An Experimental Study of the Production and Time Course of Poststenotic Dilatation in the Femoral and Carotid Arteries of Adult Dogs

By Margot R. Roach, B.Sc., M.D., C.M., Ph.D.

Poststenotic dilatation occurs clinically beyond almost every type of arterial constriction, both intrinsic (e.g., valvular stenoses and arteriosclerotic plaques) and extrinsic (e.g., compression of the subclavian artery by a cervical rib). The cause of this dilatation is still not known although many theories have been proposed to explain it.

**Natural Occurrence**

Although there is little data on the exact incidence of poststenotic dilatation, it is common with some types of constriction such as pulmonary and aortic valve stenoses\(^1\)\(^2\) but rare with others such as infundibular pulmonary stenosis\(^1\)\(^3\) or supravalvular aortic stenosis.\(^4\) It occurs with both congenital\(^1\)\(^3\) and acquired\(^1\)\(^5\)\(^6\) aortic stenosis.

Skandalakis et al.,\(^7\) in a survey of the literature from 1928 to 1958, found that 51.6% of the 106 aneurysms reported with coarctation of the aorta were distal to the stenosed segment. Kiçler et al.\(^8\) found 19 cases of mycotic aneurysm distal to a coarctation reported up to 1961 (9 of them ruptured). Zaroff et al.\(^9\) observed poststenotic dilatation distal to coarctation of the abdominal aorta, and Arvidsson et al.\(^10\) and Orell et al.\(^11\) described it beyond coarctation of the peripheral pulmonary arteries.

Poststenotic dilatation occurs with renal arterial stenoses, especially those due to arteriosclerotic plaques or medial fibromuscular hyperplasia,\(^12\) and may help to detect the hypertensive patients most likely to respond to renal artery surgery (Luke et al.\(^13\) and Perloff et al.\(^14\)). It also develops beyond arteriosclerotic plaques in the carotids,\(^15\) femorals, and other medium-sized arteries. These dilatations are small, and seldom rupture or complicate surgery.

Poststenotic dilatation also occurs in arteries which are narrowed by some external force, e.g., in the subclavian artery compressed by a cervical rib or enlarged scalenus anticus muscle (Halsted\(^16\) and Eden\(^17\)), and in the popliteal artery compressed by the adductor magnus tendinous hiatus, or the arcuate popliteal ligament (Gedge\(^18\)).

Thus poststenotic dilatation may occur in almost any artery that is adequately constricted. It may help to delineate the area of stenosis, since arteriography often demonstrates the dilatation more clearly than the stenosis; to separate valvular from infundibular pulmonary stenosis; or to indicate if arterial repair is likely to be beneficial.\(^11\)\(^13\)\(^14\)

Since a few of these dilated areas may thrombose (McCormack\(^19\)) or rupture (Skandalakis et al.\(^3\)), their presence can affect the prognosis.

**Experimental Production of Poststenotic Dilatation**

Luigi Porta,\(^20\) in 1845, noticed a large poststenotic dilatation in the experimentally constricted abdominal aorta of dogs but apparently did not realize its significance. Halsted\(^16\) was probably the first to investigate this phenomenon experimentally and to suggest that there might be a common denominator in all cases of poststenotic dilatation. He produced a constriction in the abdominal aorta of a large number of adult dogs and concluded...
that the circumscribed dilatation that developed with partial constriction of the lumen (65 to 75% occluded) was due to the same mechanism that caused subclavian artery aneurysms beyond cervical ribs. He suggested that the \textquoteleft abnormal, whirlpool-like play of the blood in the relatively dead pocket just below the site of the constriction and the lowered pulse pressure may be the chief factors concerned in the production of the dilations.'

In 1918 Halsted\textsuperscript{21} attempted to cure aneurysms in human beings by partially occluding the artery proximal to the lesion with an aluminum band. His results were often quite good, but he reported one remarkable case of a 50-year-old woman with a large aneurysm of the right subclavian artery treated by banding the innominate. Much to his surprise, the right common carotid artery distal to the band became markedly dilated and remained so even after the original aneurysm had disappeared.

