Changes in leg vein filling and emptying characteristics and leg volumes during long-term head-down bed rest

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Lousy, Francis, Philippe Schroiff, and Antonio Güell. Changes in leg vein filling and emptying characteristics and leg volumes during long-term head-down bed rest. J. Appl. Physiol. 82(6):1726–1733, 1997.—Leg venous hemodynamics [venous distensibility index (VDI), arterial flow index (AFI), half-emptying time (T1/2)], and leg volumes (LV) were assessed by mercury strain-gauge plethysmography with venous occlusion and volometry, respectively, in seven men before, during, and after 42 days of 6° head-down bed rest. Results showed a high increase in VDI up to day 26 of bed rest (50% vs. control at day 26, P < 0.05), which tended to subside thereafter (+20% increase vs. control value at day 41, P < 0.05). VDI changes were associated with parallel changes in T1/2 (+54% vs. control at day 26 of bed rest, P < 0.05, and +25% vs. control at day 41, P < 0.05) and with a decrease in AFI (−49% at day 41 vs. control, P < 0.05). LV continuously decreased throughout bed rest (−13% vs. control at day 41, P < 0.05) and was correlated with VDI only during the first month of bed rest. These results show that during long-term 6° head-down bed rest alterations of leg venous compliance are associated with impairment of venous emptying capacities and arterial flow. Changes in skeletal muscle mass and fluid shifts may account for venous changes during the first month of bed rest but, subsequently, other physiological factors, to be determined, may also be involved in leg venous hemodynamic alterations.

weightlessness; leg venous compliance; skeletal muscle mass

IT HAS BEEN SHOWN, during both spaceflights and ground simulation studies, that leg venous hemodynamics were greatly modified under the effects of prolonged microgravity (2, 3, 5, 9, 10, 18). These changes are part of the cardiovascular deconditioning syndrome and are probably one of the main causes of the orthostatic intolerance exhibited by a great number of astronauts when they return to Earth (13).

In practically all these studies, venous hemodynamics have been assessed in terms of venous compliance. However, venous compliance is not sufficient by itself to characterize venous hemodynamics. In our opinion, venous hemodynamics has to be defined by two types of parameters: filling (venous distensibility and compliance, arterial flow) and emptying parameters (emptying time). These physiological variables determine what is called the venous return to the heart, expressed as a flow and representing the sum of the venous return flows from various areas of the body (subcutaneous tissues, muscles, splanchnic areas, etc.). Leg hemodynamics plays a significant role in the determination of the venous return (15, 16) and is greatly involved in processes regulating cardiac performance and arterial pressure. Therefore, changes in venous filling as well as changes in venous emptying parameters should be taken into consideration to describe with more accuracy venous hemodynamics in lower limbs.

Ground simulation models, at least those designed for the study of changes in leg venous hemodynamics, have usually been utilized for periods of observation not exceeding 1 mo. In some of these studies, the increase in venous compliance or distensibility tended to lessen between the third and the fifth week of bed rest (9, 10, 18). The question is then whether a new state of equilibrium may be established in the venous system during the second month of simulated microgravity exposure and what the nature of this new state of equilibrium may be. In addition, correlations have been established between leg venous compliance changes and leg volume (LV) changes (representing skeletal muscle mass) (5, 9), suggesting that leg venous compliance depended in part on LV. However, these correlations have been tested from measurements made either at the end or just after bed rest. The problem is to determine whether these correlations existed throughout the entire bed rest and to investigate the significance of these correlations.

In the present experiment, long-term weightlessness exposure was simulated by 42 days of 6° head-down bed rest to assess leg venous hemodynamic changes, using 1) mercury strain-gauge plethysmography for measurement of filling (venous distensibility and compliance, arterial flow) and emptying parameters (emptying time), and 2) optoelectronic sensor plethysmography (volometry) for measurement of LV changes.

METHODS

This study was part of a joint project between the Centre National d’Etudes Spatiales, France, and European Spatial Agency and was designed to develop countermeasures for future space missions on board the International Space Station Alpha. It was performed at the Institut de Médecine Aéronautique (MEDES; Toulouse, France).

