260 | 2.2 | 1,805 | 520 | 2.5 | 1,767 | 784 | 2.8 | 1,518 | 1,044 | 2.6 | 1,513 | — | — | — | 784 | 2.8 | 1,380 |
| Mean | | 0 | 3.0 | 1,465 | 0 | 2.1 | 1,881 | 265 | 2.8 | 1,533 | 530 | 3.0 | 1,541 | 797 | 3.2 | 1,375 | 1,044 | 2.6 | 1,513 | 810 | 3.6 | 1,253 | 797 | 3.2 | 1,300 |

Cum. Hem. Vol. ml. = Cumulative Hemorrhage Volume (ml.).
CI = Cardiac Index (L./m²/min.).
TPR = Total Peripheral Resistance (dynes·sec·cm.$^{-5}$).
Hemorrhage Period 1, 2, 3 = ≃250 ml. successive hemorrhages except for rapid bleeds where the entire blood loss was in Hemorrhage Period 1.
Transient Additional Hemorrhage = An additional withdrawal of blood which was replaced immediately after hemodynamic measurements were taken.
SV = Slow Venous.
RV = Rapid Venous.
SA = Slow Arterial.
RA = Rapid Arterial.
Ex. Tr. = Exchange Transfusion: Simultaneous withdrawal and infusion of blood by two venous catheters resulting in no *net* deficit.
* 30 seconds after hemorrhage.
† 5–10 minutes after hemorrhage.
#3–10 minutes after hemorrhage.

TABLE 4. *Stroke Volume Measurements Before, During, and After Hemorrhage*

| Subject | Type of Hemorrhage | Stroke Volume ml./beat | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Recovery Period | |
| | | | Hemorrhage Period | | | | Time After Last Hemorrhage (min.) | |
| | | Control Period | 1 | 2 | 3 | Transient Additional Hemorrhage | 16–110 Mean = 70 | 55–215 Mean = 131 |
| C. R. | Slow venous | — | — | — | — | — | — | — |
| A. F. | Slow venous | — | — | — | — | — | — | — |
| T. G. | Slow venous | 66 | 61 | 61 | 56† | 47 | 60 | 72 |
| S. B. | Slow venous | 66 | 59 | 62 | 49† | — | 55 | 67 |
| Mean | | 66 | 60 | 62 | 53† | 47 | 58 | 70 |
| S. K. | Rapid venous | 61 | 48** | — | — | 38 | 60 | 52 |
| R. W. | Rapid venous | 71 | 48** | 54*** | — | 67 | — | 64 |
| Mean | | 66 | 48** | 54*** | — | 53 | 60 | 58 |
| P. Q. | Slow arterial | 105 | 85 | 78 | 71† | — | 90 | 100 |
| R. R. | Rapid arterial | 85 | 58** | — | — | 42 | 51 | 67 |
| S. R. | Rapid arterial | 82 | 35** | 44*** | — | 43 | 48 | 45 |
| Mean | (Rapid arterial) | 84 | 47** | 44*** | — | 43 | 50 | 56 |
| Controls | | | | | | | | |
| E. D. | Exchange transfusion* | 81 | 82 | 87 | 81 | — | 84 | 87 |
| T. G. | Exchange transfusion* | 68 | 50 | 72 | 68 | 68 | — | 63 |
| Mean | | 75 | 66 | 80 | 75 | 68 | 84 | 75 |

* Exchange Transfusion: Simultaneous withdrawal and infusion of blood by two venous catheters resulting in no *net* deficit.
** 30 seconds after hemorrhage.
*** 5 minutes after hemorrhage.
† 3–10 minutes after hemorrhage.

lowed shortly thereafter by a fall in arterial pressure. With the Valsalva maneuver sustained, the arterial pressure begins to level off. At the moment straining is stopped there is an abrupt fall in CVP and a transient further drop of arterial pressure coincident with a delayed return of blood to the left ventricle secondary to refilling of the pulmonary vascular tree. A rebound rise, or overshoot phase, of arterial pressure then occurs, which in turn is followed by a reflex bradycardia.

After hemorrhage the arterial pressure is lower than before hemorrhage, and respiratory fluctuations are marked. At this time even a less forceful Valsalva maneuver causes a greater drop in arterial pressure and a very blunted or absent overshoot phase. The right side of Figure 5 shows the end of the Valsalva maneuver both before and after hemorrhage. After hemorrhage the arterial tracing is almost flat, an indication that effective left ventricular output is minimal.

Electrocardiographic changes with the Valsalva maneuver after hemorrhage are seen in Figure 6 (subject P. Q.). The increased heart rate during the Valsalva is followed afterwards by bradycardia. The 6th and 7th heart beats after Valsalva show an inverted T wave. The 9th and 12th heart beats are ventricular premature beats, a possible indication of transient myocardial irritability and/or ischemia. These electro-

