Pulsed Doppler: Diameter, Blood Flow Velocity and Volumic Flow of the Brachial Artery in Sustained Essential Hypertension

M. E. Safar, M.D., P. A. Peronneau, M.D., J. A. Levenson, M.D., J. A. Toto-Moukouo, M.D., and A. Ch. Simon, M.D.

SUMMARY Diameter, blood flow velocity and volumic flow of the brachial artery were measured in 36 patients with sustained essential hypertension and compared with 25 normal subjects. Both hypertensives and control subjects were classified according to age into those younger than and those older than 40 years. For the determinations, a pulsed Doppler velocimeter with an adjustable range-gated time system and a double transducer probe was used. With the apparatus, the error in the determination of the angle between the ultrasound beam and the flowing stream of blood was less than 2%. In addition, the overestimation of the arterial diameter due to the sample volume size did not exceed 0.035 ± 0.015 cm. In hypertensives, the diameter of the brachial artery was significantly increased. The value was 0.482 ± 0.013 cm in subjects younger than 40 years and 0.517 ± 0.013 cm in those older than 40 years; in the corresponding controls, the values were 0.422 ± 0.011 cm and 0.436 ± 0.013 cm (p < 0.01; p < 0.001). Blood flow velocity was reduced (p < 0.05; p < 0.01) and volumic flow remained within normal ranges. Both in the younger and the older groups, a significant positive correlation was observed between mean arterial pressure and the arterial diameter (r = 0.75; r = 0.60). In hypertensives, i.v. dihydralazine decreased mean arterial pressure from 120 ± 7 to 102 ± 7 mm Hg (p < 0.001). Arterial diameter also significantly decreased (p < 0.01) and returned toward normal. The study demonstrated that the diameter of the brachial artery was significantly increased in sustained essential hypertension and suggested that, with the chronic elevation of blood pressure, the large arteries dilate excessively, contributing to the mainenance of arterial blood flow within normal ranges.

LARGE ARTERIES of hypertensives have been shown to be thicker and stiffer than normal vessels in both experimental animals\(^6\)\(^-\)\(^9\) and in human subjects.\(^6\)\(^-\)\(^8\) However, in humans, these observations resulted either from invasive studies of the pressure-volume relationship of the brachial artery in vivo,\(^6\) or from the measurements of the thickness of the aorta at autopsy.\(^6\) Little information is available for intact large arteries, probably because of lack of appropriate techniques.

We have developed a pulsed Doppler velocimeter\(^7\)\(^-\)\(^12\) particularly suitable for determining blood flow in peripheral arteries. In addition to its pulsed emission, the apparatus has an adjustable range-gated time system and a double transducer probe.\(^12\)\(^-\)\(^14\) With the double transducer probe, the angle of the ultrasound beam relative to the flowing stream of blood can be simply evaluated so that the diameter of the artery can be calculated.\(^12\)\(^-\)\(^14\) This method has been applied to the determination of the diameter, the blood flow velocity and the volumic flow of the brachial artery in 36 patients with essential hypertension. The measurements have been compared with those of 25 normal subjects of the same age.

Materials and Methods

Patients

The study was performed in 61 men, 36 with sustained essential hypertension and 25 normal subjects of same age. Age range was 24-60 years in normal subjects and 16-65 years in hypertensives. All subjects were investigated while on a 110-mEq/day sodium diet. All treatment was discontinued at least 1 month before the study.

The 25 healthy normal men had no cardiovascular disease and clinical and routine laboratory investigations were normal. The 36 hypertensives had a diastolic pressure of at least 90 mm Hg at the third day of hospitalization. Extensive examination including plasma and urinary electrolytes, creatinine clearance, urinary catecholamine assay and timed i.v. pyelography, were normal. All hypertensives were listed as essential hypertensives. None had any renal, cardiac or neurologic involvement. Creatinine clearance was constantly higher than 80 ml/min (mean 104 ± 8 ml/min) (mean ± sem). Patients with coronary heart failure, cerebrovascular disease or peripheral vascular disease were excluded from the study. Both hypertensives and control subjects were classified according to age into those younger than and those older than 40 years. Clinical characteristics are listed in table 1. The investigation was approved by Institut National de la Santé et de la Recherche Médicale (INSERM). All patients gave informed consent after a detailed description of the procedure.
The Pulsed Doppler Velocimeter

