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# Hemodynamic effects of pneumonia: *II. Expansion of plasma volume*

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# Hemodynamic Effects of Pneumonia

## II. EXPANSION OF PLASMA VOLUME

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ABSTRACT Previous work has demonstrated that approximately one-third of patients with pneumonia have a hypodynamic circulatory response. This response is characterized by an abnormally wide arteriovenous oxygen difference, a low cardiac output, increased peripheral resistance, and an increased hematocrit. This state was found to abate in convalescence. In an attempt to elucidate the pathogenesis of this hypodynamic state, nine additional patients were studied hemodynamically during the acute phase of pneumonia before and during acute expansion of blood volume by low molecular weight dextran (seven patients) or normal saline (two patients). Five patients were restudied before and during acute blood volume expansion in convalescence.

Three patients with pneumonia had a normal arteriovenous oxygen difference ($< 5.5$ vol %), and six patients were hypodynamic in that their arteriovenous oxygen differences were greater than 5.5 vol %. With expansion of blood volume in the acute phase of pneumonia, all patients showed an increase in cardiac output, a decrease in arteriovenous oxygen difference, and a decrease in peripheral vascular resistance; however, the percentage change in the hypodynamic patients was not as great as occurred in the patients with normal hemodynamics nor as great as occurred when restudied in convalescence. Likewise, all patients had a normal or near normal hemodynamic profile in convalescence. In addition, ventricular function in the acute phase of pneumonia was depressed. The findings suggest that the hypodynamic state associated with acute pneumonia is due to depressed myocardial contractility to which relative hypovolemia may contribute.

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## INTRODUCTION

A hypodynamic circulatory response to lobar pneumonia was first described from this laboratory in 1964 (1). Subsequent studies (2–4) demonstrated that approximately one-third of patients without other cardiovascular or pulmonary disease have a hypodynamic response to pneumonia rather than the predicted hyperdynamic response (5). This was manifested by an abnormally wide calculated arteriovenous oxygen difference (A-V $O_2$ difference) which returned to normal in convalescence. Central venous pressure was normal. Although no significant deficit in blood volume could be demonstrated, increased hematocrit was often associated with this hypodynamic state and suggested that alterations or shifts in blood volume might play an etiologic role. If such a mechanism predominated, expansion of plasma volume should convert the hypodynamic into a normal or hyperdynamic response. However, if this were not the case, depression of myocardial function would have to be invoked to explain the observations.

The present study was planned to elucidate the pathogenesis of the hypodynamic circulatory response to pneumonia. Nine additional patients with pneumonia were studied in the acute phase, before and after expansion of plasma volume. The response was reassessed during convalescence in five patients.

## METHODS

Nine patients in the acute stage of pneumonia were studied within 24 hr of admission to the hospital, none later than the 3rd day of illness. Patients 70 yr or older as well as patients with cardiovascular, renal, hepatic, or chronic pulmonary disease were excluded.

Patients were selected on the basis of informed consent by the patient and his physician.