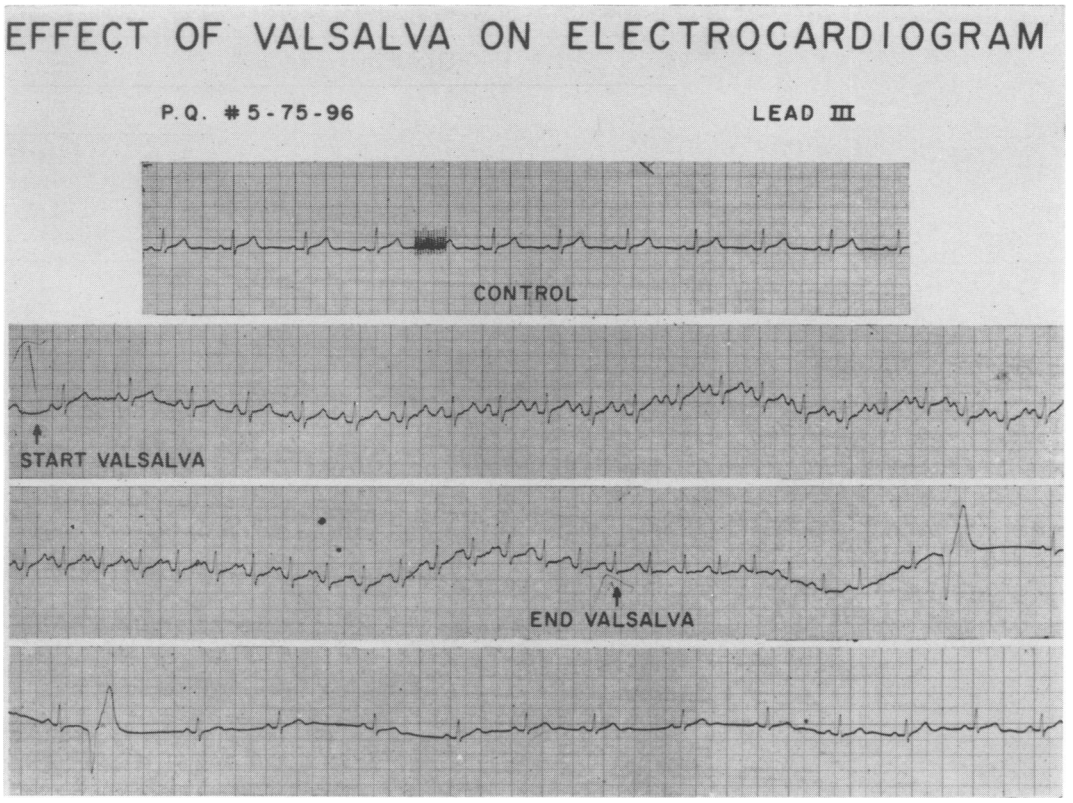



FIG. 6. The increased heart rate during the Valsalva is followed by marked bradycardia. The 5th, 6th, and 7th beats after the Valsalva show inversion and flattening of the T wave. The 9th and 12th beats are ventricular premature beats.

cardiographic changes were not seen with Valsalva before hemorrhage.

Cardiac output measurements made during the Valsalva maneuver are unreliable because of the nonsteady state conditions. The complete holdup of a dye bolus injected during the performance of a Valsalva maneuer, however, is impressive evidence of a marked temporary cessation of effective left ventricular output (Fig. 7). This temporary holdup of the dye bolus was noted in three of the five subjects before hemorrhage and in all five subjects after hemorrhage.

**Breath Holding.** Figures 8 and 9 show typical effects of breath holding and the Valsalva maneuver in subject R. W. before and after a rapid venous hemorrhage. Expiratory breath holding (EBH) did not impose a significant circulatory stress. Arterial pressure and CVP showed no consistent change over control values. Inspiratory breath holding (IBH) at maximal vital capacity produced bradycardia, a rise in CVP (5 mm. Hg), and a rise in systolic and diastolic pressure before hemorrhage. After hemorrhage IBH produced slight bradycardia and a rise in CVP (3 mm. Hg), but with a depression of arterial blood pressure. Cardiac index decreased consistently with IBH—this decrease being greater after hemorrhage than before hemorrhage (Table 6). IBH was associated with a decrease in CI in two of the three volunteers after hemorrhage. Mean CI dropped more with IBH than with EBH both before and after hemorrhage in the three subjects in whom these comparisons could be made.

TABLE 5. *The Effect of Hemorrhage on Pulse Rate and Central Venous Pressure*

| | | Pulse Rate (Beats/min.) | | | Central Venous Pressure (mm. Hg.) | | |
|---|---|---|---|---|---|---|---|
| | | Control | Hemorrhage Period | Recovery Period | Control | Hemorrhage Period | Recovery Period |
| Subject | Type of Hemorrhage | Mean | Mean | Mean | Mean | Mean | Mean |
| C. R. | Slow venous | 60 | 67 | 65 | — | — | — |
| A. F. | Slow venous | 64 | 71 | 67 | — | — | — |
| T. G. | Slow venous | 73 | 84 | 83 | 2 | 2 | 1 |
| S. B. | Slow venous | 80 | 91 | 89 | 4 | 4 | 3 |
| Mean | | 69 | 78 | 76 | 3 | 3 | 2 |
| S. K. | Rapid venous | 75 | 88 | 86 | 3 | 2 | 2 |
| R. W. | Rapid venous | 77 | 74 | 76 | 5 | 4 | 4 |
| Mean | | 76 | 81 | 81 | 4 | 3 | 3 |
| P. Q. | Slow arterial | 68 | 81 | 85 | 3 | 4 | 2 |
| R. R. | Rapid arterial | 73 | 86 | 77 | 3 | 2 | 1 |
| S. R. | Rapid arterial | 76 | 83 | 94 | 3 | 2 | 1 |
| Mean | (Rapid arterial) | 75 | 85 | 86 | 3 | 2 | 1 |
| Controls | | | | | | | |
| E. D. | Exchange transfusion* | 76 | 77 | 78 | 6 | 5 | 6 |
| T. G. | Exchange transfusion* | 70 | 70 | 77 | 4 | 4 | 4 |
| Mean | | 73 | 74 | 78 | 5 | 5 | 5 |

* Exchange Transfusion: Simultaneous withdrawal and infusion of blood by two venous catheters resulting in no *net* deficit.

## Representative Individual Hemodynamic Patterns

**1. Subject T. G., #1–20–61. Slow Venous Hemorrhage.** 784 ml. in 79 minutes (Fig. 10). A decrease in CI is seen only after the transient additional hemorrhage of 100 ml. Mean arterial blood pressure decreased gradually by 11.5% during hemorrhage, and mean CVP decreased 1 mm. Hg in the recovery period. The decrease in BP is mainly in the systolic component. Pulse rate gradually rose with hemorrhage.

*Comment.* Hemodynamic changes developed very gradually in this slowly bled subject.

**2. Subject S. K., #5–83–42. Rapid Venous Hemorrhage.** 810 ml. in 14 minutes (Fig. 11). Cardiac index increased slightly after hemorrhage. In spite of this there was a marked transient fall in systolic and diastolic pressure associated with a marked fall in TPR. Central venous pressure fell during hemorrhage and during the transient additional hemorrhage. Pulse rate rose as the hemorrhage increased.

*Comment.* This subject was the only one to show an increase in CI immediately after hemorrhage. Though CI and pulse rate increased, he was still unable to maintain arterial pressure because his TPR dropped markedly.