In addition to the classic pulsed Doppler method, the present apparatus (Echovar Doppler pulse, Alvar Electronic) has two main original characteristics: the pulsed emission is associated with an adjustable range-gated time system and a double transducer system provides a bidimensional blood velocity measurement, which considerably minimizes the errors induced by the observation angle between the ultrasonic beam and the vessel axis.

Briefly, a single transducer acts alternatively as emitter and receiver (fig. 1). The emitter is a ferroelectric ceramic used at a frequency of 8 MHz, with emission duration of 0.5–2 μsec, and pulsed at a repetition of 15 or 30 μsec. Between the emission pulses, the transducer operates as a receiver and an electronic gate selects the signals reflected at a settled time from this emission. This time represents the time delay (t) of the reception. Moreover, the reception duration (τ) can also be selected at a given value. Adjustments of time delay (t) and reception duration are made by using a constant step of 0.5 μsec. Thus, any value between zero and the interval time of two successives emissions (32 or 64 μsec) can be selected. A high-pass filter with a cutoff frequency of 250 Hz eliminates the possible contribution of the vessel wall motion. With such an adjustable range-gated time system, the exact distance (d) can be determined between the red cell and the transducer, according to the echographic relation \( d = c / 2 \tau \), where \( c \) is the ultrasonic speed in tissues (1540 m/sec) and (t) the reception time. In these conditions, 0.5 μsec represents 0.4 mm; the interval between two successive emission pulses (32 or 64 μsec) corresponds to the maximum distance of measurement from the transducer (25 or 50 mm); the time delay and the duration reception represent, respectively, the depth and the thickness of the measurement volume along the beam axis. A small gate duration enables local velocity to be measured. This procedure can be applied to the determination of the diameter and the cross-sectional blood velocity of the vessel. The gate width is chosen to obtain the smallest sample volume size that is convenient with significant energy (1 μsec for an emission duration of 1 μsec). Then, the time delay is progressively increased stepwise by 0.5 μsec so that the lumen vessel could be crossed.

The time delay of the first velocity wave (\( t_1 \)) and the time delay of the last one (\( t_2 \)) indicate the region where the sample volume is close to the proximal and the distal arterial walls from the transducer (fig. 2). However, the smallest sample volume size is finite and not a point; errors will be introduced at the entering and the coming out the vessel because a part of the sample volume is out of the vessel lumen. This can be minimized by using focused lenses that are put on the transducer and prevent the divergence of the ultrasonic beam. Knowing the values \( t_1 \) and \( t_2 \), it is possible to obtain the cross-sectional velocity of the blood by superimposing the sample volume on the proximal and distal arterial walls. Moreover, the apparent echo diameter of the vessel (D) is deduced from the difference (\( t_2 - t_1 \)), according to the formula

\[
D = \frac{c}{2} \cdot (t_2 - t_1) \sin \theta
\]

where \( \theta \) is the angle between the ultrasonic beam and the vessel axis. Thus, a precise evaluation of angle \( \theta \) is required.

With the double transducer system used in the present pulsed Doppler velocimeter, the difficulty of

![Figure 1. Diagram of the Doppler signal analysis. Emission (E) has an oscillation frequency of 8 MHz and a duration of 0.5, 1, 1.5 or 2 μsec. The interval between two emission pulses is 32 or 64 μsec. The reception is defined by its time delay from the emission (t) and its duration (τ). Angle θ represents the angle between the ultrasonic beam and the velocity vector of the blood column.](image)