TABLE I

*Hemodynamic Data, Acute Pneumonia, and*

| Case No. | Age | Sex | Rectal temperature at initial study | Status | Amount infused* | Rate of infusion | Body surface area | Heart rate | Central venous pressure | Brachial artery pressure mean | $O_2$ consumption |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | *yr* | | *°F* | | *ml* | *ml/min* | *m²* | *beats/min* | *mm Hg* | *mm Hg* | *ml/min* |
| 1 | 45 | F | 100.8 | Acute | | | | | | | |
| | | | | pre-infusion | | 18.5 | 1.67 | 102 | 8 | 82 | 207 |
| | | | | infusion | 1000* | | | 99 | 6 | 75 | 197 |
| | | | | infusion | 1500* | | | 96 | 6 | 75 | 197 |
| 2 | 40 | M | 101.3 | Acute | | | | | | | |
| | | | | pre-infusion | | 14.4 | 1.74 | 90 | 4 | 93 | 322 |
| | | | | infusion | 450 | | | 88 | 8 | 98 | 348 |
| | | | | infusion | 650 | | | 90 | 10 | 98 | 351 |
| | | | | Convalescent | | | | | | | |
| | | | | pre-infusion | | 14.1 | 1.74 | 78 | 4 | 102 | 320 |
| | | | | infusion | 460 | | | 84 | 9 | 96 | 313 |
| | | | | infusion | 650 | | | 84 | 10 | 98 | 315 |
| 3 | 58 | F | 103.2 | Acute | | | | | | | |
| | | | | pre-infusion | | 55.5 | 1.50 | 111 | 1 | 74 | 257 |
| | | | | infusion | 1000* | | | 117 | 6 | 80 | 257 |
| | | | | Convalescent | | | | | | | |
| | | | | pre-infusion | | 31.3 | 1.45 | 111 | 0 | 76 | 190 |
| | | | | infusion | 1000* | | | 124 | 5 | 82 | 193 |
| 4 | 60 | F | 102.0 | Acute | | | | | | | |
| | | | | pre-infusion | | 7.9 | 1.86 | 95 | 3 | 94 | 293 |
| | | | | infusion | 350 | | | 95 | 10 | 106 | 270 |
| | | | | infusion | 500 | | | 100 | 10 | 106 | 296 |
| | | | | Convalescent | | | | | | | |
| | | | | pre-infusion | | 10.2 | 1.82 | 90 | 6 | 110 | 234 |
| | | | | infusion | 350 | | | 90 | 9 | 126 | 174 |
| | | | | infusion | 500 | | | 93 | 12 | 128 | 243 |
| 5 | 50 | F | 101.0 | Acute | | | | | | | |
| | | | | pre-infusion | | 13.5 | 1.71 | 93 | 3.5 | 92 | 324 |
| | | | | infusion | 230 | | | 100 | 10.5 | 94 | 338 |
| 6 | 64 | M | 100.0 | Acute | | | | | | | |
| | | | | pre-infusion | | 20 | 1.46 | 96 | 1.5 | 95 | 276 |
| | | | | infusion | 700 | | | 96 | 7.5 | 95 | 288 |
| | | | | Convalescent | | | | | | | |
| | | | | pre-infusion | | 9.4 | 1.54 | 84 | 4 | 114 | 172 |
| | | | | infusion | 740 | | | 102 | 10 | 128 | 255 |
| 7 | 48 | M | 101.3 | Acute | | | | | | | |
| | | | | pre-infusion | | 11.2 | 1.58 | 108 | 4 | 82 | 300 |
| | | | | infusion | 370 | | | 105 | 10 | 88 | 299 |
| | | | | Convalescent | | | | | | | |
| | | | | pre-infusion | | 14.3 | 1.57 | 93 | 1 | 84 | 263 |
| | | | | infusion | 500 | | | 90 | 5 | 90 | 232 |
| 8 | 40 | M | 100.2 | Acute | | | | | | | |
| | | | | pre-infusion | | 10.8 | 2.04 | 84 | 4 | 122 | 439 |
| | | | | infusion | 530 | | | 80 | 7 | 120 | 458 |
| 9 | 32 | M | 99.3 | Acute | | | | | | | |
| | | | | pre-infusion | | 14.8 | 1.77 | 51 | 5 | 118 | 308 |
| | | | | infusion | 400 | | | 60 | 8 | 114 | 277 |
| | | | | infusion | 650 | | | 56 | 10 | 107 | 277 |

* Normal saline in cases 1 and 3; dextran in all other cases.

‡ Van Slyke.

§ Calculated from pH and $Pa_{O_2}$.