**3. Subject P. Q., #5–90–48. Slow Arterial Hemorrhage.** 825 ml. in 107 minutes (Fig. 12). Cardiac index was unchanged until 30 minutes after bleeding when it rose from 3.0 L./m.$^2$/min. to 4.0 L./m.$^2$

TABLE 6. *Cardiac Index Measurements During Inspiratory and Expiratory Breath Holding*

| Subject | Type of Hemorrhage | Cardiac Index L./m.²/min. Control: Before Hemorrhage | Inspiratory Breath Holding (IBH): Before Hemorrhage | Inspiratory Breath Holding (IBH): Comment | Inspiratory Breath Holding (IBH): After Hemorrhage | Inspiratory Breath Holding (IBH): Comment | Expiratory Breath Holding (EBH): Before Hemorrhage | Expiratory Breath Holding (EBH): Comment | Expiratory Breath Holding (EBH): After Hemorrhage | Expiratory Breath Holding (EBH): Comment |
|---|---|---|---|---|---|---|---|---|---|---|
| R. W. | Rapid venous | 2.7 | 2.0 | 38 sec. IBH through exponential* | 1.4 | 45 sec. IBH through exponential* | 4.5 | 30 sec. EBH through exponential* | 1.7 | 38 sec. EBH through exponential* |
| R. R. | Rapid arterial | 3.2 | 2.7 | 30 sec. IBH through exponential* | 2.3 | 30 sec. IBH through exponential* | 2.8 | 28 sec. EBH through exponential* | 2.8 | 30 sec. EBH through exponential* |
| S. R. | Rapid arterial | 2.7 | 1.9 | 36 sec. IBH through exponential* | 1.2 | 35 sec. IBH through exponential* | 3.2 | 28 sec. EBH through exponential* | 1.6 | 28 sec. EBH through exponential* |

* Through Exponential: Indicates that the dye curve appearance time was not changed by the maneuver.

/min. With this rise in CI, TPR fell but arterial pressure remained practically unchanged (2.8% mean decrease). Central venous pressure dropped during the second and third blood removal periods. Pulse rate rose gradually during the study.

*Comment.* Hemodynamic changes were gradual to develop during this slow bleed.

**4. Subject S. R., #5–96–27. Rapid Arterial Hemorrhage.** 780 ml. in 19 minutes (Fig. 13). Cardiac index decreased immediately after hemorrhage. Arterial pressure fell precipitously during hemorrhage, but returned to almost baseline value by the end of hemorrhage. Total peripheral resistance increased markedly after hemorrhage. Central venous pressure fell during hemorrhage and the transient additional hemorrhage. Pulse rate increased just before the hypotensive episode to 100 beats per minute, but then fell to 73 beats per minute as arterial pressure returned towards baseline value.

*Comment.* Transient hypotension was not associated with bradycardia in this subject.

**5. Subject T. G., #1–20–61. Control: Exchange Transfusion.** 784 ml. in 81 minutes (Fig. 14). Mean CI increased gradually with exchange transfusion, then decreased and returned to control value afterwards. Three hours later mean CI showed a second rising trend. Arterial pressure and CVP showed no change. Pulse rate increased from a mean of 70 beats per minute during the control and exchange transfusion periods to a mean of 77 beats per minute during the recovery period.

*Comment.* This subject, who showed minimal hemodynamic changes with his slow venous hemorrhage study 6 months earlier, shows even fewer changes with his exchange transfusion.

## Discussion

Shenkin and co-workers [17] using healthy men, categorized the effects of hemorrhage into three stages of severity. The first stage was characterized by the absence of symp-

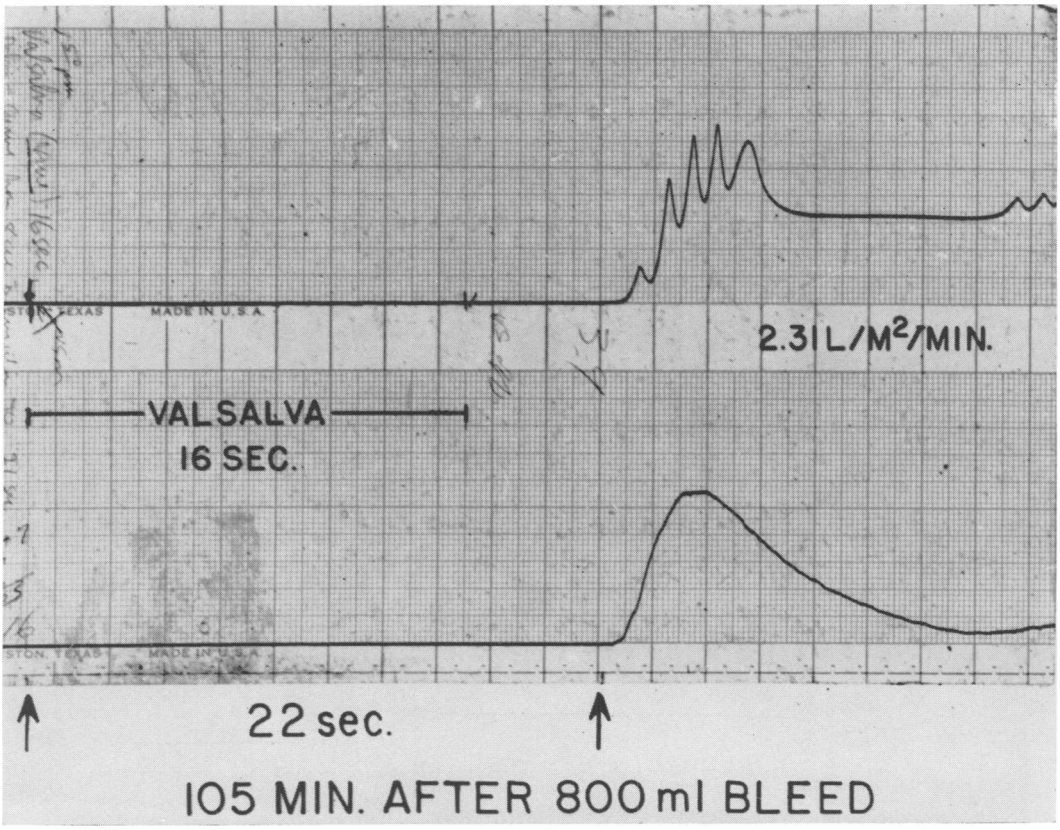



FIG. 7. The complete holdup of the cardiogreen dye bolus performed 105 minutes after an 800 ml. slow venous hemorrhage in subject S. B. is shown during a 16 second Valsalva. The 22 second appearance time indicates that the dye bolus appeared at the brachial artery sampling site 6 seconds after the end of the Valsalva. A low cardiac index value of 2.3 L./m.²/min. was obtained in this instance.

toms and by a pulse rate and blood pressure within normal limits when lying down. On standing, however, pulse rate increased and blood pressure decreased significantly. In the second stage pulse and blood pressure showed no changes at rest, but syncope occurred rapidly on standing. In the third stage sweating, restlessness, and syncope, with profound hypotension and bradycardia occurred even though the subject was lying down. The effects of hemorrhage reported in this paper do not uniformly coincide with Shenkin's categories.