Little experimental work was done on poststenotic dilatation from the time of Halsted, until Holman\textsuperscript{22} aroused interest in the subject in 1954. One of the major reasons for this was the problem of pressure necrosis which occurs with most types of band, especially in the thoracic aorta.\textsuperscript{23} Holman et al.\textsuperscript{24} found that this did not occur if the aorta of newborn pups was banded (without constriction), so that the stenosis developed gradually as the animal grew. Poststenotic dilatation was present when the dogs were sacrificed several months later. In a few cases, aortograms were used to demonstrate the dilatation. These authors also produced poststenotic dilatation in two or three constricted rubber tubes perfused with saline with pulsatile flow. Permanent dilatations developed after 21 to 96 hours. They claimed that the increased side pressure produced by the turbulence present in the poststenotic area weakened the wall by a process of \textquoteleft structural fatigue\textquoteright so that a poststenotic dilatation eventually developed.

About the same time, Robicsek,\textsuperscript{25} on the basis of experiments in glass and rubber models, suggested that turbulence or cavitation might lead to poststenotic dilatation even though he found that the pressure distal to the stenosis decreased rather than increased. He suggested, from his results and those of van Buchem,\textsuperscript{26} that turbulence probably destroyed the elastic fibres in the poststenotic segment.

De Vries and van den Berg\textsuperscript{27} later showed, by an ingenious set of experiments with rigid and elastic tubes and isolated and intact aortae, using steady and pulsatile flow, that the pressure was always normal, or lower than normal, distal to a stenosis, and that if turbulence was present, the pressure was always decreased even more. From this they suggested that congenital weakness of the wall was the most likely cause of poststenotic dilatation clinically.

In 1961, Bruns et al.\textsuperscript{28} reported that rubber (Penrose) tubes would dilate if distended with water that was artificially vibrated without flow. The dilatation always occurred near the tip of the vibrating rod, so they postulated that a stenosis might create periodic wakes or vortices (instead of turbulence) which caused vibration of the wall distal to the constriction, and hence produced a poststenotic dilatation.

The existence of poststenotic dilatation in arteries is beyond dispute, but its cause is still controversial. It occurs in a low pressure region,\textsuperscript{27} and hence cannot be attributed to distension by increased pressure. Our experiments were designed to find the cause of the dilatation and the time required for it to develop.

\textbf{Methods}

\textbf{PRODUCTION OF STENOSIS}

Stenoses were produced in the femoral and/or carotid arteries of twenty-six large adult dogs (14 to 25 kg) with aseptic technique. These arteries were chosen because they were a convenient size, easily exposed, fairly resistant to pressure necrosis,\textsuperscript{29} and paired so that each dog could serve as its own control.

The dogs were anesthetized with intravenous sodium pentobarbital (approximately 0.43 cc/kg), and the femoral and carotid arteries were exposed and gently dissected free from connective tissue.
tissue and nerve. Small branches were tied and cut, large ones were left intact.

Bands were made of nylon taffeta, an inert substance that could be autoclaved and cut to approximately the right size. It was doubled, wrapped twice around the artery, and fastened with a mattress suture of 4-0 atraumatic silk in such a way that the suture did not touch the artery, so that the risk of pressure necrosis was decreased. The loose ends of the band were then cut off (it was important to leave them long enough so that unraveling would not reach the suture), and another mattress suture was inserted as above. The skin was closed, and the wound was covered with collodion. Each dog received 2 cc of S.R.S. penicillin (300,000 IU Penicillin G Procaine, 1 g streptomycin sulphate, 100,000 IU Penicillin G Potassium) prophylactically.

Three degrees of stenosis produced in this way were defined as: 1. minimum stenosis if there was no palpable change in distal pulsation and no thrill or bruit (seven arteries); 2. moderate stenosis if there was distal turbulence as indicated by the presence of a thrill and bruit (thirty-nine arteries); 3. severe stenosis if there was a marked decrease or absence of palpable distal pulsation, and no thrill or bruit (four arteries).

The dogs were sacrificed from 24 hours to 10 months later, and the degree of stenosis and amount of dilatation proximal and distal to the band were determined by caliper measurements at 0.25-cm intervals.

**TIME COURSE OF DILATATION**

Daily arteriograms and indwelling catheters were unsatisfactory. We developed a method for making the arterial wall radiopaque, so that the diameter of the artery proximal and distal to the stenosis could be measured from daily radiograms. Thorium dioxide (British Drug House) was made into a thick paste with normal saline and painted on the artery before it was banded. The "paint" was easy to apply, dried rapidly, and remained in place for long periods (at least ten months, which was the maximum duration of our experiments).

