Responses of Isolated Dog Cerebral and Peripheral Arteries to Prostaglandins after Application of Aspirin and Polyphloretin Phosphate

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SUMMARY  In helically cut strips of dog cerebral, coronary, mesenteric and femoral arteries, the contractile response to prostaglandin (PG) F2, and E2, relative to contractions induced by 30 mM K+*, did not appreciably differ, whereas relaxations induced by PGE2 relative to those induced by 10−4 M papaverine were significantly different; the least in cerebral arteries and the greatest in mesenteric arteries. The relaxation of human cerebral arteries in response to PGE2, was similar to that of dog cerebral arteries. Treatment for 60 min with polyphloretin phosphate (3 × 10−4 and 10−3 g/ml) suppressed the contractile response to PGE2 and E2 but did not alter the response to 25 mM K+. The relaxing effect of PGE2, was not influenced. Aspirin (5 × 10−4 and 2 × 10−4 M) significantly potentiated the contractile response to PGE2 and E2 but did not alter the relaxation induced by PGE2. In contrast, contractions induced by serotonin were attenuated. It is concluded that dog cerebral, coronary, mesenteric and femoral arteries relaxed differently in response to PGE2. It appears that arterial responses to vasoconstricting PGs, but not to the vasodilating PG, are significantly attenuated by polyphloretin phosphate and potentiated by aspirin.

PROSTAGLANDINS (PGs) induce changes in systemic blood pressure, regional blood flow and tone of vascular smooth muscle. Alterations induced by a variety of PG derivatives differ markedly, and even the same PGs sometimes elicit opposite actions on vessels from various species. Different responses of cerebral vessels to PGE2 and E2 have been reported, however, it is generally agreed that PGF2α causes constriction in cerebral vessels.

The ability of polyphloretin phosphate (PPP) to antagonize the effect of PGE2 on intraocular pressure was first demonstrated by Beitch and Eakins.7 PPP does not antagonize all actions of PGs on uterine, tracheal and bronchial smooth muscles.8−10 Aspirin-like anti-inflammatory agents inhibit the biosynthesis of PGs in isolated tissues and whole animals,11,12 but the interaction between PGs and aspirin or indomethacin, related to responses of vascular smooth muscles, has not been clarified.

The present study was undertaken to compare the actions of PGE1, E2 and F2α on isolated dog cerebral arteries with their actions on coronary, mesenteric and femoral arteries and to analyze the antagonistic action of PPP in these arteries.Alterations in the response of the arteries to PGs after aspirin and indomethacin application were also investigated.

Methods

Mongrel dogs of both sexes, weighing 7 to 15 kg, were anesthetized with intraperitoneal injections of sodium pentobarbital in a dose of 50 mg/kg and sacrificed by bleeding from common carotid arteries. The brain and heart were rapidly removed. Basilar and middle cerebral arteries (0.5 to 0.8 mm outside diameter) and ventral interventricular branches of the left coronary artery (0.6 to 0.9 mm) were isolated.

Distal portions of the mesenteric (0.5 to 0.8 mm) and femoral arteries (0.5 to 0.8 mm) were also removed. The arteries were helically cut into strips, the length being approximately 20 mm. The specimen was vertically fixed between hooks in a muscle bath containing nutrient solution, which was maintained at 37 ± 0.5°C and aerated with a mixture of 95% O2 and 5% CO2. Hooks anchoring the upper end of the strips were connected to the lever of a force-displacement transducer (Nihonkoden Kogyo Co., Tokyo, Japan). The resting tension was adjusted to 1.5 g, which was determined to be optimal for obtaining maximum contraction.13−14 Composition of the nutrient solution was (mM): Na+, 162.1; K+, 5.4; Ca2+, 2.2; Mg2+, 1.0; Cl−, 159.0; HCO3−, 14.9 and dextrose, 5.6. The pH of the solution was 7.2 to 7.3. Osmotic adjustment was not made when K+ (up to 30 mM) was added to the bathing media. Before the start of experiments, all preparations were allowed to equilibrate for 90 to 120 min in the control media during which time the fluids were replaced every 15 to 20 min.

Seven human cerebral arteries (4 intracranial internal carotid and 3 basilar) were obtained during autopsy from 4 humans, 50-, 61-, 65- and 81-year-old males, within 8 hours after death. The causes of death were lung cancer, peritoneal carcinomatosis, and urinary bladder cancer. Human arteries were cut into helical strips, which were fixed at a resting tension of 2 g in the bathing media, as described above.