Transient hypotension plus bradycardia, commonly known as vasovagal syncope * [7] occurred in three of the nine bled subjects after approximately 750 ml. blood loss. Two of these three subjects, R. W. and S. R., had rapid hemorrhages, one venous and one arterial, respectively. Subject A. F. had a vasovagal episode after only 520 ml. of slow venous hemorrhage. In contrast, one subject (S. K.) developed an increased pulse rate with his transient precipitous hypotension following an 810 ml. rapid venous hemorrhage.

Rapid hemorrhage caused a greater and briefer change in blood pressure, CI, and stroke volume than did slow hemorrhage. While rapid blood loss produces more dramatic hemodynamic changes, slow blood loss—especially from the veins—may well represent a much greater hazard to a

* Vasovagal syncope: as recently differentiated from vagovagal syncope.[7]

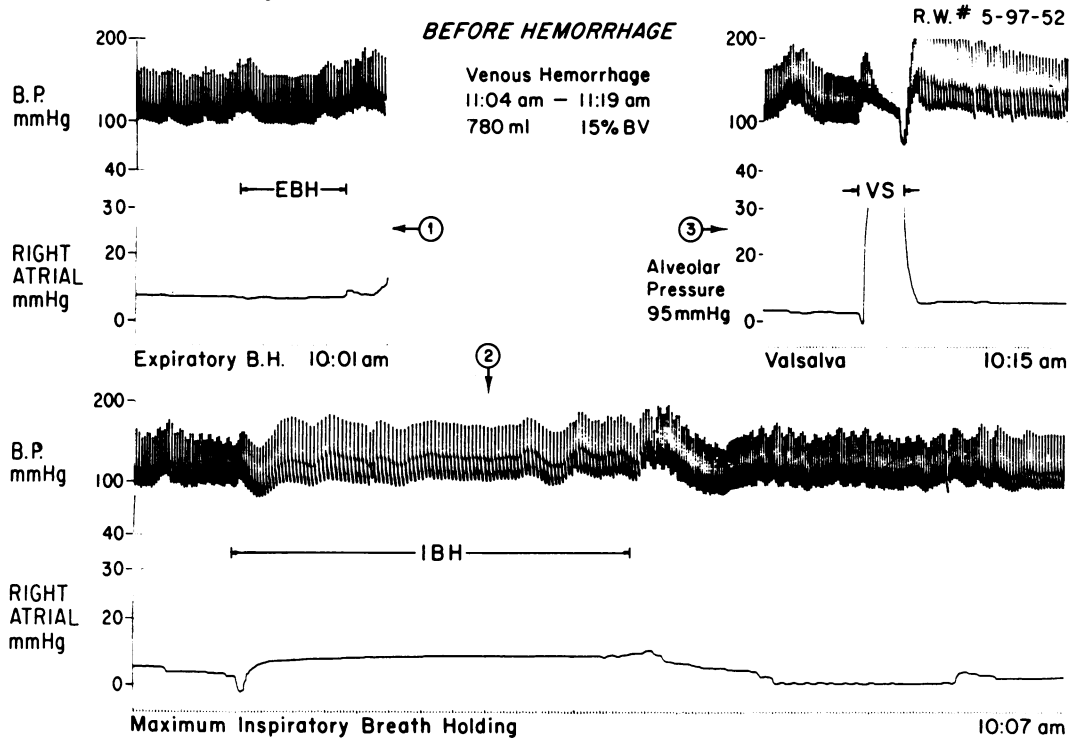


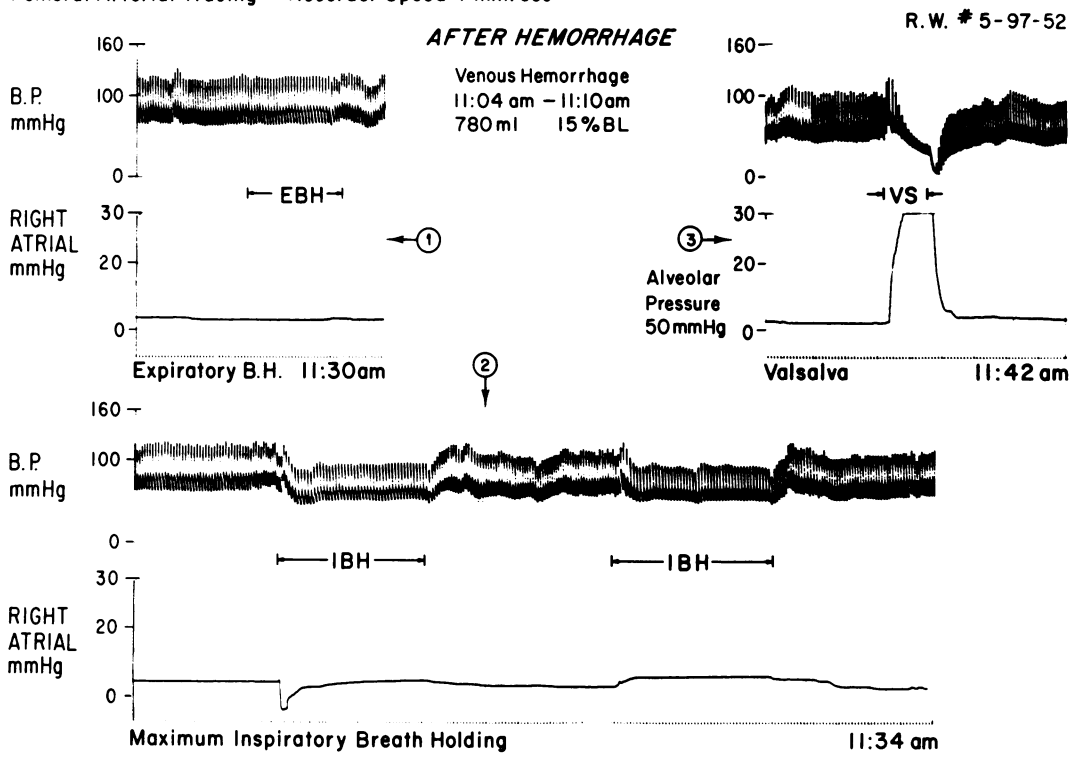

FIG. 8, 9. Breath holding: The bradycardia seen with inspiratory breath holding ((IBH) is not observed with expiratory breath holding (EBH) in the tracing before hemorrhage. Nonrespiratory oscillations in arterial pressure (0.05 cycles/second) are seen in the IBH tracing before hemorrhage. Right atrial pressure rises gradually with IBH. After hemorrhage arterial

bleeding patient. The prolonged hypotension in the slow hemorrhage group and in the venous hemorrhage group gives support to this concept.