![Figure 2. Location of the sample volume close to the vessel walls: \( t_1 \) and \( t_2 \) values represent the time delays of the sample volume corresponding to the first and the last signal obtained by Doppler at the entering and the coming out of the vessel lumen. \( D = \) internal diameter of the vessel.](image)
measuring precisely the angle $\theta$ can be overcome.\textsuperscript{14} Two transducers 5 mm in diameter are symmetrically located at the extremity of a probe and form a definite angle $\alpha$ between them (fig. 3). The probe is designed so that the crossing volume of the beam corresponding to each transducer is located close to the vessel lumen. Each transducer is successively activated and a simple computation provides the longitudinal velocity within the plane defined by the ultrasonic beam and the vessel axis. Thus, the velocity vector is defined by its two components rectangularly projected on the beam axis of each transducer which form the angle $\alpha$. By adjusting the probe position so that the two vector components are equal in absolute values, i.e., in practice, when the probe is perpendicular to the vessel axis, the $\theta$ angle between each ultrasonic beam and the axis vessel equals $\alpha/2$. In the present system, the $\alpha$ angle of the transducers was fixed at 120°, so that the $\theta$ incidence angle of the ultrasonic beam could be adjusted by this procedure at 60°.

The accuracy of the Doppler determinations was studied with a hydraulic test device in which calibrated latex tubes and flow velocity could be controlled and measured. The test device was filled with a dilute suspension of starch particles in distilled water and placed on a beaker full of water. Pulsatile flow was obtained from a pump so that velocity could be changed between 5 and 100 cm/sec. The ultrasonic velocimeter was tested on the calibrated tubes through the water beaker used as an ultrasound conductor medium. The distance of the transducers from the tubes was similar to the distance encountered between the brachial artery and the skin. The two-transducer system was used as described above. The diameters of the calibrated tubes were compared to the calculated parent echo Doppler diameters. A strong positive relationship ($r = 0.99$) was observed, and the slope ($0.99 \pm 0.02$) was not significantly different from 1. The intercept was equal to 0.035 ± 0.015 cm. This value was not significantly different from zero. In addition, flow velocities measured with the studied system were within 95% of that controlled by the hydraulic test device for flow velocities of 5–100 cm/sec.

System Use of the Pulsed Doppler Velocimeter

Patients were examined in the supine position after 20 minutes of rest. The room temperature was 20–23°C. Blood pressure was measured at least three times on the left arm. The auscultatory technique was used, the criterion for the diastolic pressure being the disappearance of Korotkoff sounds. With the patient in the supine position, the right arm was placed on a horizontal plane corresponding to one-third of the distance between the anterior chest wall and the examination table. The investigator confirmed the pathway of the right brachial artery with his finger tips at the flexion side of the elbow joint. An ultrasonic gel was used as coupling medium between the probe and the skin. A loudspeaker was used as a monitor for listening to the Doppler output. The analog curve of velocity was derived from a zero crossing detector, transcribed on a Siemens apparatus with the ECG and simultaneously monitored throughout the examination with the loudspeaker. Some training was necessary to recognize the arterial Doppler beat by monitoring with the loudspeaker.

Determination of the Ultrasonic Beam Incidence Angle

An approximation of the location of the brachial artery was set first by adjusting the time delay and the gate width.\textsuperscript{15} The time delay was fixed at 10–20 $\mu$sec, corresponding nearly to the usual depth of the artery. The gate width was adjusted 5–10 $\mu$sec to overlay the whole section of the vessel. In this condition, the two velocity curves corresponding to the two described transducers were easily recorded. Probe position was adjusted so that the two velocities successively recorded during 10 cardiac cycles were equal in absolute values (fig. 4).\textsuperscript{13–14} In this case, the incidence probe was 60°, as demonstrated above. Once the adequate position was obtained, the probe was fixed in position over the course of artery by means of a stereotaxis device placed around the arm. This procedure was repeated throughout the examination before each velocity measurement. The accuracy of the method was tested as follows: The ratio between the surface of the velocity curves obtained from the two transducers during the examination was calculated in each patient. The mean value of the ratio was $1.02 \pm 0.02$, which corresponds to a maximal variation of 1° from the expected 60° angle.