Isometric contractions and relaxations were recorded on an ink-writing oscillograph (Sankei Sokki Co., Tokyo, Japan). The contractile response to 30 mM K+* was first obtained. PGs and serotonin were added directly to the bathing media in cumulative concentrations, and contractions relative to those induced by 30 mM K+* are presented. Arterial strips were contracted with either PGF2α or K+* before the addition of PGE2. Relaxations induced by 10−4 M papaverine were taken as 100% and relaxations induced by PGE2, relative to papaverine-induced relaxations are...
presented. Preparations were exposed for 60 min to PPP or for 20 min to other blocking agents, before the dose-response curve of PGs was obtained. Results shown in the text and figures represent mean values ± standard errors of the means. Statistical analyses were made using the Student's t-test. Drugs used were PGA₂, A₂, E₂ and F₂α (Ono Co., Osaka, Japan), serotonin creatinine sulfate, acetyl salycylic acid (aspirin), indomethacin, sodium polyphloretin phosphate (PPP), chlorpheniramine maleate, phen tolamine mesylate, methysergide bimaleate, dl-propranolol hydrochloride, atropine sulfate, cimetidine, aminophylline and papaverine hydrochloride.

Results

Responses of Different Arteries to PGs

In helically cut strips of dog cerebral, coronary, mesenteric and femoral arteries, the addition of PGF₂α in concentrations ranging from 10⁻⁷ to 10⁻⁶ M caused a dose-related contraction (fig. 1, left). Further increase in the concentration above 5 × 10⁻⁵ M relaxed the arterial strips by 20 to 35%, as compared with the maximum contraction induced at 10⁻⁵ M. The dose-response curve found for cerebral arteries was almost identical with the curves from other arteries. In 4 out of 16 cerebral, 3 out of 16 coronary and 2 out of 14 mesenteric arteries, slight and transient relaxation was observed in response to 2 × 10⁻⁸ and 10⁻⁷ M PGF₂α. In the remaining preparations, even though contracted with serotonin or K⁺, no relaxation was obtained.

The addition of PGE₂ (2 × 10⁻⁸ to 10⁻⁶ M) also elicited dose-dependent contractions; the maximum contraction was attained at 10⁻⁵ M (fig. 1, right). Dose-response relationships in cerebral, coronary, mesenteric and femoral arteries were similar, although the highest concentration of PGE₂ (10⁻⁶ M) produced greater contractions in femoral than in cerebral arteries (P < 0.02).

In 2 human cerebral arteries, PGF₂α and E₂ produced a dose-related contraction.

PGA₁ and A₂ (10⁻⁷ to 10⁻⁵ M) caused contractions in isolated dog cerebral, coronary and mesenteric arteries. Maximum contraction of cerebral arteries induced by 10⁻⁵ M PGA₁, A₂, F₂α and E₂, relative to those induced by 30 mM K⁺, averaged 53.1 ± 5.6% (N = 16), 56.0 ± 8.1% (N = 13), 60.8 ± 6.1% (N = 16) and 73.4 ± 8.4% (N = 14), respectively.

The addition of PGE₁ failed to contract cerebral (N = 2), coronary (N = 5), mesenteric (N = 2) and femoral arteries (N = 2). PGE₁ (2 × 10⁻⁸ to 10⁻⁵ M) relaxed arteries contracted with PGF₂α in a dose-dependent manner (fig. 2, left). Different responses of a basilar arterial strip to PGF₂α, E₁ and E₂ are demonstrated in figure 3. At 10⁻⁵ M PGE₁ caused slight contractions in 6 out of 13 mesenteric arteries.

**Figure 1.** Dose-response curves of PGF₂α and E₂ for isolated dog cerebral, coronary, mesenteric and femoral arterial strips. Contraction induced by 30 mM K⁺ was taken as 100%; mean absolute values in cerebral, coronary, mesenteric and femoral arteries were 978 ± 139 mg (N = 16), 1486 ± 123 mg (N = 16), 2174 ± 228 mg (N = 14) and 1246 ± 158 mg (N = 6), respectively (left figure), and those were 872 ± 139 mg (N = 14), 1512 ± 123 mg (N = 13), 1850 ± 237 mg (N = 12) and 1368 ± 225 mg (N = 5), respectively (right figure). Vertical bars represent standard errors of means. Figures in parentheses indicate the number of preparations used.
FIGURE 2. Dose-response curves of PGE₁ for isolated dog cerebral, coronary, mesenteric and femoral arteries and human cerebral arteries. Left figure: preparations were contracted with PGF₂α (5 × 10⁻⁵ to 3 × 10⁻⁴ M). Right figure: coronary arterial strips were contracted with either K⁺ (10 to 17 mM) or PGF₂α. Relaxation induced by 10⁻⁴ M papaverine was taken as 100%. Mean absolute values in cerebral, cerebral (human), coronary, mesenteric and femoral arteries were 672 ± 86 mg (N = 24), 1753 ± 299 mg (N = 7), 840 ± 72 mg (N = 23), 602 ± 87 mg (N = 13) and 702 ± 79 mg (N = 8), respectively (left figure), and those in coronary arterial strips contracted with PGF₂α and K⁺ were 840 ± 72 mg (N = 23) and 771 ± 217 mg (N = 8), respectively (right figure).