**Nonrespiratory Oscillations of Arterial Pressure.** Race and Rosenbaum [14] have described nonrespiratory oscillations in systemic arterial pressure in dogs before and after graded hemorrhage and after infusion of pentolinium, epinephrine, norepinephrine, and angiotensin II. Maintenance of systemic arterial pressure depends on a control system containing multiple feedback loops, among which are the carotid and aortic baroreceptors, cerebral ischemic response, and chemoreceptors.[13] As suggested by Race and Rosenbaum, the increase of amplitude and frequency of the blood pressure fluctuations after hemorrhage in the present studies is probably, at least in part, due to nonlinearity in the baroreceptors causing changes in input pressure to be reflected in changes of gain at the receptor site.

Race and Rosenbaum [14] noted an increase in the nonrespiratory oscillations after hemorrhages greater than 20% of the blood volume. Subject R. W. (Fig. 7) showed less prominent nonrespiratory oscillations after blood loss in the IBH tracing than in his control period. This conflicting finding may be due to different experimental conditions and a smaller hemorrhage volume in this study.

*Pulse rate.* An increased mean pulse rate during hemorrhage developed in eight of




pressure does not change with EBH, but drops significantly with IBH. Valsalva: A typical Valsalva with pronounced overshoot and reflex bradycardia is shown before hemorrhage. After hemorrhage the arterial pressure drop is greater, even though airway pressure is less, and the overshoot and bradycardia are absent.

the nine subjects ($p < 0.025$). Shenkin and his co-workers [17] reported that slowing of the pulse was more common after a large hemorrhage. He concluded that the pulse rate could not be used to diagnose hemorrhage. (The mean amount and duration of Shenkin's large bleeds was 1,029 ml. in 14.1 minutes.) In the present studies, although bradycardia occurred transiently in three of the four subjects who developed precipitous changes in blood pressure, only in subject, R. W., was it persistent throughout the hemorrhage and recovery periods. In most of Shenkin's studies, the observation period was short and confined to the actual hemorrhage period—hence his findings of consistent bradycardia in contrast to the increased pulse rate seen after hemorrhage in this study.

**Arterial Pressure Pulse Contours.** The first clinical estimation of cardiac output from pressure pulse contours in man was made by Erlanger and Hooker in 1904.[3] These workers investigated pulse rate and arm cuff blood pressures under varying physiological conditions and attempted to relate the product of these measurements as an index of the relative velocity of blood flow.

Warner and co-workers,[22] testing the theoretical basis for measuring the beat to beat changes in stroke volume from the central arterial pulse contours in man (using the left subclavian artery or the

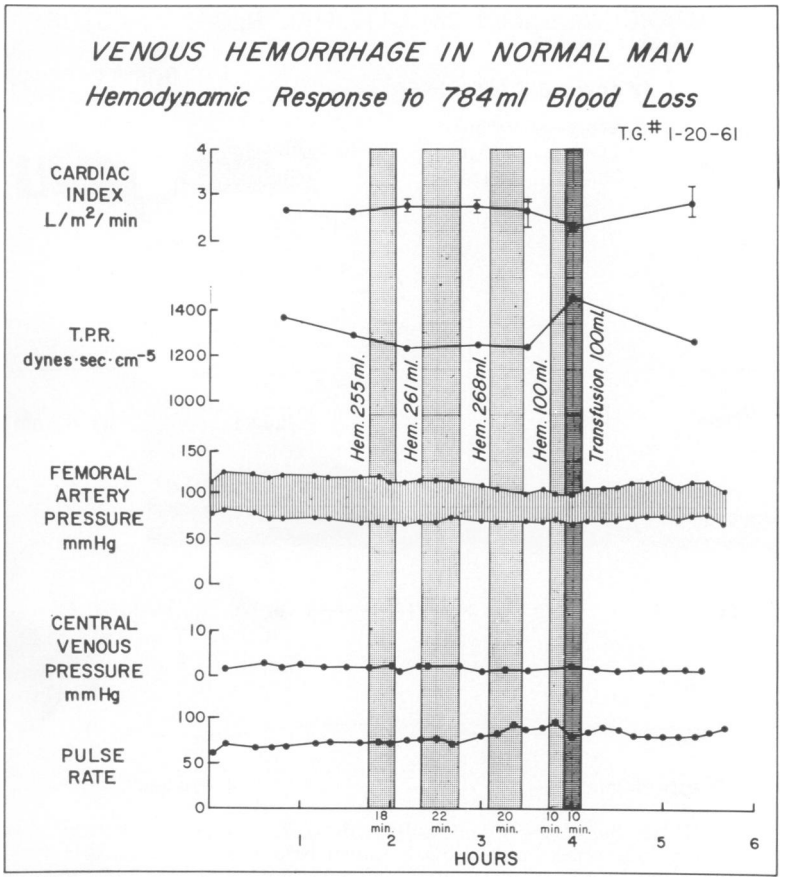



FIG. 10. Slow venous hemorrhage: Cardiac index (CI) drops only after the 100 ml. transient additional hemorrhage (dots are mean values; bars represent individual separate values). Systolic pressure decreases slightly. Mean central venous pressure drops only in the recovery period (by 1 mm. Hg). Pulse rate shows a gradual rise. (TPR = total peripheral resistance.)

aorta), found good agreement between this method and the standard methods of cardiac output estimation using the direct Fick or dye-dilution principle.

Although quantitation of the stroke volume from the femoral artery pulse contours was not attempted in the present studies, it is significant that the area under the femoral artery pressure pulse curve was uniformly reduced after hemorrhage in all of the bled subjects. As Herd and coworkers [6] point out, pulse pressure area and stroke volume would be proportional to each other only if heart rate remains constant. In subject R. W. (Fig. 2) there was no significant change in pulse rate. A direct ratio between area and stroke volume, therefore, can be observed in his study only.

The two control subjects having exchange transfusions did not show this reduction of arterial pulse contour area.