Subjects. Seven healthy young male subjects gave their written consent to participate in this 42-day 6° head-down tilt bed-rest exposure in the medical facility of the MEDES. Before giving their written informed consent, all subjects were explained the procedures and potential hazards. The experiment was submitted to and approved by the Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale Midi-Pyrénées I (France). Subjects were submitted to a medical investigation including medical history and physical examination before entry into the study to make sure there was not history of cardiovascular, especially venous, pathology. Biometric characteristics of the subjects were as follows: age 27.9 ± 2.6 yr, height 176.3 ± 1.3 cm, and body weight 74 ± 3.3 kg.
Bed-rest protocol. The protocol consisted of a 15-day ambulatory control period (BDC) followed by 42 days of bed rest in the 6h head-down tilt (HDT) and 13 days of recovery after bed rest (R). During bed rest, the subjects remained in the head-down position continuously for all activities, with the head-down position being monitored around the clock by a video system. Subjects ingested no caffeine or alcohol and were not allowed to smoke throughout bed rest. The average daily caloric intake was 2,500–2,700 kcal. The average dietary sodium and potassium intakes were approximately 2,700 and 3,500 mg/day, respectively. Fluid intake was ad libitum. The bedrooms were air conditioned, and the temperature was kept below 28°C at all times.

Techniques. Venous hemodynamics was assessed by mercury strain-gauge plethysmography with venous occlusion. This technique was first used by Whitney in 1953 (20). The principle of this technique, developed to describe changes in LV, is the measurement of changes in circumference of the leg by use of a mercury strain gauge in the form of a Silastic tube filled with mercury. This tube has a small diameter (ID = 0.5 mm), and its wall thickness is ~0.8 mm. Each end of the tube is connected to a copper fitting making an electrical contact with the mercury column. The stretching of the gauge changes the electrical resistance of the mercury column, and a Wheatstone bridge is used to record this change in gauge resistance. The gauge is a dual-thread gauge placed around the limb in which changes in volume are to be measured. It is connected to a Wheatstone bridge equipped with a thermal compensation device to take into consideration temperature fluctuations during the measurement. With this device, Whitney showed that a proportional relation existed between leg circumference according to the following formula

\[
\Delta A/A = \Delta V/V = 2\Delta L/L_0
\]

where \(L_0\) is optimal length and \(\Delta\) is change. When venous occlusion is applied to the thigh by use of an air cuff inflated to a pressure lower than diastolic arterial pressure, the recording shows a typical curve that provides several types of information (Fig. 1). The first part of the curve is an ascending slope followed by a plateau, the height of which depends on the applied counterpressure. The rapid increase in LV at the beginning is caused by arterial flow (arterial flow index (AFI)). Once the plateau has been reached, pressure in the plethysmograph is suddenly released, restoring venous outflow. The limb gradually recovers its initial volume, first rapidly, then more slowly. Venous capacity (\(\Delta V_{max}\)) represents the emptying volume. It is a venous capacity as it corresponds to the maximum quantity of blood that can be contained in the venous network at the considered counterpressure. Venous emptying is quantified by the half-emptying time (\(T_{1/2}\)), which is the time necessary for one-half venous emptying. This parameter reflects venous elasticity and resistance to venous flow. When several counterpressures (10, 20, 30, 40, 50, and 60 mmHg) are applied to the cuff, corresponding values of \(\Delta V_{max}\) are obtained. A pressure-volume curve can then be drawn, the slope of which indicates the compliance of the venous network. To assess the value of this slope, we calculated the venous distensibility index (VDI) as follows

\[
\frac{\Delta V_{max}}{50 - \Delta V_{max}} \times 10^{-2}
\]

VDI is expressed in ml·100 ml⁻¹·mmHg⁻¹, and the inverse value is the venous tone index.