*Convalescence, Before and During Infusion*

| Cardiac output | A–V $O_2$ difference | Stroke volume | Peripheral vascular resistance | HCT | Plasma volume | Total blood volume | Central blood volume | $O_2$ saturation | $Pao_2$ | $Paco_2$ | pH |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *liters/min* | *vol %* | *ml/beat* | *dyne-sec-cm$^{-5}$* | *%* | *liters* | *liters* | *liters* | *%* | *mm Hg* | *mm Hg* | |
| 5.52 | 3.75 | 54.0 | 1072 | 41.2 | 3.04 | 5.02 | 1.30 | 92.0‡ | — | — | — |
| 6.08 | 3.24 | 61.0 | 908 | 37.0 | — | — | 1.30 | — | — | — | — |
| 6.65 | 2.96 | 69.0 | 830 | 34.6 | 3.38 | 5.07 | 1.39 | — | — | — | — |
| 6.20 | 5.20 | 68.8 | 1148 | 37.0 | — | — | 1.17 | 96.3§ | 82 | 31 | 7.50 |
| 7.23 | 4.81 | 82.1 | 996 | 31.4 | — | — | 1.32 | — | — | — | — |
| 8.20 | 4.28 | 91.1 | 878 | 29.6 | — | — | 1.33 | 96.2§ | 82 | 34 | 7.48 |
| 5.64 | 5.67 | 72.3 | 1390 | 37.7 | 2.29 | 3.61 | 1.07 | 94.0§ | 77 | 36 | 7.42 |
| 7.79 | 4.02 | 92.7 | 893 | — | — | — | 1.36 | — | — | — | — |
| 7.54 | 4.17 | 89.8 | 934 | 30.9 | 3.65 | 5.19 | 1.14 | 94.3§ | 77 | 40 | 7.39 |
| 4.88 | 5.26 | 44.0 | 1197 | 38.2 | 2.59 | 4.09 | 0.75 | 94.3§ | 78 | 19 | 7.38 |
| 6.15 | 4.18 | 52.6 | 963 | 37.1 | 2.36 | 3.66 | 0.97 | 93.7§ | 77 | 20 | 7.35 |
| 3.74 | 5.08 | 35.3 | 1626 | 30.8 | 2.08 | 2.95 | 0.65 | 94.4§ | 72 | 36 | 7.47 |
| 4.91 | 3.93 | 49.6 | 1254 | 26.4 | 2.35 | 3.15 | 0.77 | 93.3§ | 68 | 39 | 7.44 |
| 5.22 | 5.61 | 55.0 | 1395 | 34.1 | 2.40 | 3.57 | 0.75 | 91.4§ | 73 | 28 | 7.51 |
| 5.44 | 4.96 | 57.0 | 1412 | 28.7 | — | — | 0.85 | — | — | — | — |
| 6.10 | 4.85 | 61.0 | 1259 | 27.7 | 3.24 | 4.47 | 0.89 | 90.0§ | — | — | — |
| 4.14 | 5.65 | 46.0 | 2010 | 28.1 | 2.57 | 3.53 | 0.79 | 96.4§ | 84 | 35 | 7.49 |
| 5.68 | 3.06 | 63.1 | 1648 | 24.9 | — | — | 1.05 | 96.9§ | 89 | 37 | 7.48 |
| 6.16 | 3.94 | 66.2 | 1506 | 24.0 | 2.82 | 3.62 | 0.81 | — | — | — | — |
| 5.10 | 6.35 | 54.8 | 1379 | 32.8 | 3.05 | 4.45 | 0.84 | 94.3§ | 66 | 31 | 7.54 |
| 5.73 | 5.89 | 57.3 | 1208 | 29.1 | 3.68 | 5.11 | 0.85 | 95.2§ | 72 | 32 | 7.52 |
| 3.91 | 7.05 | 40.7 | 1912 | 36.2 | 2.67 | 4.09 | 0.85 | 96.2§ | 80 | 33 | 7.51 |
| 4.97 | 5.70 | 51.8 | 1409 | 26.2 | 3.79 | 5.07 | 0.84 | 97.2§ | 89 | 32 | 7.50 |
| 4.14 | 4.15 | 49.3 | 2126 | 39.6 | 2.79 | 4.50 | 1.13 | 98.0§ | 106 | 35 | 7.47 |
| 5.50 | 4.63 | 54.0 | 1716 | 33.4 | 3.47 | 5.07 | 1.15 | 97.2§ | 98 | 35 | 7.44 |
| 3.78 | 7.39 | 35.0 | 1530 | 37.2 | 3.20 | 4.98 | 0.84 | 98.0‡ | — | — | — |
| 4.35 | 6.87 | 41.0 | 1434 | 32.8 | 3.64 | 5.28 | 0.98 | 98.2‡ | — | — | — |
| 5.28 | 4.98 | 57.0 | 1258 | 31.2 | 2.84 | 4.06 | 1.17 | 95.8§ | 83 | 37 | 7.45 |
| 6.22 | 3.50 | 69.0 | 932 | 24.8 | 3.62 | 4.75 | 1.02 | — | — | — | — |
| 5.17 | 8.49 | 61.5 | 1826 | 39.1 | 3.90 | 6.43 | 1.32 | 98.0§ | 104 | 32 | 7.49 |
| 6.20 | 7.38 | 77.4 | 1458 | 33.2 | 4.88 | 7.68 | 1.56 | 98.5§ | 110 | 25 | 7.58 |
| 3.66 | 8.41 | 71.7 | 2470 | 41.8 | 2.86 | 4.78 | 1.17 | 94.7‡ | 104 | 28 | 7.50 |
| 4.05 | 6.83 | 67.0 | 2096 | 37.0 | — | — | 1.29 | — | — | — | — |
| 4.01 | 6.90 | 71.6 | 1935 | 34.7 | 3.93 | 5.90 | 1.41 | 93.0‡ | 113 | 28 | 7.50 |