**Cardiac Index and Stroke Volume.** Cardiac index fell with blood loss in five of the seven subjects in whom it was measured, but this fall was not statistically significant ($0.1 > p > 0.05$). Stroke volume, however, fell in all seven of these subjects ($p < 0.001$). (Mean control CI was 2.8 $\pm$ 0.3 L./m.²/min. [1 S.D. of the mean].) Guyton [5] has pointed out that comparison of CI values among individuals is not always meaningful because cardiac output does not relate closely to body surface area. This probably explains the standard deviation of 0.3 L./m.²/min. seen in the mean control CI value for the entire group. When CI is compared within an individual,

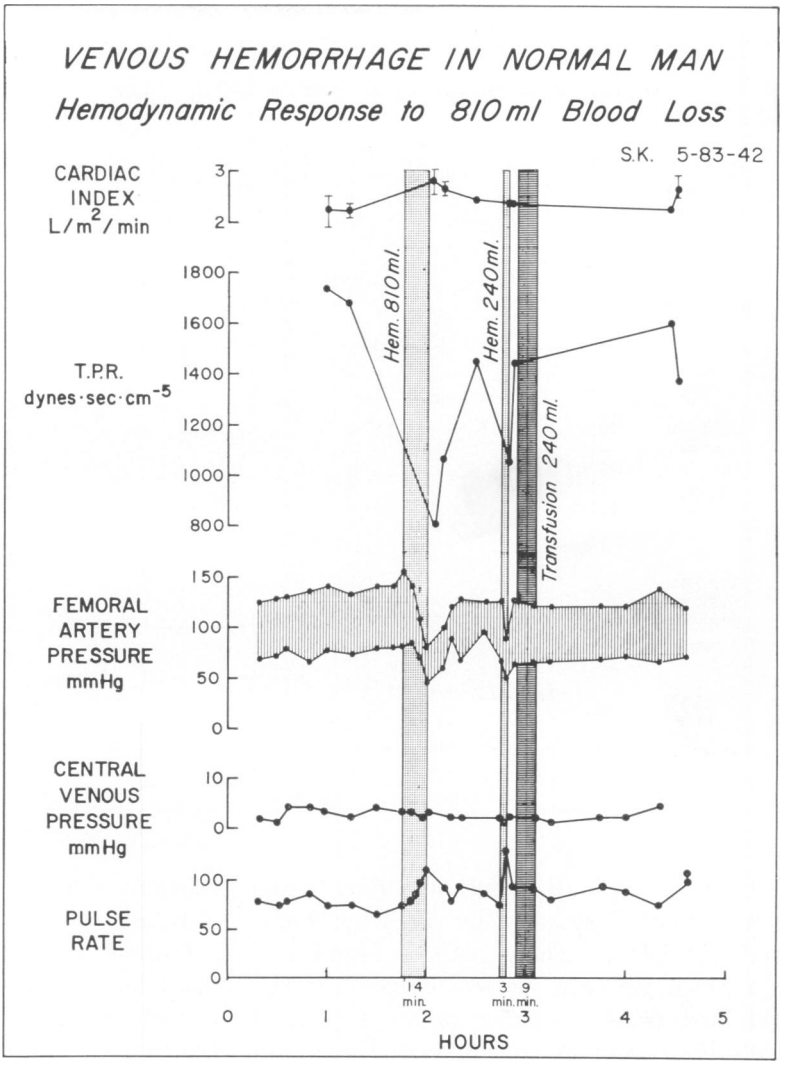



FIG. 11. Rapid venous hemorrhage: This is the only bled subject whose CI increased after hemorrhage. Central venous pressure drops toward the end of the bleed. Arterial pressure and TPR drop precipitously for a brief period after hemorrhage. These drops are associated with a rise in pulse rate.

however (by multiple cardiogreen injections approximately 45 seconds apart), the reproducibility of CI measurements at any given time is demonstrated (Fig. 13, subject S. R.). The largest variation found on a clustered series of dye-dilution injections during the entire study was that of subject T. G. 2½ hours after exchange transfusion (mean CI = 3.7 ± 1.4 L./m.²/min. [1 S.D. of the mean]).

Warren, Stead, and co-workers,[20, 23] using the direct Fick method with 2-minute collections of expired gas for the determination of cardiac output, were unable to detect consistent changes in cardiac output after hemorrhage in normal volunteers. Two possible sources of error are present in Warren's studies. It is likely that 2-minute periods of expired gas collection are too brief for a steady state determination of oxygen consumption. Also, as pointed out by these authors, variations in cardiac index may result from difficulties encountered in obtaining true mixed venous blood samples.

Use of the analog computer to analyze

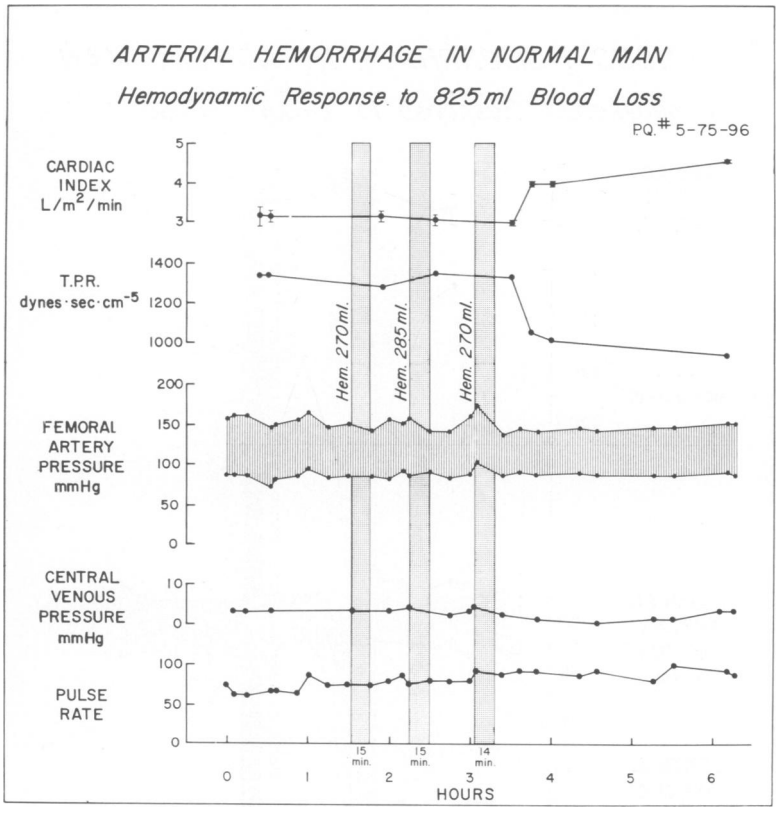



FIG. 12. Slow arterial hemorrhage: CI drops very little with hemorrhage. As CI increases after hemorrhage, TPR drops while arterial pressure stays constant. CVP drops 1 mm. Hg (mean) after hemorrhage.

cardiac output dye-dilution curves has been reported recently by Sinclair, Duff, and MacLean.[18] These authors found no difference between cardiac output values obtained from computer analyzed curves and those from manual Stewart-Hamilton replots.