LV was measured by optoelectronic plethysmography or volumetry. The plethysmograph with optoelectronic sensors or volumeter (Bösl, Medizintechnik, Aachen, Germany) is an optoelectronic measurement system for determining the volume of an extremity from the measurements of its diameters (horizontal and vertical diameters). It is composed of clamps for limb fixation, proximal and distal with respect to the measured limb segment, a sliding frame equipped with light transmitters and receivers, and a microprocessor. After pressing the measuring head, the frame is moved from a preestablished initial position to the area to be measured, in ~2 s. During this time, one vertical and one horizontal diameter are measured at 225 successive points and stored into a microcomputer. A sensor incorporated in the frame determines the traveled distance and subsequently the location at which each measurement is made. The computer terminates the measuring operation after a distance of 36 or 40 cm or any other selected distance of travel. The device operates under the assumption that the extremity cross section is elliptical. The limb is divided into 225 single layers by the computer. After the extremity has been positioned into the frame, the volometer measures 225 individual diameters within ~2 s along the predetermined measuring distance. The principle of limb volume measurement by optoelectronic plethysmography is illustrated in Fig. 2 showing a diagram of the frame equipped with the optoelectronic sensors, with the cross section of a limb in its center. To the right of the limb and below the limb, the frame includes 120 phototransistors placed in staggered rows ("receivers") spaced every 2.5 mm along the line. Opposite each one of these rows of receivers is a corresponding row of infrared-emitting semiconductor diodes ("transmitters"). All light transmitters and receivers can be individually controlled by the microprocessor in accordance with its program to obtain 120 vertical and 120 horizontal light barriers. Limb diameters are measured by automatically switching on vertical and horizontal barriers successively in their respective rows. The number of light barriers interrupted by the limb is the measure of the limb diameter. For each point of the limb, the computer measures two perpendicular diameters, a horizontal and a vertical diameter, stores them, and records their distance from the reference (initial) point on the limb within ~0.01 s. Knowing the successive cross-section areas over a given distance, calculated from the two measured diameters, the computer determines the entire volume of the measured stretch.

\[
\begin{align*}
\text{Venous capacity (ml/100ml)}
\end{align*}
\]
Measurement protocol. Plethysmographic and volumetric measurements were always made simultaneously. For each subject, measurements were made before bed rest (BDC); on days 1, 4, 7, 14, 21, 26, 34, and 41 of bed rest (HDT1, HDT4, HDT7, HDT14, HDT21, HDT26, HDT34, and HDT41, respectively); and on days 1, 3, 7, 11, and 30 of recovery from bed rest (R + 1, R + 3, R + 7, R + 11, and R + 30, respectively). Before each measurement, subjects remained supine for ~20 min to achieve total muscle relaxation. After this period of rest, the volume of the right leg was measured by using the volometer. The leg was elevated 20 cm above the bed to ensure venous emptying. By principle, to be reproducible, the volumetric measurement requires that the position of the leg with respect to the sliding frame be strictly identical from one measurement to the next. Centimetric marks were made on the frame to position the leg with great accuracy (in height, laterally, and longitudinally with respect to the center of the frame). Three positioning measurements were thus available for each subject, and the leg was placed exactly in the same position for all measurements. This volumetric measurement was followed by the strain-gauge plethysmographic measurement. The position of the leg was identical to the position used for volumetric measurements, with the leg elevated 20 cm above the bed. The volume of the leg was allowed to rise to its peak value for each counterpressure applied to the thigh. Then the counterpressure was suddenly released to obtain the same emptying curve as the initial curve. The different counterpressures (10, 20, 30, 40, 50, and 60 mmHg) were applied in random order.

All plethysmographic and volumetric measurements were made under the same experimental conditions. Room temperature was maintained between 22 and 28°C. In each measurement session, measurements were scheduled at the same time of day for the same subject, at least 2 h after the last meal.

Statistical analysis. Results are expressed as means ± SE. All parameters (VDI, T1/2, AFI, and LV) were analyzed with an analysis of variance for repeated measures. If a significant difference appeared in the overall test, values were then compared by pairs using Fisher's test, with the reference being the control value. To examine the relationship between changes in LV and changes in leg venous compliance, correlations were generated between the relative (percent) changes in VDI and percent changes in LV calculated during three different periods of the experiment: total period of bed rest (BDC to HDT41), first period of bed rest (BDC to HDT28), and the recovery period (R + 3 to R + 30). For all statistical tests, the level of significance was set at P < 0.05.

RESULTS

Changes in leg venous hemodynamics (VDI, T1/2, and AFI) and in LV during and after bed rest are shown in Table 1 (expressed in absolute values) and in Fig. 3 (expressed in %changes compared with BDC).