Thorium is the radiopaque substance in Thorotrast, a contrast medium formerly used for arteriography. Clinically, it has caused fibrosis, and even malignancy of the liver and other tissues after fifteen or twenty years or more, probably due to the alpha-radiation produced by the thorium. Since arteries are quite radioresistant, it seemed likely that this side effect would not be important for the relatively short-term experiments planned (i.e., one year or less). Thorium dioxide is readily available commercially, is quite inert chemically, and is known to be phagocytosed rapidly by reticulo-endothelial cells such as those in the adventitia of arteries. Tension-length diagrams obtained from pressure-volume studies on segments of painted and unpainted artery from the same dog (either two segments of the same artery, or one segment from each of paired arteries) showed that the thorium did not change the elastic properties of the artery for periods up to ten months (fig. 1).

If the artery was painted before it was banded, the length and diameter of the stenosis were clearly visible on the radiograms (fig. 2). Immediately after operation the dog was X-rayed. The animal was placed on its back, with the shoulders supported in a wooden brace and the hips resting on the cassette. The hips and knees were flexed to approximately 90°. The X-ray tube was always 63.5 cm from the plate and was centered over the midline of the abdomen at the level of the femoral arteries. The last six dogs were also X-rayed in the prone position with the thorax resting on the flexed forepaws in the brace, and the hips and knees flexed to 90° and supported on the cassette. The tube was centered over the junction of the tail and body. In the prone position it was essential to expose the film at the end of the expiration since the legs

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*Parke, Davis & Co.*

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(and hence the arteries) moved with the chest during respiration.

Consistent results were obtained only if the artery was exactly the same distance from both the film and the tube every day. Both the height of the hip and the knee, and the degree of flexion of these joints, determined the size of shadow the artery cast on the film. If the legs were extended, the arteries simultaneously elongated and decreased in diameter. Plaster moulds were made to maintain the position in two animals but did not improve the consistency of the results and so were abandoned.

The radiograms were placed on a viewing box, and each end of the stenosis was marked with pencil. Distances were measured proximal and distal to this at about 0.25-cm intervals. The diameter at each of these points was then measured with pointed vernier calipers. The inner edge of the paint was used since it was sharp and showed the boundary between the media and adventitia (histological examination showed that the thorium particles were distributed in the reticulo-endothelial cells in the adventitia). The outer limit of the paint was less reproducible since it depended both on the amount of thorium applied and on the diameter of the artery.

The distal diameters at each point were expressed as a percentage of the average proximal diameter of the same artery. This decreased the daily variations (e.g., those due to slight differences in position) and also allowed comparison of the measurements from dogs of different sizes. It is obvious from tables 1 and 3 and figures 5 and 6 that the "relative diameter" of the distal segment compared to that of the proximal was always less than 100% unless a poststenotic dilatation was present. This was particularly apparent in the femoral artery, where the exit of branches decreased the diameter of the main trunk. In addition, the stenosis produced a decrease in pressure distally, and hence decreased the diameter even more. Since the normal value for the true distal diameter seemed uncertain, we decided to express all values as "relative diameters," so that the proximal diameter, which was seldom changed by the band, showed the rate of dilatation in each case. If radiograms were available for both the prone and supine positions, the measurements were averaged to obtain the daily value.

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A similar method was used for the four carotids that were painted. Radiograms were obtained with the dog in a lateral position with the neck extended, and in a few cases with the dog on its back and the neck extended as before. This position was difficult to maintain, and the results were less consistent than those in the lateral position. In addition, the thorium did not remain in the carotid wall as well as in the femoral, but tended to "track" down toward the mediastinum. The carotids were difficult to study together (since their shadows often were superimposed on the radiogram), and altogether were found to be less satisfactory for our purposes than the femorals.

FREQUENCY ANALYSIS OF MURMURS

In our experiments, the poststenotic dilatation always developed if a thrill and bruit were present, but never developed if they were absent. The murmurs were recorded on magnetic tape with an Ampex 601-2 tape recorder immediately after the original operation, and again just before the conclusion of the experiment. The microphone was held firmly on the skin overlying the region of maximum intensity of the murmur (and, in a few cases, directly over the artery). The small size of the stenosed arteries made intra-arterial phonocatheters impractical.

The frequency spectrum of the recorded murmurs was determined by connecting the output of the tape recorder through four band-pass filters (Krohn-Hite 310-AB) connected in series to an oscilloscope (Dumont 304 H). This arrangement gave a total cut-off of 96 decibels/octave. The intensity of each frequency component of the murmur (as recorded above) was determined by varying the frequency setting of the filters and then measuring the amplitude of that component on the oscilloscope. Measurements with a General Radio type 760-B sound analyzer were not possible since the murmurs occurred only during systole.

Results

COMPLICATIONS

This method had a low mortality and morbidity rate. Two dogs died shortly after the operation (probably from anaesthesia) during the thirty-seven operations.