Location of the Arterial Walls

With the probe adequately located at a 60° incidence angle, emission duration and gate width were
selected at 1 μsec. Arterial walls were located by moving the time delay from 0.5 to 0.5 μsec (i.e., 0.4 to 0.4 mm) along the beam axis with an advance speed synchronized with the ECG. With this procedure, the peak velocity distribution throughout the whole arterial section was obtained and recorded with a paper speed of 5 mm/sec.

Figure 4 shows an example of n velocity peaks corresponding to (n-1) intervals. The speed of the step advance was coupled with the ECG, so the interval between two successive waves equals the step advance of the time delay (0.5 μsec, i.e., 0.4 mm). Thus, the accuracy obtained for the exact location of proximal and distal arterial walls equals the value of the step of the time delay (0.4 mm). In the conditions of the study, the arterial diameter can be considered as being between a minimal value \( D_1 \), so that

\[
D_1 (\text{mm}) = (n-1) \times 0.4 \times \sin 60^\circ
\]

and a maximal value \( D_2 \), so that

\[
D_2 (\text{mm}) = (n + 1) \times 0.4 \times \sin 60^\circ.
\]

Thus, the apparent echo Doppler diameter \( D \) can be obtained from the formula

\[
D (\text{mm}) = (D_1 + D_2)/2 = n \times 0.4 \times \sin 60^\circ.
\]

After determining \( D \), the velocity over the vessel cross section was obtained by adjusting the time delay to the proximal arterial wall and the gate width to the diameter \( D \). The calibration voltage of the apparatus corresponds to a velocity of 38 cm/sec for an incidence angle of 60°. Velocity was recorded at a paper speed of 50 mm/sec. Mean velocity (\( V_m \)) was calculated by electronic integration of the velocity curve and was the mean value of 10 successive cardiac cycles on each transducer. The estimated mean volumic flow (\( Q \)) was calculated according to the formula

\[
Q = \pi D^2/4 \times V_m.
\]

In this study, the flow was expressed in ml/min and ml/min/m² after correction for body surface area. All the determinations were repeated at least twice in each patient. The reproducibility was 7 ± 2% for the apparent echo Doppler diameter and 5 ± 2% for the mean velocity.

**Administration of Vasodilating Drug**

In nine sustained hypertensives, the Doppler measurements were performed before and 30 minutes after i.v. administration of 7.5 mg of dihydralazine. One ampoule of 25 mg of the drug was diluted into 30 ml of isotonic saline. Nine milliliters (7.5 mg) of the drug were infused within 5 minutes to obtain a 15–20% decrease in mean blood pressure.

The Doppler measurements after dihydralazine were compared to those in basal conditions in the nine hypertensives and those in nine age-matched normal subjects investigated in basal conditions.

Means, standard errors of the mean and correlation coefficients were calculated according to standard statistical methods. Regression analysis were performed using the least-squares method. Differences in means were assessed by the \( t \) test.

**Results**

**Younger Group**

Figure 5 summarizes the values of diameter, blood flow velocity and volumic flow of hypertensives in comparison with normal subjects. The diameter was significantly increased \((0.482 ± 0.013 \text{ vs } 0.422 ± 0.011 \text{ cm}, p < 0.01)\). Seven of the hypertensives were above the upper limit of normal subjects. The velocity was slightly reduced \((6.4 ± 0.6 \text{ vs } 9.1 ± 0.9 \text{ cm/sec}, p < 0.05)\). The volumic flow was within normal ranges both in ml/min \((72 ± 7 \text{ vs } 78 ± 11 \text{ ml/min})\) and in ml/min/m² \((40 ± 4 \text{ vs } 44 ± 6 \text{ ml/min/m²})\).

Figure 6 shows, in the overall population, a positive correlation between the arterial diameter and mean
arterial pressure ($r = 0.75$, $p < 0.001$). Velocity and blood flow were not correlated with blood pressure.