**Total Peripheral Resistance (TPR).** The lack of generalized increase in arteriolar vasoconstriction which has been noted by Warren and co-workers [3] was also noted in this study. Of the seven bled subjects in whom TPR was measured the only two whose TPR increased after hemorrhage were the two who underwent rapid arterial hemorrhages (subjects R. R. and S. R.) (Fig. 13, subject S. R.). The lack of a consistent rise in TPR after hemorrhage may be related to a predominant increase of epinephrine secretion, a catecholamine fraction which lowers the peripheral resistance.[24, 25]

**Central Venous Pressure (CVP).** The small but important fall in CVP observed with hemorrhage was associated with a transient decrease of venous return, a decrease which was reflected by a slight drop in cardiac output. Warren and co-workers [23] also noted a fall in right atrial pressure with hemorrhage, and concluded that there was no compensatory mechanism to maintain a constant pressure. Pappenheimer and Soto-Rivera,[12] however, showed that this decrease in venous pressure is a potent stimulus to the transcapillary refilling * of the blood volume after hemorrhage, a

* Transcapillary refilling describes an influx of new fluid into the plasma volume from an area not formerly included in the 40-minute distribution volume of Evans blue.[8]

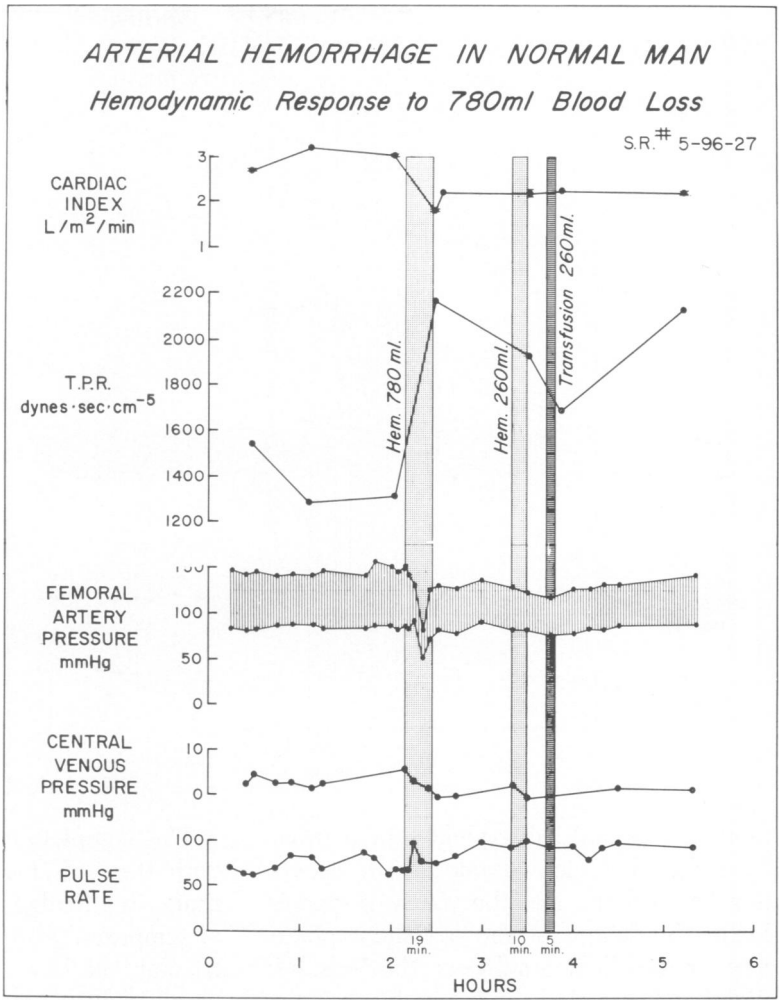



FIG. 13. Rapid arterial hemorrhage: As bradycardia occurs during hemorrhage, CI and arterial pressure drop sharply and transiently. TPR increases markedly as arterial pressure returns rapidly to a normal range. CVP drops markedly during the bleed. Pulse rate gradually rises throughout the study.

mechanism which will eventually restabilize the venous pressure at its previous normal value.

**The Valsalva Maneuver.** The Valsalva maneuver has been used to test vasomotor control of the circulation.[4, 16] Recently Coffin, Gann, and Drucker [1] studied the effect of the Valsalva maneuver in the anesthetized dog after graded hemorrhage, reinfusion, and subsequent overexpansion with dextran and saline. Their results suggest that this maneuver may be a useful test to measure effective circulatory volume. On application of a positive airway pressure of 20 mm. Hg for 10 seconds, normovolemic dogs showed a definite Valsalva overshoot phase, whereas the hypovolemic dogs (bled 20% of their blood volume) lacked the overshoot phase. A similar lack of the overshoot phase after hemorrhage in the dog had been noted previously by Sarnoff and co-workers.[16]

In the present studies almost all of the volunteers showed an overshoot phase associated with a reflex bradycardia before hemorrhage. When the Valsalva maneuver was tested after hemorrhage, five of the nine subjects did not show an overshoot phase or bradycardia. It is likely that larger hemorrhages would consistently abolish