Two dogs developed moderately severe wound infections with local swelling, heat, redness, and pus formation. Both responded to systemic antibiotic therapy in less than a week. Five others developed slight redness and heat, but this disappeared in less than two days after an antiseptic powder was applied. No systemic antibiotics were used. No infections occurred in the neck after carotid surgery.

No gross pressure necrosis developed, although histological preparations always showed tissue atrophy under the band microscopically.

DEVELOPMENT OF POSTSTENOTIC DILATATION

The dogs were sacrificed from 24 hours to 10 months postoperatively. The results are shown in table 1. All of the arteries with moderate stenosis (and distal turbulence) had developed some poststenotic dilatation, but none of the others had (fig. 3). The largest dilatations seemed to be associated with the loudest murmurs, but there was considerable variation in different dogs. In some dogs, a thrill extended into the main branches of the arteries, and these branches, as well as the main trunk of the artery proximal and distal to the division, were all dilated (fig. 4).
Left femoral artery of dog 13 thirteen days after operation. The band (B), poststenotic dilatation (PSD), and direction of flow (shown by the arrow) are marked. The upper photograph shows that the dilatation extended into the branches (where a thrill was palpable), and the lower one (with the branches removed) shows that the dilatation extended beyond the origin of the branches.

**TABLE 1**

<table>
<thead>
<tr>
<th>Type of stenosis</th>
<th>Per cent decrease in lumen</th>
<th>Turbulence</th>
<th>No. of arteries</th>
<th>Proximal dilatation</th>
<th>Poststenotic dilatation</th>
<th>Duration of experiment (operation to sacrifice)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>5-35</td>
<td>0</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>1 day to 8 months</td>
</tr>
<tr>
<td>Moderate</td>
<td>23-76</td>
<td>Weak</td>
<td>6</td>
<td>6</td>
<td>12</td>
<td>1 day to 10 months</td>
</tr>
<tr>
<td>Strong</td>
<td>85-100</td>
<td>Strong</td>
<td>18</td>
<td>9</td>
<td>27</td>
<td>1 day to 10 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>1 day to 7 months</td>
</tr>
</tbody>
</table>

*Relative diameter = \( \frac{100 \times \text{distal diameter}}{\text{proximal diameter}} \) as measured with vernier calipers at sacrifice.

Summary of the effects of different degrees of stenosis on the femoral and carotid arteries of twenty-six adult dogs. The "relative diameters" shown are the maximum ones obtained at the time of sacrifice.
POSTSTENOTIC DILATATION

TABLE 2

Measurements of Left Femoral Artery of Dog 13

<table>
<thead>
<tr>
<th></th>
<th>Day</th>
<th>Prox. diam (cm)</th>
<th>Distal diam (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray (inside edge of thorium) (corrected for artifact)</td>
<td>0</td>
<td>0.42</td>
<td>0.38</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>0.41</td>
<td>0.50</td>
</tr>
<tr>
<td>Arteriogram (corrected for artifact)</td>
<td>28</td>
<td>0.40</td>
<td>0.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.39</td>
<td>0.48</td>
</tr>
<tr>
<td>External diameter at sacrifice (with calipers)</td>
<td>30</td>
<td>0.40</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Comparison of different types of measurement on the femoral artery of one dog. The values at the end of the experiment are not significantly different.

TIME COURSE OF THE DILATATION

When the absolute values of the diameter (from the radiograms) were plotted against time, there was always some daily variation (probably due to slight differences in position). There was a consistent decrease in values in the first 24 to 48 hours in almost all cases, probably due to phagocytosis of the thorium particles on the surface by cells inside the adventitia, since this process is known to occur rapidly. This hypothesis was supported by the observation that the paint was easily washed off the artery soon after it was applied, but had to be dissected off 24 hours postoperatively. At sacrifice the white thorium was clearly visible in the vessel wall (figs. 3 and 4) without any evidence of accompanying edema, inflammation, or fibrosis (except in the two dogs where considerable bleeding and/or muscle contamination with thorium had occurred). The faintly basophilic granules, said to be typical of thorium, could be seen in the adventitia microscopically. Although no granules were seen in the media and intima, it is impossible to state that they were not there. However, as McDonald points out, the thickness of the wall of the femoral and carotid arteries is, at most, only 0.05 to 0.08 times the diameter of the arterial lumen so that, even if the thorium were not arrested at the medial-adventitial boundary, this would introduce an error of not more than 8%, and even such an error should not affect significantly the difference between the proximal and distal segments. The effect of turbulence on the migration of thorium was not assessed, but there was no gross difference between the proximal and distal segments in these vessels, and as noted above, the maximum error produced would not exceed 8%.