<table>
<thead>
<tr>
<th>Days of Bed Rest</th>
<th>VDI, 10−2 ml·100 ml−1·mmHg−1</th>
<th>T1/2, s</th>
<th>AFI, ml/100 ml</th>
<th>Leg Volumes, ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDC</td>
<td>4.5 ± 0.3</td>
<td>3.8</td>
<td>2.1 ± 0.2</td>
<td>2.714 ± 103</td>
</tr>
<tr>
<td>HDT1</td>
<td>5.5 ± 0.6*</td>
<td>5.1</td>
<td>1.5 ± 0.2*</td>
<td>2.612 ± 92*</td>
</tr>
<tr>
<td>HDT4</td>
<td>6.3 ± 0.6*</td>
<td>5.9</td>
<td>1.5 ± 0.1*</td>
<td>2.578 ± 64*</td>
</tr>
<tr>
<td>HDT7</td>
<td>6.7 ± 0.5*</td>
<td>5.8</td>
<td>1.6 ± 0.1*</td>
<td>2.538 ± 99*</td>
</tr>
<tr>
<td>HDT14</td>
<td>6.5 ± 0.6*</td>
<td>5.8</td>
<td>1.7 ± 0.1*</td>
<td>2.497 ± 85*</td>
</tr>
<tr>
<td>HDT21</td>
<td>6.5 ± 0.5*</td>
<td>5.7</td>
<td>1.4 ± 0.1*</td>
<td>2.447 ± 78*</td>
</tr>
<tr>
<td>HDT26</td>
<td>6.8 ± 0.5*</td>
<td>5.9</td>
<td>1.8 ± 0.1*</td>
<td>2.437 ± 76*</td>
</tr>
<tr>
<td>HDT34</td>
<td>5.9 ± 0.5*</td>
<td>5.1</td>
<td>1.3 ± 0.1*</td>
<td>2.419 ± 92*</td>
</tr>
<tr>
<td>HDT41</td>
<td>5.4 ± 0.4*</td>
<td>4.8</td>
<td>1.1 ± 0.1*</td>
<td>2.353 ± 88*</td>
</tr>
<tr>
<td>R + 1</td>
<td>4.4 ± 0.8</td>
<td>3.7</td>
<td>1.2 ± 0.2*</td>
<td>2.467 ± 89*</td>
</tr>
<tr>
<td>R + 3</td>
<td>4.9 ± 0.6</td>
<td>3.2</td>
<td>2.4 ± 0.1</td>
<td>2.562 ± 92*</td>
</tr>
<tr>
<td>R + 7</td>
<td>4.9 ± 0.6</td>
<td>3.2</td>
<td>2.7 ± 0.3*</td>
<td>2.587 ± 100*</td>
</tr>
<tr>
<td>R + 11</td>
<td>4.4 ± 0.6</td>
<td>3.2</td>
<td>2.8 ± 0.2*</td>
<td>2.607 ± 83*</td>
</tr>
<tr>
<td>R + 30</td>
<td>4.9 ± 0.6</td>
<td>3.4</td>
<td>2.2 ± 0.1</td>
<td>2.713 ± 96</td>
</tr>
</tbody>
</table>

Values are means ± SE. VDI, venous distensibility index; T1/2, half-emptying time; AFI, arterial flow index; BDC, bed-rest control period; HDT, head-down-tilt period; R, recovery period; nos. following HDT and R are nos. of days. *Significant differences from BDC (P < 0.05).
VDI tended to increase significantly all along bed rest, from the very first day of simulation (5.5 ± 0.6 \(10^{-2}\) ml·100 ml\(^{-1}\)·mmHg\(^{-1}\) at HDT1, +22%, \(P < 0.05\) compared with BDC). At the end of the week, venous compliance reached a maximum (6.7 ± 0.5 \(10^{-2}\) ml·100 ml\(^{-1}\)·mmHg\(^{-1}\), +67%, \(P < 0.05\) compared with BDC) and was maintained at this level until HDT26. From then on, and until the end of bed rest, leg venous compliance tended to decrease while remaining elevated compared with its control value. During recovery, VDI was rapidly restored to its initial level.

Mean T\(_{1/2}\) basically followed the same course as venous compliance, i.e., there was a rapid and significant increase during the first week, with a peak (5.4 ± 0.4 s at HDT4, +54%, \(P < 0.05\) compared with BDC) maintained until HDT26, and then there was a tendency for T\(_{1/2}\) values to decrease until the end of bed rest, followed by a rapid return to normal during recovery.