**Older Group**

Figure 5 is a summary of the values of diameter, blood flow velocity and volumic flow of hypertensives compared with normal subjects. The diameter was significantly increased ($0.517 \pm 0.013$ vs $0.436 \pm 0.013$ cm, $p < 0.001$). Twelve hypertensive patients were above the upper limit of normal subjects. The velocity was reduced ($6.0 \pm 0.5$ vs $9.8 \pm 1.5$ cm/sec, $p < 0.01$). The volumic flow was within normal ranges: $77 \pm 8$ vs $89 \pm 15$ ml/min) and $41 \pm 4$ vs $50 \pm 8$ ml/min/m². Because mean body weight was significantly increased in the hypertensives of the older group (table 1), 13 of them were weight-matched with the corresponding control subjects. Table 2 indicates that body weight did not affect the results.

Figure 6 shows, in the overall population, a positive correlation between the arterial diameter and mean arterial pressure ($r = 0.60$, $p < 0.001$). Velocity and blood flow were not correlated with blood pressure.

**Administration of Dihydralazine**

After dihydralazine administration, mean blood pressure decreased from $120 \pm 7$ to $102 \pm 7$ mm Hg ($p < 0.001$) and heart rate increased from $73 \pm 2$ to $96 \pm 5$ beats/min ($p < 0.001$). Velocity did not in-
TABLE 1. Clinical Characteristics

<table>
<thead>
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<th>Younger group</th>
<th>Older group</th>
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<tr>
<td></td>
<td>Normal subjects</td>
<td>Hypertensive patients</td>
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<tr>
<td>Number</td>
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<td>14</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30 ± 2</td>
<td>32 ± 2</td>
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<tr>
<td>Weight (kg)</td>
<td>66 ± 2</td>
<td>72 ± 3</td>
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<td>Height (m)</td>
<td>1.70 ± 0.01</td>
<td>1.71 ± 0.02</td>
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<tr>
<td>Body surface area (m²)</td>
<td>1.76 ± 0.03</td>
<td>1.83 ± 0.04</td>
</tr>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td>120 ± 2</td>
<td>170 ± 5†</td>
</tr>
<tr>
<td>Diastolic arterial pressure (mm Hg)</td>
<td>79 ± 1</td>
<td>104 ± 5†</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)*</td>
<td>92 ± 1</td>
<td>126 ± 4‡</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>68 ± 3</td>
<td>71 ± 3</td>
</tr>
</tbody>
</table>

*Calculated as diastolic pressure plus one-third of pulse pressure.
†p < 0.05.
‡p < 0.005.

TABLE 2. Diameter, Velocity and Volumic Flow in Normal Subjects and in Weight-matched Hypertensives of the Older Group

<table>
<thead>
<tr>
<th></th>
<th>Normal subjects</th>
<th>Hypertensive patients</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
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<td>13</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47 ± 1</td>
<td>50 ± 1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69 ± 3</td>
<td>70 ± 2</td>
</tr>
<tr>
<td>Height (m)</td>
<td>173 ± 2</td>
<td>172 ± 1</td>
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<tr>
<td>Arterial diameter (cm)</td>
<td>0.436 ± 0.013</td>
<td>0.497 ± 0.013†</td>
</tr>
<tr>
<td>Velocity (cm/sec)</td>
<td>9.8 ± 1.5</td>
<td>6.1 ± 1*</td>
</tr>
<tr>
<td>Volumic flow (ml/min/m²)</td>
<td>44 ± 6</td>
<td>40 ± 6</td>
</tr>
</tbody>
</table>

Values are mean ± sem.
*p < 0.05.
†p < 0.01.

crease significantly (4 ± 3%). When blood pressure returned toward normal values after dihydralazine, the arterial diameter significantly decreased (0.463 ± 0.024 vs 0.495 ± 0.026 cm, p < 0.01) and returned toward normal (fig. 7).

Figure 8 shows a significant positive correlation (r = 0.75) between the change in blood pressure and the change in arterial diameter after the drug administration.

Discussion

Our choice of the brachial artery to evaluate peripheral blood flow represented a technical advantage with respect to the deep and curved vessels, such as the aorta. Although animal experiments have shown that the Doppler method was valid with arteries that were 2 mm in diameter, the small diameter of the brachial artery could represent a problem for non-invasive determinations in men. The validity of the pulsed Doppler system has been discussed in detail.