In all of the dogs, caliper measurements at the end of the experiment agreed well with measurements from the radiograms. In dog 13, an arteriogram was done two days prior to death, and the three types of measurements of the arterial diameter agreed remarkably well (table 2). Actually, the values from both the arteriogram and the radiogram (X-ray) are probably slightly greater than they should be since the artery was about 1.0 to 1.5 cm deep to the anterior surface of the leg and so was that distance from the film. Since the X-ray tube was set at 63 cm from the film, a correction factor of 1 to 2% was applied. These values exclude the possibility that the apparent dilatation is only a change in thickness of the vessel wall.

Figure 5 shows the average curves obtained from measurement of the radiograms of six dogs with a minimum stenosis of one femoral artery and a moderate stenosis of the other. Those with minimum stenosis and no distal turbulence did not change appreciably in diameter throughout the experiment. However, those with moderate stenoses and distal turbulence increased significantly for about ten days and then remained unchanged up to
Average time course for the development of poststenotic dilatation in the femoral arteries of dogs. "Relative diameter" or (100 \times \text{distal diameter at any point/average proximal diameter}) is plotted against days after operation for different distances distal to the band. The dots show the average from radiograms of six arteries with minimum stenoses (no turbulence) and do not change with time. The crosses show averages from radiograms of fifteen arteries with moderate stenoses (distal turbulence). These arteries started to dilate within twenty-four to forty-eight hours, increased for ten days, and then remained unchanged for up to ten months. The first change, and the largest dilatation, was usually between 0.50 and 1.0 cm distal to the band.

Three types of response to the presence of turbulence occurred initially (fig. 7). This probably explains why the average values shown in figure 5 were so variable in the first few days. The middle curve (14RF) shows the most typical response, i.e., a gradual increase in the dilatation for about ten days, and then essentially no change for up to ten months. The top curve (9RF), which occurred in four arteries, shows the same initial response but some "overshoot" before the steady state was reached. The bottom curve (13RF) occurred only in this one artery, and so was quite atypical. Although an immediate dilatation developed within a few minutes after the stenosis was produced in about one-third of the arteries, it rarely lasted more than a few seconds or minutes. However, 13RF developed an "immediate dilatation" which lasted for at least an hour, since the relative diameter was 132% in the first radiogram. By the next day, the artery appeared to be in spasm because the distal diameter was considerably decreased, and decreased even more the following day. After this, a dilatation developed and progressed in the usual way and reached a steady state by the tenth day.

Four arteries had severe stenoses (i.e., stenoses so tight that no pulsation could be felt distal to the band at operation, and no thrill or bruit was present). They developed a temporary proximal dilatation (probably due to increased pressure) and a distal collapse. Both the proximal and distal diameters tended to return toward normal as collaterals developed in three or four days. No poststenotic dilatations were present at postmortem. The presence of a severe stenosis had no appreciable effect on the animal if it was in a carotid artery (three cases). However, in the one dog with a severe stenosis of the femoral artery, the leg was quite cold but the dog did not limp. The leg and foot started to feel warmer by the third or fourth day, and by ten days postoperatively were not appreciably different from the other leg and foot. At autopsy, large collateral vessels were seen bypassing the area of stenosis.
POSTSTENOTIC DILATATION

One unplanned experiment illustrates how important turbulence is for the development of a poststenotic dilatation. Figure 8 shows the measurements obtained from the radiograms of the right femoral artery of dog 11 (11EF) at a point about 0.75 cm distal to the band. A moderate stenosis, with a grade 3 or 4 murmur, was present in this dog immediately after operation. A poststenotic dilatation began to develop in the usual way but disappeared rapidly in a few days as the murmur decreased and disappeared. Soon thereafter the abdomen appeared larger than normal and it became apparent that the dog was pregnant. Within twenty-four hours after she delivered seven full-term puppies the murmur reappeared and a poststenotic dilatation again developed, as shown. Presumably, as the uterus enlarged, it decreased the flow through the iliac arteries either by compressing them or by diverting the flow to the enlarged uterine vessels and hence through the femorals, so that the velocity fell below that needed to produce turbulence. After delivery the flow increased and turbulence reappeared. Since a poststenotic dilatation developed in the usual way in the right ca-

rotid artery of the same dog, the hormonal changes of pregnancy cannot be blamed for the peculiar results that occurred in the femoral artery.