AFI was significantly depressed from the very first days of bed rest (1.5 ± 0.2 ml·min\(^{-1}\)·100 ml\(^{-1}\), −30%, \(P < 0.05\) compared with BDC) and remained low throughout the entire simulation, with the greatest decrease being observed at the end of bed rest (1.1 ± 0.1 ml·min\(^{-1}\)·100 ml\(^{-1}\), −49%, \(P < 0.05\) compared with BDC). Surprisingly, a significant increase in AFI was measured at the end of the period of recovery (2.4 ± 0.1 ml·min\(^{-1}\)·100 ml\(^{-1}\), i.e., +11%; 2.7 ± 0.3 ml·min\(^{-1}\)·100 ml\(^{-1}\), i.e., +29%; and 2.8 ± 0.2 ml·min\(^{-1}\)·100 ml\(^{-1}\), i.e., +31% at R+1, R+7 and R+11, respectively, \(P < 0.05\) in all instances).

Changes in LV were measured throughout the entire bed-rest period to establish a possible correlation with changes in venous compliance. A rapid and significant decrease in LV was observed from the very first day of bed rest (2,714 ± 267 ml at BDC vs. 2,612 ± 240 ml at HDT41, \(P < 0.05\)), followed by a more moderate but persistent decrease until the end of bed rest (2,353 ± 228 ml at HDT41, −13%, \(P < 0.05\) compared with BDC). After bed rest, LV increased, first rapidly, starting on R+1 (2,467 ± 230 ml, +4% compared with HDT41), then more slowly, and was restored to its initial value at R+30.

Percent changes in VDI were inversely correlated with percent changes in LV when this regression was observed during the first period of bed rest (from BDC to HDT28, \(P = 0.02\), \(r = 0.5\)) (Fig. 4), whereas no correlation existed between these two variables when the regression was examined throughout the entire bed-rest period (\(P = 0.3\)) or during the recovery period (\(P = 0.7\)).

**DISCUSSION**

Changes in leg venous compliance are representative of venous compliance changes occurring in lower limbs.
during exposure to simulated or actual microgravity. The increase in leg venous distensibility evidenced under these conditions may account for the decreased orthostatic tolerance arising in astronauts during reentry, because of the excessive amount of blood pooling in the extremities and the subsequent effect on venous return (5, 13). However, the characteristics of lower limb venous adaptation to microgravity are relatively unknown for several reasons: 1) only few astronauts were submitted to hemodynamic venous assessment during spaceflights, a fact that prevents us from inferring definitive conclusions about physiological adaptation of the venous system under microgravity; 2) until now, limb venous hemodynamics has been described during simulation studies only in terms of venous compliance; however, a complete analysis of venous hemodynamics has to take into account parameters of venous filling (arterial inflow, venous compliance, or distensibility) as well as parameters of venous emptying (T1/2); and 3) most of simulation studies have been generally performed for periods shorter than 1 mo. The aims of the present study were, therefore, to 1) give a complete description and assess the consistency of leg venous changes during weightlessness simulated by 6° head-down tilt for 42 days; and 2) assess, under these conditions, the correlations between venous changes and skeletal muscle changes, which have been evidenced in earlier studies (5, 9) for periods of bed rest shorter than 1 mo.

Leg venous compliance changes and correlations with leg venous volume. Results of this study show that leg venous hemodynamics during exposure to 42 days of simulated weightlessness are characterized by 1) a progressive increase in venous compliance, completed as early as the end of the first week, maximal up to the end of the first month, and tending to subside thereafter; and 2) a lack of parallelism between changes in LV and changes in leg venous compliance after 30 days of simulated microgravity.

The increase in leg venous compliance has been shown to correlate with the decrease in cross-sectional areas (CSA) of leg muscle during simulation studies lasting <30 days (5, 9). Based on this relationship, it was hypothesized that leg venous overdistensibility was caused by the reduction of skeletal muscle masses surrounding deep veins in the muscle, with these muscles no longer playing their role of natural counter-pressure against the distension of venous walls. Results of this study should be an invitation to reconsider physiological factors underlying venous distensibility. First, the novelty of this experiment was that it has been possible to measure continuously and simultaneously the respective course of leg venous compliance and LV throughout the entire bed rest. It was thus possible to assess correlations between these two parameters at different phases of bed rest. In the study of Convertino et al. (5), correlations between relative changes in calf muscle CSA and calf volume on the one hand and calf compliance on the other hand have only been generated with results obtained after bed rest. In the study of Louisy et al. (9), the correlations have been tested between changes in leg venous compliance measured at day 27 of bed rest and changes in triceps surface area measured immediately after bed rest. In the present study, a clear relation was evidenced between changes in leg venous compliance and LV during the first part of bed rest, as was demonstrated by the significant correlation existing between these two parameters up to HDT28. The significance of such a relation is probably not equivocal, and we have to distinguish between short-term and mid-term vs. long-term changes in these two parameters.