TABLE II

*Statistical Analysis of Hemodynamic Effects of Expansion of Plasma Volume*

| Parameters | State | n | Control | | Infusion | | Difference | | P |
|---|---|---|---|---|---|---|---|---|---|
| | | | Mean | SD | Mean | SD | Mean | SD | |
| Heart rate, *beats/min* | Acute | 9 | 92.2 | 17.6 | 93.3 | 17.2 | 1.1 | 4.8 | NS |
| | Convalescent | 5 | 91.2 | 12.5 | 98.6 | 15.6 | 7.4 | 8.3 | NS |
| Central venous pressure, *mm Hg* | Acute | 9 | 3.8 | 2.0 | 8.6 | 1.9 | 4.8 | 2.8 | <0.001 |
| | Convalescent | 5 | 3.0 | 2.4 | 8.4 | 3.2 | 5.4 | 0.9 | <0.001 |
| Brachial artery pressure mean, *mm Hg* | Acute | 9 | 94.7 | 16.0 | 95.9 | 14.0 | 1.2 | 17.1 | NS |
| | Convalescent | 5 | 97.2 | 16.5 | 105.2 | 21.6 | 8.0 | 8.5 | NS |
| $O_2$ consumption, *ml/min* | Acute | 9 | 303 | 63 | 317 | 72 | 4 | 18 | NS |
| | Convalescent | 5 | 236 | 59 | 248 | 44 | 12 | 43 | NS |
| Cardiac output, *liters/min* | Acute | 9 | 4.82 | 0.87 | 5.82 | 1.23 | 0.99 | 0.48 | <0.001 |
| | Convalescent | 5 | 4.58 | 0.82 | 6.06 | 0.98 | 1.48 | 0.47 | <0.005 |
| A–V $O_2$ difference, *vol. %* | Acute | 9 | 6.39 | 1.59 | 5.45 | 1.48 | 0.94 | 0.35 | <0.001 |
| | Convalescent | 5 | 5.11 | 0.62 | 4.03 | 0.41 | 1.07 | 0.89 | <0.01 |
| Stroke volume, *ml/beat* | Acute | 9 | 55.9 | 12.4 | 63.6 | 15.2 | 9.7 | 7.1 | <0.005 |
| | Convalescent | 5 | 52.0 | 13.8 | 65.7 | 15.7 | 13.7 | 5.9 | <0.01 |
| Peripheral vascular resistance, *dynes-sec-cm*$^{-5}$ | Acute | 9 | 1548 | 450 | 1264 | 348 | 284 | 153 | <0.001 |
| | Convalescent | 5 | 1682 | 378 | 1268 | 347 | 413 | 69 | <0.001 |
| Hematocrit, % | Acute | 9 | 37.6 | 3.0 | 31.7 | 3.7 | 5.9 | 2.6 | <0.001 |
| | Convalescent | 5 | 33.5 | 4.9 | 27.9 | 4.1 | 5.6 | 1.2 | <0.001 |
| Plasma volume, *liters* | Acute | 8 | 2.96 | 0.46 | 3.61 | 0.71 | 0.65 | 0.46 | <0.01 |
| | Convalescent | 5 | 2.51 | 0.32 | 3.18 | 0.57 | 0.67 | 0.45 | <0.05 |
| Total blood volume, *liters* | Acute | 8 | 4.68 | 0.87 | 5.28 | 1.17 | 0.60 | 0.58 | <0.025 |
| | Convalescent | 5 | 3.73 | 0.58 | 4.36 | 0.92 | 0.63 | 0.59 | NS |
| Central blood volume, *liters* | Acute | 9 | 1.00 | 0.24 | 1.14 | 0.28 | 0.14 | 0.09 | <0.005 |
| | Convalescent | 5 | 0.96 | 0.23 | 0.97 | 0.18 | 0.02 | 0.10 | NS |

The clinical evaluation included full history, physical examination, routine laboratory studies, 12 lead electrocardiogram, chest roentgenograms, and fluoroscopy. Between admission to the hospital and the initial study, therapy initiated by the physician responsible for the patient always included appropriate antibiotics and, in most cases, parenteral fluid therapy. Five patients permitted repetition of the study during convalescence, at least 4 days after the initial study. The convalescent state was defined as absence of fever for more than 72 hr and disappearance of radiologic evidence of pulmonary lesions.