FREQUENCY ANALYSIS OF MURMURS

Figure 9 shows the results obtained from frequency analysis of the murmurs in several

TABLE 3

<table>
<thead>
<tr>
<th>Distance from distal end of band (cm)</th>
<th>Relative diameter* (average)</th>
<th>Difference of the means (per cent)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With turbulence</td>
<td>Without turbulence</td>
<td></td>
</tr>
<tr>
<td>0.25</td>
<td>103.2</td>
<td>89.2</td>
<td>14.1</td>
</tr>
<tr>
<td>0.55</td>
<td>110.2</td>
<td>89.0</td>
<td>21.2</td>
</tr>
<tr>
<td>0.75</td>
<td>108.4</td>
<td>89.3</td>
<td>19.1</td>
</tr>
<tr>
<td>1.05</td>
<td>107.3</td>
<td>88.5</td>
<td>18.8</td>
</tr>
<tr>
<td>1.25</td>
<td>103.7</td>
<td>89.7</td>
<td>14.0</td>
</tr>
<tr>
<td>1.55</td>
<td>96.6</td>
<td>86.4</td>
<td>10.2</td>
</tr>
<tr>
<td>1.75</td>
<td>93.4</td>
<td>86.0</td>
<td>7.4</td>
</tr>
<tr>
<td>2.05</td>
<td>91.5</td>
<td>86.7</td>
<td>4.8</td>
</tr>
</tbody>
</table>

*Relative diameter = \( \frac{\text{distal diameter}}{\text{avg proximal diameter}} \times 100. \)

P is the probability that the differences obtained are due only to chance, so that P < 0.01 means there is only 1 chance in 100 that the two groups are not different.

Statistical analysis of the difference in relative diameter with moderate vs. minimum stenoses. The values shown are averages from the radiograms of six dogs with a moderate stenosis (turbulence) in one artery, and a minimum stenosis (no turbulence) in the other. The maximum dilatation occurred 0.55 cm distal to the band, and decreased steadily on either side of this point.

_Circulation Research, Volume XIII, December 1965_
TABLE 4A
Average Diameters of Femoral Arteries of Six Dogs with Standard Deviations (at 0.75 cm from Band)

<table>
<thead>
<tr>
<th></th>
<th>Days 0-9</th>
<th>Days 10-31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turbulence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal diam.</td>
<td>0.49 ± 0.01 cm</td>
<td>0.50 ± 0.02 cm</td>
</tr>
<tr>
<td>Distal diam.</td>
<td>0.47 ± 0.02 cm</td>
<td>0.55 ± 0.03 cm</td>
</tr>
<tr>
<td>No turbulence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal diam.</td>
<td>0.48 ± 0.03 cm</td>
<td>0.52 ± 0.02 cm</td>
</tr>
<tr>
<td>Distal diam.</td>
<td>0.45 ± 0.03 cm</td>
<td>0.47 ± 0.02 cm</td>
</tr>
</tbody>
</table>

Average diameters (in centimeters) of femoral arteries of six dogs with a minimum stenosis (no turbulence) of one femoral artery and a moderate stenosis (turbulence) of the other. Diameters shown are 0.75 cm on either side of the band and were measured on the radiograms with vernier calipers. The two columns show the initial or transitional period (days 0-9), and the final or steady state period (days 10-31).

TABLE 4B
Statistical Analysis of Change of Diameter with Time

<table>
<thead>
<tr>
<th></th>
<th>Turbulence</th>
<th>No turbulence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal diam.</td>
<td>ΔM</td>
<td></td>
</tr>
<tr>
<td>0.9—(10-31)</td>
<td>-0.01</td>
<td>-0.04</td>
</tr>
<tr>
<td>(cm)</td>
<td>±0.01</td>
<td>±0.02</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.5</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>Distal diam.</td>
<td>ΔM</td>
<td></td>
</tr>
<tr>
<td>0.9—(10-31)</td>
<td>-0.08</td>
<td>-0.02</td>
</tr>
<tr>
<td>(cm)</td>
<td>±0.02</td>
<td>±0.02</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.01</td>
<td>&lt; 0.3</td>
</tr>
</tbody>
</table>

Statistical analysis of data from table 4A. ΔM is the difference of the means between the initial and final periods. ΔM is the standard deviation of the difference of the means, and P is the probability that the two groups are not different.