In the first 24 h of bed rest, rapid and significant changes in LV paralleled rapid and significant changes in leg venous compliance. These rapid changes in volume cannot be attributed to alterations of muscle mass. The factors that could be accounted for by such changes have been investigated in previous studies. Data obtained during spaceflights (14) as well as during ground studies (19) show that the source of LV changes is a fluid shift from the legs to the upper part of the body, with a relatively rapid shift of blood followed by interstitial and probably intercellular fluid. An additional total volume loss probably completes fluid shifts to contribute to decreases in LV during the first hours of exposure to actual or simulated microgravity. Now it is known that changes in intravascular volumes or interstitial volumes and pressures alter venous hemodynamics by modifying transmural pressure or the zone of free...
distensibility, as was previously stated (8, 16). It is, in fact, well known that veins only require low transmural pressures to maintain their circular contours. If these pressures become too low, veins tend to become elliptical or flat. Under such conditions, significant volume changes can then take place without appreciable pressure changes. Other factors with rapid implementation, especially the role of nerves, may be hypothesized to explain early venous compliance changes: alteration of venous smooth muscle tone or baseline tone of skeletal muscles surrounding the veins and alteration of venosomatic (21) or venoarteriolar reflexes (17). Data available in this experiment do not allow us to isolate the effects of these factors. Hence, we cannot rule out the possibility that bed rest caused physiologically significant alterations in one or more of these determinants of venous compliance. However, the results presented here and those previously reported in the literature permit us to reasonably assume that changes observed in leg venous compliance during the first hours or the very first days of head-down tilt are caused by fluid shifts.

The increase in leg venous compliance has also been described for long-term head-down tilts, at least for periods shorter than 30 days. However, none of the studies attempted to assess correlations between changes in leg venous compliance and LV vs. time during bed rest. Previous studies established correlations between equivalent parameters but only from unique measurement points acquired either at the end of bed rest (5) or immediately post-bed rest (9). The significant correlation existing between relative changes in LV and relative changes in leg venous compliance measured throughout the first month of bed rest strengthens the hypothesis that, at least during this period, the decrease in LV, and in muscle mass, may explain the increase in venous compliance in the lower limbs. At this point of the discussion, we have to question the significance of LV changes noted during bed rest. In fact, LV is composed of several compartments, the size of which partly determines this volume (bone, subcutaneous adipose, muscle, intravascular, and extravascular water). One can intuitively assume that changes in bone compartment, as noted in earlier studies (6), only play a very minor role in overall LV changes. The shift and reduction in body fluids have already been demonstrated to occur during the very first days of weightlessness exposure (3–4 days) and to stabilize thereafter (14). Calf subcutaneous tissue has been shown to be reduced during bed rest (6). However, the small reduction of fat stores observed in the latter study after 1 mo of bed rest (~4%), associated with the fact that fat only represents ~15% of total leg CSA, allow us to attribute to fat store changes only a minor part of the LV changes observed after 42 days of bed rest in our experiment. Therefore, one can reasonably assign to muscle changes the major changes in LV and so to changes in leg skeletal muscle mass.

After the first month of bed rest, the increase in leg venous compliance tended to lessen, and the correlation between changes in LV and changes in leg venous compliance no longer existed. However, this tendency should not be interpreted as a normalization, because venous compliance continued to be higher than control values. Such a phenomenon has already been described during exposure to actual or simulated weightlessness. In Skylab 4 astronauts, Thornton and Wyckliffe Hoeffler (18) related a tendency for leg venous compliance to decrease between the fourth and the fifth week of spaceflight after a primary increase. In bed-rest studies, Louisy et al. (9, 10) also described such a change in leg venous distensibility after 3–4 wk of bed rest. It is as if there was a tendency for the venous system to reestablish equilibrium after a primary disadaptation. The significance of this phenomenon is hard to interpret. The lack of correlation between LV changes and leg venous compliance means that it is not linked to leg muscle mass. However, one cannot rule out the possibility that a relationship with changes in surrounding skeletal muscle tone might exist. These venous changes were not paralleled by similar changes in plasma volume (personal communication), which means that fluid volume status was not involved. As was reported earlier in this study, other physiological parameters may be considered as candidates to account for such evolution of leg venous compliance during exposure to weightlessness. The hypothesis of the involvement of these parameters will have to be tested in experiments on animal models.