Patients were brought to the cardiac catheterization laboratory without premedication. In all patients a polyethylene catheter (I.D. 1.14 mm) was advanced percutaneously from the antecubital vein to the right side of the heart. The catheter was judged to be intrathoracic by length and by the marked drop in pressure with inspiration. By means of an injection of Cardiografin (85% methylglucamine diacetylamidotriiodobenzoate)[1] at the end of the study, it was demonstrated to be in the right atrium in 10 studies and in the superior vena cava in two. A second identical polyethylene catheter was introduced into the brachial artery percutaneously. Base line measurements included blood gases, heart rate, venous pressure, arterial pressure, cardiac output, and blood volume. After base line measurements, all patients were infused until the central venous pressure increased to above 6 mm Hg. In seven patients Rheomacrodex 10% (low molecular weight dextran, average molecular weight 40,000)[2] in normal saline was infused. The total amounts of 230–700 ml were infused in 17–63 min; the average rate of infusion was 15.3 ml/min (Table II). Two patients (cases 1 and 3) received normal saline, 1500 and 1000 ml, in 30 and 81 min, respectively. During infusion venous and arterial pressures were monitored every 5 min. At the end of infusion hemodynamic measurements were repeated in all patients. Cardiac output was measured at an intermediate stage in six studies.

Hemodynamic methods were similar to those described in a previous report (4). Electrocardiogram, pressures, and cardiac output were recorded on a multichannel oscillograph (Hewlett-Packard Co., Waltham, Mass.).

Pressures were measured by strain gauge manometers (Statham P23D or P23G, Statham Instruments, Inc., Los Angeles, Calif.) with the exception of case 5, in which venous pressure was measured by saline manometer. All pressures were referred to a point 10 cm above the patient's back. The details of the measurements and the derivation of the calculated parameters have been described (4).

[1] Cardiografin was supplied by E. R. Squibb & Sons, New York.

[2] Rheomacrodex 10% in normal saline was supplied by Pharmacia Fine Chemicals Inc., Piscataway, N. J.

Cardiac output was measured by means of the indicator dilution method using Indocyanine green dye, and calibration was carried out by the integrated sample technique (6). Plasma volume was determined by means of intravenous injection of Evans blue dye and by analyzing an arterial blood sample drawn 10 min later. Arterial $Pa_{O_2}$, $Pa_{CO_2}$, and pH were measured as described previously (4). Oxygen saturation was measured by the method of Van Slyke and Neill in four patients; in others it was calculated from $Pa_{O_2}$ and pH using the nomogram of Severinghaus (7). Arteriovenous $O_2$ difference was calculated as described previously (4). An abnormally wide A-V $O_2$ difference was defined as equal to or greater than 5.50 vol %, based on the data of 202 normal subjects (8) who had a mean A-V $O_2$ difference of 3.84 vol %, SD 0.63 vol %; the range of A-V $O_2$ differences for 99% confidence ($P < 0.01$) based on $t$ test was 2.20–5.48 vol %.

Peripheral vascular resistance (dynes-sec-cm$^{-5}$) was calculated as:

$$\frac{(\text{MAP} - \text{RAP}) \times 60 \times 1.322}{\text{cardiac output (liters/min)}}$$

where MAP = mean arterial pressure and RAP = mean right atrial pressure (in mm Hg).

Statistical significance was calculated by paired and unpaired $t$ test.

## RESULTS

Hemodynamic data are presented in Table I and a summary of statistical analyses is given in Table II.

*Clinical evaluation.* In eight patients a diagnosis of pneumococcal pneumonia was made based upon positive blood culture in three (D. Pneumoniae type 1, 7, and 22 in cases 3, 4, and 8 respectively) and sputum smear or culture in the remaining six patients. One patient (case 7) had Klebsiella pneumonia (K. pneumoniae type 1) as proven by sputum culture. All patients had a definite pneumonic infiltration of at least one lobe and none had cardiomegaly by roentgenogram.