TABLE 4C
Statistical Analysis of Data from Table 4A

<table>
<thead>
<tr>
<th></th>
<th>Turbulence</th>
<th>No turbulence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IP-ID</td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>+0.02</td>
<td>-0.05</td>
</tr>
<tr>
<td>ΔM ± σΔM</td>
<td>±0.01</td>
<td>±0.01</td>
</tr>
<tr>
<td>P</td>
<td>&lt; 0.2</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>Distal</td>
<td>+0.03</td>
<td>+0.05</td>
</tr>
<tr>
<td>ΔM ± σΔM</td>
<td>±0.02</td>
<td>±0.02</td>
</tr>
<tr>
<td>P</td>
<td>&lt; 0.2</td>
<td>&lt; 0.02</td>
</tr>
</tbody>
</table>

Proximal
| T-NT | ±0.01 | -0.02 |
| ΔM ± σΔM | ±0.02 | ±0.01 |
| P | < 0.6 | < 0.2 |

Distal
| T-NT | +0.02 | +0.08 |
| ΔM ± σΔM | ±0.02 | ±0.02 |
| P | < 0.3 | < 0.01 |

Statistical analysis of data from table 4A. The top two sets (Turbulence and No turbulence) show the difference in the means of the immediate proximal (IP) and immediate distal (ID) diameters, with the standard deviation (ΔM) of the difference of the means with turbulence (T) and without turbulence (NT). None of the groups was significantly different in the initial period. In the final period, there is a marked difference (P << 0.01) in the diameters of the distal segments in the groups with and without turbulence; but no difference (P < 0.2) in the proximal diameters of the same two groups. The proximal and distal diameters in each group are significantly different (in opposite directions) as shown.

Discussion

These experiments show conclusively that poststenotic dilatation always develops if arteries before and after a dilatation developed. There was no evidence of a definite frequency pattern, or of resonance, in any of the murmurs studied. The absolute amplitude values are arbitrary since the amplification of the tape recorder was different when they were recorded. However, the relative amplitudes shown for each murmur are accurate due to the flat frequency response of all of the apparatus. There was a wide variation of frequencies from 100 to 1400 cycles/sec, with no apparent resonant points.

These experiments show conclusively that poststenotic dilatation always develops if
turbulence (as shown by the presence of a thrill and bruit, and often by eddies visible through the vessel wall) is present distal to the band; a dilatation never develops if there is no turbulence. This strongly suggests that turbulence causes the dilatation, although the mechanism is not apparent.

The rate of dilatation was surprisingly similar in different arteries and a steady state value was always reached by the tenth postoperative day. Many factors probably influenced the rate and amount of dilatation, but the presence of turbulence appeared essential. Table 1 suggests that low-grade murmurs were associated with small dilatations, and loud murmurs with large dilatations. Unfortunately, there is still no way to measure turbulence quantitatively, so it is impossible to determine the exact correlation between the amount of turbulence and the size of the dilatation. Many secondary factors are probably important. For example, De Vries and van den Berg showed that the pressure decreased progressively as the stenosis was increased, and dropped further as turbulence developed. This would tend to counteract the increase in diameter due to turbulence.

Age decreases the distensibility of human arteries and probably affects those of dogs also. Our animals were mongrels, of unknown age, so this factor could not be controlled.

The steady state value reached about ten days postoperatively may have been modified by the type (length, shape, etc.) and degree of stenosis, and by the elastic properties of the constricted artery. The gradual increase in diameter that occurred during the initial period was probably caused by a progressive weakening of the wall by some forces associated with turbulence. However, the "immediate" dilatation, which developed in about one-third of the arteries at operation, cannot be explained in this way. The mechanism is obscure. The rapidity with which the "immediate" dilatation disappeared (a few seconds or minutes) suggested that some sort of "reflex" response to stretching might be involved. The marked constriction that occurred in 13RF (fig. 7), which was the only artery where the "immediate" dilatation persisted for more than a few minutes, supports this conclusion. The nervous pathways, if any, responsible for this phenomenon are also completely unknown. There was no apparent correlation between the transient "im-
Graphs to show the effects of pregnancy on the development of poststenotic dilatation in the femoral artery of one dog. The upper graph shows the "relative diameter" and the lower graph shows the actual diameters 0.75 cm on either side of the band plotted against time. A moderate stenosis, with a loud murmur, was produced on day 0, and the artery began to dilate immediately (upper graph). The absolute diameter decreased slightly, owing to phagocytosis of the thorium dioxide by reticuloendothelial cells in the adventitia. The murmur became faint at a, and inaudible at b. At c the abdomen appeared large and the dog was assumed to be pregnant. At d, seven full-term pups were delivered spontaneously, and at e a murmur became audible again, and a poststenotic dilatation developed. There was probably no change in pressure, since the proximal diameter did not change.

mediate" dilatation and the gradual one that developed over about ten days. It is still impossible to say why a steady state was reached after ten days, but obviously by this time the restoring forces became equal to the destructive ones.