Changes in other venous hemodynamic parameters.

For the first time, we showed in this study that the alteration of venous distensibility was associated with equivalent alterations of the venous emptying capacities, i.e., a relative inability for the venous network to expel blood to the heart. This was demonstrated by the fact that changes in \( T_{1/2} \) strictly paralleled those of venous compliance. These results are in contrast with others, which demonstrated that, in some instances (e.g., endurance-trained subjects), increase in venous compliance is not associated with impairment of emptying capacities (11). Therefore, assessment of leg venous compliance always has to be completed by information on venous emptying to give a full description of venous hemodynamic characteristics. In our study, alteration of venous emptying may denote either a degradation of viscoelastic properties of the veins or/and a change in the tone of surrounding skeletal muscles. This may hinder effective recoil of venous wall for complete emptying of blood from venous network. Venous emptying is an important feature of cardiovascular hemodynamics because of its key role in venous return, cardiac filling, and cardiac output regulation. It is suspected that alterations of venous emptying during exposure to weightlessness may account, at least partly, for changes in orthostatic tolerance occurring in astronauts during reentry or the immediate postflight period.

The AFI in the leg was significantly modified during and after bed rest. During bed rest, it was significantly
decreased, but not regularly, as shown by the unstable contours of the mean AFI1 curve and the discrepancies between subjects’ curves. This instability of arterial flow, probably due to vasomotor regulation disorders in lower limbs, has already been described in previous studies (1). After bed rest, the AFI transiently increased in the leg area. This response should be correlated with an overall increase in vascular flows in lower limb muscle areas, characterized by relative hyperactivity compared with bed rest and by the restoration of muscle masses by a hypertrophic process.

Use of optoelectronic sensor plethysmography for measuring LV changes. In the present study, we assessed LV changes by using optoelectronic sensor plethysmography. For the first time, we achieved this kind of measurement with a device easy to implement in comparison to other more complex and expensive systems (X-ray scanography, nuclear magnetic resonance). We were able to measure LV changes appearing at different stages of bed rest, and we showed earlier in this text that these changes had several meanings. In addition to the interpretation given to LV changes at the beginning of and throughout bed rest, we evidenced a rapid increase in LV during the first 24 h after bed rest (+4%), which corresponded to fluid shifts toward the lower part of the body. This phase was followed by a slower increase in LV (~0.5% per 24 h) until day 30 of recovery, corresponding to the gradual restoration of muscle mass under the effect of reloading. The accuracy and reproducibility of this method have been stated earlier (7, 12) and are compatible with the range of variations observed in this study. Optoelectronic sensor plethysmography or volometry, therefore, appears to be a very accurate and reliable method to measure limb volume and to study fluid shifts and muscular deconditioning following exposure to real or simulated microgravity.

In conclusion, we demonstrated in this study a significant increase in leg venous compliance, which was completed and maximal during the first month of ~6° head-down tilt and tended to subside afterward. Several physiological factors can account for venous changes, depending on which phase of bed rest they occur (alteration of fluid status, changes in surrounding skeletal muscle mass). After the first month, the course of leg venous compliance changes was not paralleled by changes in these physiological parameters, which means that other parameters were involved and have to be investigated. During the entire bed rest, leg venous changes were accompanied by parallel changes in venous emptying and by an alteration of arterial flow. The use of volometry to measure LV changes allowed us to test the feasibility of a simple, reliable, and reproducible method aimed at assessing vascular and muscular deconditioning during exposure to weightlessness.

The authors are grateful to D. Freund for assistance in correcting the English in this paper. The authors also thank the staff of the Institut de Médecine Aérospatiale for their technical and administrative assistance.

This work was supported by grants from the Centre National d’Études Spatiales and by the European Space Agency.

Received 20 November 1996; accepted in final form 3 January 1997.

REFERENCES