Figure 7. Effect of dihydralazine on blood pressure and arterial diameter in nine hypertensives. The p values represent comparisons of the basal values of the nine hypertensives and the basal values of nine age-matched normal subjects. *p < 0.05; **p < 0.01; ***p < 0.005.
Elsewhere,9,  10,  12 Thus, the main technical problem of this study was to evaluate the validity of the determination of the apparent echo Doppler diameter in a vessel as small as the brachial artery in normal subjects and in hypertensives.

Factors that relate to this problem are mainly the angle between the ultrasonic beam and the vessel axis and the sample volume size. The angle problem appeared to be easily overcome by the two-transducer system and the stereotaxis device, which prevented the probe movements. In contrast, the definition of the sample volume and its interference on the measurement were more difficult to assess. The sample volume size depends on the size of the transducer, the shape of the ultrasonic beam, the emission and gate duration.10  13 The distortion introduced by the sample volume interfered mainly close to the arterial walls, leading to an overestimation of the echo Doppler diameter.13 The superficial position of the brachial artery gave an optimal signal-to-noise ratio for the frequency used. In addition, the selection of short emission and gate duration permitted us to get a very small sample volume. Finally, with the laboratory testing, an adequate evaluation of the error due to the sample volume was obtained. The intercept of the curve between the diameters of the calibrated tubes and the echo Doppler calculated diameters gave a quantitative idea of the overestimation due to the sample volume size. The value of the intercept (0.035 ± 0.015 cm) was not statistically different from zero and could be neglected in clinical practice. For this reason, the measured diameter was called "apparent" echo Doppler diameter of the brachial artery.

With the method, a noninvasive measurement of diameter, blood flow velocity and volumic flow of brachial artery can be proposed in man. In normal subjects, the mean value of the diameter was 0.422 ± 0.011 cm in patients younger than 40 years and 0.436 ± 0.013 cm in those older than 40 years. Such data, obtained on intact brachial arteries, were the first to be performed in man and, therefore, lacked comparison. However, the values were in reasonable agreement with previous anatomic or operative findings in other major branches of the arterial tree, such as carotid17, 18 or femoral arteries.19, 20 Estimated mean volumic flow was 44 ± 6 ml/mm/m² in subjects younger than 40 years and 50 ± 8 ml/mm/m² in those older than 40 years. The forearm is almost entirely irrigated by the brachial artery, so the value was consistent with the previous determinations of forearm blood flow made by plethysmography.21

In hypertensives, the diameter of the brachial artery was significantly increased and the velocity was slightly reduced, while volumic flow remained within normal range. The results were observed in subjects younger than and older than 40 years; age did not seem to influence greatly the hemodynamic characteristics of the brachial artery. The increased diameter

\[ r = 0.75 \]
\[ P < 0.02 \]

**FIGURE 8.** Effect of dihydralazine: relationship between the change in arterial diameter and the change in blood pressure.
and the decreased velocity could be more likely related to the chronic elevation of blood pressure. This interpretation is consistent with two observations: the findings of increased arterial diameter in chronic renal experimental hypertension and the positive correlation observed between arterial diameter and mean blood pressure in the present study (fig. 6). However, the dilatation of the brachial artery could be either a state simply associated with sustained essential hypertension or a consequence of the chronic elevation of blood pressure. In the present study, the effects of dihydralazine in hypertensives favored the latter possibility. The dilatation of small arteries due to dihydralazine reduced blood pressure while the diameter of brachial artery decreased toward the normal range. Moreover, the decrease in pressure after dihydralazine was directly correlated with the decrease in arterial diameter (fig. 8). Thus, the results agree with the concept that, with high blood pressure, the large arteries dilate excessively and so contribute to the maintenance of arterial blood flow within normal ranges.

Folkow reported that adaptive changes of the resistance vessels were characteristic of hypertension. The present investigation provides evidence that in man the adaptive vascular changes are not restricted to arterioles, but also involve the large arteries.

Acknowledgment

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References

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