Our experiments were limited to the femoral and carotid arteries of adult dogs. It is conceivable that the time course and extent of the dilatation vary considerably in different species. However, it seems likely that turbulence is the most important factor, since poststenotic dilatation developed both in vivo and in vitro (results to be published) only if turbulence was present.

Although our experiments show that poststenotic dilatation develops only if a thrill and bruit are produced by the stenosis, our statement that "turbulence was defined by the presence of a thrill and bruit" might be questioned, since there is considerable doubt about what causes murmurs. It is generally agreed that laminar flow is silent, but the type of nonlaminar flow most likely to produce sound is still controversial. As McDonald points out, so little fundamental work has been done on how sound is generated in a liquid, that any discussion of murmur production is likely to be purely speculative. The pulsatile flow and branching elastic tubes, with or without valves, which are common in biological material add further complications.

Three types of nonlaminar flow have been proposed as the cause of murmurs:

1. Cavitation or bubble formation probably does not occur unless the fluid is supersat-

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urated with gas, or there is more negative pressure than is likely to occur biologically.  

2. Vortex formation or periodic wake fluctuations occur in the fluid between two streamlines which have been separated by a stationary object held in a moving stream.  

With rapid flow, the stream may develop turbulence or eddies. Bruns proposed that this was the only type of nonlaminar flow that could produce enough acoustical energy to create a murmur. However, as McDonald points out, Bruns neglected the fact that the heterogeneous arterial wall could vibrate, and assumed that flow through an orifice was identical to flow past a stationary or rotating obstacle held in the center of the stream.  

3. Turbulence has been defined as completely random flow by Bruns and as any nonlaminar or unsteady flow by Rushmer and McDonald. If the general definition is accepted, murmurs must be due to turbulence. If Bruns' definition is used, all murmurs may not be attributable to turbulence, since completely random motion would probably produce very little acoustical energy, although vibration of the arterial wall might produce a murmur. Since turbulence cannot be measured quantitatively, vague qualitative measurements must be used to detect its presence — e.g., distorted dye patterns, nonlinear pressure-flow curves, and high Reynolds numbers. However, most authors seem to agree that even though the production of murmurs by turbulence is indirect, some relationship seems to exist between them.  

Table 5 summarizes some of the ways of differentiating the three types of nonlaminar flow. De Vries and van den Berg found a small drop in pressure (a few mm Hg) beyond a stenosis if a murmur was present. The murmurs in our dogs had a wide frequency distribution (fig. 9) with no resonant points and no frequencies over 1500 cycles/sec. Model experiments, where a constriction was produced in a long piece of Tygon tube, showed a random type of nonlaminar flow without eddies or bubbles. On this basis, we feel that, at least in our experiments, if the arterial stenosis was associated with a thrill and bruit, turbulence was present. Therefore, we have concluded that poststenotic dilatation develops in vivo only if turbulence, as defined by the presence of a thrill and bruit, is produced by the constriction. If turbulence is present, a dilatation always develops. The dilatation develops rapidly — usually starting within 24 hours and reaching a steady state within ten days.

**Summary**  
Three degrees of stenosis were produced in the femoral and carotid arteries of twenty-six adult dogs. Minimum stenosis caused neither proximal nor distal dilatation. Moderate stenosis, defined by the presence of a distal thrill and bruit, always produced poststenotic dilatation. Severe stenosis, with a marked decrease or absence of distal pulsation caused temporary proximal dilatation. The arteries were painted with a radiopaque paste which did not change their elastic properties and allowed daily measurements of arterial diameter. Radiograms showed that if turbulence was present, the artery usually started to dilate within twenty-four hours, reached a steady state within ten days, and then remained essentially unchanged for up
to ten months. The dilatation was fusiform, and usually extended for 1.75 to 2.0 cm distal to the end of the band.

Frequency analysis of the murmurs showed a wide frequency spectrum with no resonant points and no components over 1500 cycles/sec. This type of sound is more likely to be produced by turbulence than by cavitation or vortex formation.

Dye injection in a model showed a random dye distribution starting a short distance distal to the constriction.

Analysis of pressure-volume diagrams from these arteries suggested that the dilatation was due to a weakness of the arterial wall in the poststenotic segment.

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