The pneumonic infiltrate involved the right middle lobe in three patients (cases 1, 2, and 3), the right lower lobe in three patients (cases 7, 8, and 9), the left lower lobe in two patients (cases 5 and 6), and both right and left lower lobes in one patient (case 4). All patients had an uncomplicated course and survived. Two patients were chronic alcoholics (cases 2 and 7) as defined by Jellinek (9). At the time of study there was no clinical evidence of dehydration. All patients were in normal sinus rhythm and none had cardiomegaly or gallop rhythm. The electrocardiogram was normal except in patient 5 in whom the T waves were inverted in all leads but reverted back to normal in convalescence.

*Initial hemodynamic state.* The initial hemodynamic state reflected the spectrum reported previously (4). Cases 1, 2, and 3 were characterized by normal arteriovenous oxygen differences, cardiac output, and pressures. In the remaining patients, the A-V $O_2$ difference was increased and cardiac output, central blood volume, and left ventricular stroke work tended to be low. Notwithstanding a general tendency to respiratory alkalosis, arterial oxygen tension and saturation were slightly decreased.

*Response to plasma volume expansion in the acute phase.* In response to expansion of plasma volume, central venous pressure increased in all studies except one (case 1) who was one of the two patients given 1500 ml of saline. For the group, central venous pressure increased from an average of 3.7 to 8.5 mm Hg. Heart rate and mean brachial arterial pressure did not change.

Cardiac output increased in all patients; the mean increase was 20.6%. This was accounted for predominantly by an increase in stroke volume. The oxygen consumption remained unchanged so that the calculated A-V $O_2$ difference decreased in all patients on the average by 19.8%. There was an average decrease in peripheral vascular resistance of 18.3%.

Central blood volume increased in all patients except one (case 6). At the end of plasma volume expansion, as predicted, significant increases in plasma volume and decreases in the hematocrit were evident. Total blood volume increased by 12.9%.

*Convalescent hemodynamic state.* The convalescent hemodynamic profile was within normal limits except in cases 2 and 4 who had a slightly elevated A-V $O_2$ difference. Some patients still showed evidence of slight hyperventilation. The small size of the group precludes statistical comparison with the observations made during pneumonia. However, oxygen consumption decreased in four of five patients and A-V $O_2$ difference narrowed in patients with wide differences. Cardiac output decreased in both patients who had a hyperdynamic circulatory response and increased in two of the three patients with hypodynamic response (Table I).

The response to plasma volume expansion was again characterized by a significant increase in venous pressure and blood volume. In convalescence there was a greater increase in cardiac output and a greater fall in A-V $O_2$ difference during infusion, 33 ±5 (SEM) and 24 ±3%, respectively, when compared to 17 ±2 (SEM) and 13 ±2% in six patients with hypodynamic states during pneumonia ($P < 0.02$).

*Ventricular function.* Ventricular output curves were constructed by plotting right atrial pressure against cardiac output to assesss the ventricular function in pneumonia and convalescence (Fig. 1). This method of ventricular function evaluation has been validated by Bishop and colleagues (10, 11). Since the heart rate and aortic pressure did not change during plasma volume expansion, alterations in cardiac output reflect the functional status of the myocardium. Ventricular output curves were constructed from the pooled data for six patients with hypodynamic response (cases 4–9) and three patients with normal or hyperdynamic response

(cases 1–3). Ventricular output curves obtained from five patients studied during convalescence (cases 2–4, 6, and 7) served as control. The ventricular function in patients with a hypodynamic response is depressed, whereas in patients with a normal or hyperdynamic response it is normal or above normal (Fig. 1).

## DISCUSSION

In previous studies in this laboratory approximately one-third of patients with pneumonia had a hypodynamic circulatory response as manifested by an abnormally wide A-V $O_2$ difference, a relatively low cardiac output, and an abnormally high total peripheral resistance (1–4). These patients had an increased hematocrit. The present study was designed to test the relative contribution of (*a*) depressed myocardium, and (*b*) dehydration from decreased fluid intake and/or increased insensible loss or other significant fluid shifts decreasing the effective blood volume resulting in diminished venous return and decreased cardiac output. These hypotheses were tested by volume expansion during pneumonia and convalescence.

After using saline infusions safely in two patients, low molecular weight dextran, a more potent expander of plasma volume (12, 13), was used in the remainder of the series. It was found that, except for one patient given saline, the central venous pressure could be raised in all patients with reasonable volumes of infusate without discomfort and without the devlopment of abnormally high central venous pressures.