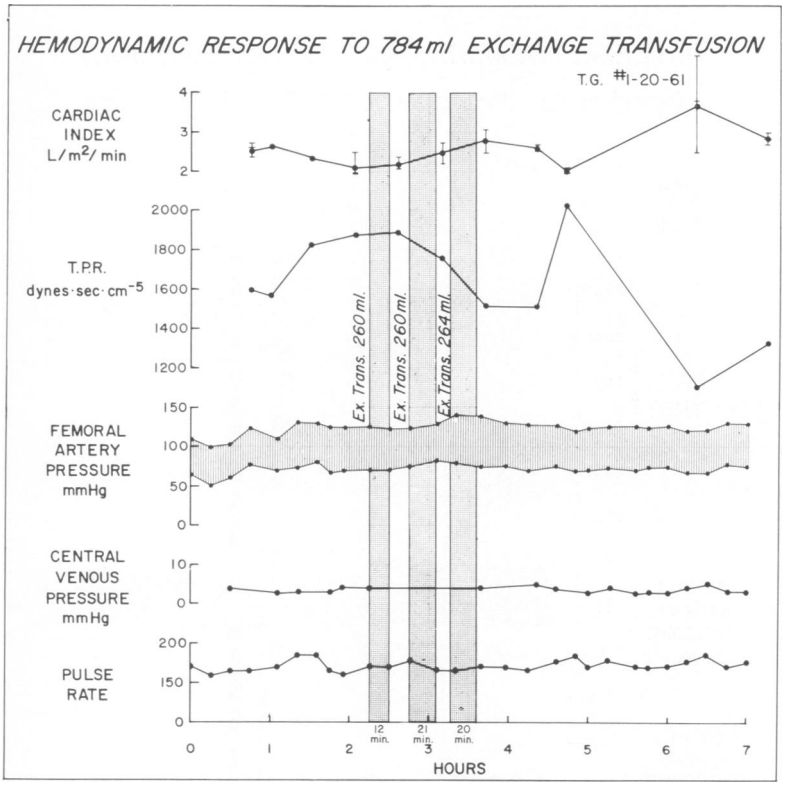



FIG. 14. Exchange transfusion (control): CI gradually rises during exchange transfusion. Large variation of CI is observed 2½ hours after exchange transfusion. Arterial pressure fluctuates in the control period and then stabilizes. Mean CVP does not change. Pulse rate increases slightly.

the overshoot and subsequent bradycardia. The reduced stroke volume which occurs after hemorrhage may be partly responsible for the failure of the overshoot phase to occur. In all nine subjects, the Valsalva following hemorrhage produced a greater drop in arterial pressure than it did in the control period, even though the maximum airway pressure was less than before hemorrhage.

Stone, Lyon, and Teirstein [21] state that the tachycardia and secondary rise in blood pressure which occur just before the end of the Valsalva infers reflex vasoconstriction. After hemorrhage, however, when the effects of increasing airway pressure accentuate the reduction in central blood volume, tachycardia may not be sufficient to maintain cardiac output, thus a secondary rise in blood pressure will not occur. This is observed in the Valsalva tracings before and after hemorrhage in subject R. W. (Figs. 8, 9).

The complete holdup of the dye bolus with the Valsalva maneuver after hemorrhage in all subjects is impressive evidence of temporarily impaired right and left ventricular outflow. Even when barely discernible pulse contours were visible on the arterial trace, the dye bolus did not appear at the femoral artery sampling site until the termination of the straining period (Fig. 7).

The usefulness of this test in critically ill patients is questionable. Although definite changes in the Valsalva maneuver occur with hypovolemia, performance of a satisfactory test requires cooperative effort. The patient in whom this maneuver might provide useful information is the very one who will have difficulty executing it. In addition, transient myocardial ischemia may be a hazard.

**Breath Holding.** Mithoefer [9] has recently reviewed the physiological aspects of breath holding. Breath holding is a stress

on the circulation which seems to be less severe than that of the Valsalva maneuver.

Changes in pulse rate and blood pressure similar to those observed before hemorrhage in subjects R. W. (Figs. 8, 9), S. R., and R. R. have been previously described by Muxworthy [11] in breath holding studies in man. Muxworthy noted a fall in heart rate, a rise in systolic and diastolic pressure, and a decrease in the rate of finger blood flow, pulse volume, and finger volume.

Murdaugh and co-workers [10] in studies in the harbor seal, *Phoca vitulina,* have reported profound bradycardia, markedly decreased cardiac output, and intense peripheral vasoconstriction which maintains the blood pressure during diving experiments. Arterial vasoconstriction is so intense in the extremities of the diving seal that these areas are, in effect, excluded from the circulation.

In subject R. W. (Table 6, Figs. 8, 9) bradycardia, decreased cardiac output, and a rise in systolic pressure occurred with IBH before hemorrhage. A slight rise in CVP was noticed just before the breaking point.* Calculated TPR increased to 2,420 dynes·sec.·cm.$^{-5}$ during IBH, evidence of intense arterial vasoconstriction similar to that observed in the seal experiments.

After hemorrhage the cardiac index in subject R. W. fell even more with IBH, but peripheral resistance did not rise as much (TPR after hemorrhage with IBH = 1,830 dynes·sec.·cm.$^{-5}$) and blood pressure dropped to 98/52 mm. Hg. The further reduction in cardiac output may be due in part to the reduced central blood volume and decreased lung volume caused by hemorrhage.[23] Subjects S. R. and R. R. (Table 6) showed similar changes.

The higher cardiac index values seen with EBH support the view that EBH is a more gentle circulatory stress than IBH. The use of breath holding to evaluate cardiovascular function and circulatory volume adequacy needs further study.

* "Breaking point" has been defined by Mithoefer as "the voluntary termination of breath holding in response to the development of a net ventilatory stimulus too strong to be further resisted by voluntary effort." [9]

## Summary

The hemodynamic effect of acute blood loss (15% of the blood volume) has been studied in nine normal male volunteers. Cardiac output (dye-dilution), intra-arterial blood pressure, central venous pressure, and the response to the Valsalva maneuver, and breath holding were tested before and after hemorrhage.

Cardiac index decreased after hemorrhage in five of the seven subjects in whom it was measured, but this fall was not statistically significant. Stroke volume decreased significantly in all the bled subjects after hemorrhage ($p < 0.005$). Arterial pressure pulse contours reflected this decrease in stroke volume. Contrary to predicted changes, calculated total peripheral resistance increased after hemorrhage in only two of the seven subjects in whom it was measured. The control subjects having exchange transfusions did not show these changes.

Central venous pressure decreased during hemorrhage or in the recovery period. Pulse rate increased significantly during the hemorrhage period in eight of the nine subjects ($p < 0.025$).

Rapid hemorrhages caused briefer and more precipitous changes in blood pressure, cardiac index, and stroke volume than did slow hemorrhages. Venous hemorrhages caused a greater and more prolonged drop in blood pressure than did arterial hemorrhages. The significance of these findings is discussed.

The Valsalva maneuver is a challenge to the circulation which has pronounced cardiovascular effects. These effects are more noticeable in the presence of hypovolemia. Breath holding is a more gentle hemodynamic stress.

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