Patients in the convalescent phase of pneumonia had essentially the same hemodynamic response to blood volume expansion as normal subjects. However, in the acute phase of pneumonia, six of the nine patients showed a definite hypodynamic state in their base line measurements associated with depressed ventricular function (Fig. 1). This was partially reversed by plasma volume expansion. However, the percentage increase in cardiac output and the percentage decrease in A-V $O_2$ difference were not as great as occurred in convalescence, nor was a normal hemodynamic state reached (Table I). In contrast, these patients had a normal hemodynamic state in convalescence, except for a slightly abnormal A-V $O_2$ difference in case 4. Thus the hypodynamic state observed in pneumonia can largely be accounted for by depressed myocardial function. It is noteworthy that this depression of ventricular function was not seen in cases with normal arteriovenous oxygen difference; in fact, ventricular function was above normal in these patients.

What might be responsible for depressed ventricular function in some patients with acute pneumonia? An inflammatory myocarditis is a possibility. Infiltration of the myocardium by inflammatory cells and degeneration of myocardial fibers have been demonstrated in 39% of cases examined in a retrospective study (14). Also, electrocardiographic T-wave changes have been described

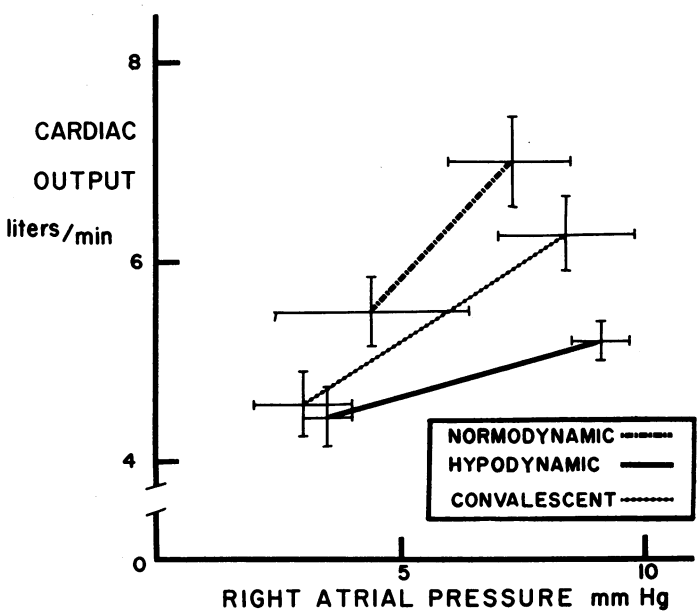


FIGURE 1 Ventricular output curves during plasma volume expansion (mean ±SEM) in three patients with normal or hyperdynamic response, and in six patients with hypodynamic response, compared to five patients during convalescence.

during acute pneumococcal pneumonia (15). A direct toxic effect of some substance released into the circulation by the bacteria or infected lung tissue is a possibility which has not been investigated. Among undetected heart diseases that one must consider is primary myocardial disease of the alcoholic. Two of the patients were chronic alcoholics. One was in the group with and the other in the group without the hypodynamic state. Furthermore, none of these had cardiomegaly nor abnormal electrocardiograms even during acute pneumonia, and none had a past history of cardiac symptoms. However, no attempt was made to pressure-load these subjects (16). Modest arterial hypoxemia was seen in most patients studied but did not differ in degree in patients with and without the hypodynamic state. Most patients were slightly alkalotic secondary to mild hyperventilation and tended to be more alkalotic in the acute phase of pneumonia. However, alkalosis has not been shown to depress ventricular function (17).

Is the hypodynamic circulatory state clinically adaptive and desirable or should it be considered pathological and undesirable? A relatively inadequate cardiac output with increased A-V $O_2$ difference lowers venous $P_{O_2}$ and hence produces tissue anoxia, a potential threat to tissues and organs such as brain, heart, and kidneys. On the other hand, increased cardiac output, even if metabolically justified, increases cardiac work, whereas decreased cardiac output may spare the myocardium, at least as long as coronary blood flow remains adequate. In the absence of evidence that the heart is overloaded, the maintenance of adequate tissue oxygenation must be considered the primary aim of physiological regulation. Regional blood flow should be appropriate to metabolic needs. While ultimate therapeutic suggestions should await elucidation of the etiology of myocardial depression in pneumonia, on the basis of the present study it may be recommended that plasma volume be expanded to a normal, or upper limits of normal, central venous pressure in order to permit as adequate a circulatory response to the acute illness as possible.

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