An increase in the concentration to 5 × 10⁻⁴ M caused additional contractions in mesenteric and slight contractions in the other arteries.

The relaxation induced by PGE₁ was significantly greater in mesenteric than in cerebral arteries. The relaxing effect on cerebral arteries did not differ in basilar and middle cerebral arteries. The average relaxations induced by 5 × 10⁻¹, 2 × 10⁻⁴ and 10⁻⁴ M PGE₁ were 15.9 ± 4.1, 41.1 ± 4.6 and 56.7 ± 4.9%, respectively (N = 18), in basilar arteries, and 12.9 ± 7.5, 51.1 ± 5.4 and 61.1 ± 5.8%, respectively (N = 8), in middle cerebral arteries. Similar dose-dependent relaxations were observed in human cerebral arteries contracted with PGF₂α (fig. 2). In 7 out of 24 cerebral and 11 out of 23 coronary arteries, slight but significant contractions were produced at low concentrations (2 × 10⁻⁴ and 10⁻⁴ M) of PGE₁. In contrast, such contractions were not observed in mesenteric and femoral arteries.

Relaxation in response to PGE₁ was also found in coronary arteries contracted with K⁺ (10 to 15 mM).

FIGURE 3. Comparison of dose-related responses to PGF₂α, E₁, and E₂ of a dog cerebral arterial strip. Concentrations from 1 to 5: 2 × 10⁻⁴, 10⁻⁴, 5 × 10⁻⁴, 2 × 10⁻³ and 10⁻² M, respectively. Before the addition of PGE₁, the strip was contracted with 10⁻⁴ M PGF₂α; the horizontal line just left of the bottom tracing represents the level prior to the addition of PGF₂α. PA: papaverine.
However, in the K+-contracted arteries, contractions seen at low concentrations of PGE₁ were greater and relaxations at high concentrations were significantly less, as compared with those in PGF₂α-contracted arteries (fig. 2, right). Similar results were observed in 3 cerebral and 2 mesenteric arteries.

Modification by PPP of Response to PGs

Contractile responses in cerebral arterial strips to PGF₂α and E₂ were unaffected by 10⁻⁶ M phentolamine, 10⁻⁶ M methysergide and 10⁻⁶ M chlorpheniramine. Relaxation induced by PGE₁ was not affected by 10⁻⁶ M propranolol, 10⁻⁶ M atropine, 10⁻⁶ M cimetidine and 2 × 10⁻⁵ M aminophylline.

Treatment for 60 min with PPP (3 × 10⁻⁵ and 10⁻⁴ g/ml) attenuated the contractile response of cerebral arterial strips to PGF₂α and E₂ (fig. 4). Similar attenuation was observed in mesenteric arteries (fig. 5). The attenuation with PGE₂ was greater than that for PGF₂α. The inhibition was reversed only partially by repeated washing of the preparations. PPP in a concentration of 3 × 10⁻⁵ g/ml did not alter the contractile response of cerebral arteries to 25 mM K⁺ but at 10⁻⁴ g/ml significantly attenuated the response (fig. 6).

Contraction induced by low concentrations of PGE₁ (2 × 10⁻⁴ and 10⁻³ M) in coronary arteries, contracted with K⁺, was unaffected by PPP (10⁻⁴ g/ml). Relaxation induced by PGE₁ in coronary and mesenteric arterial strips in concentrations ranging from 2 × 10⁻⁴ to 2 × 10⁻⁵ M was not affected by PPP, while the response to 10⁻⁴ M PGE₁ was potentiated (fig. 7).

Modification by Aspirin of Response to PGs

Contractile responses of cerebral arteries to PGF₂α and E₂ were significantly potentiated by treatment for 20 min with aspirin (5 × 10⁻⁵ and 2 × 10⁻⁴ M). This potentiation was reversed by repeated replacement of aspirin-added solutions with control fluids (fig. 8). Similar potentiation was observed in mesenteric arterial strips treated with aspirin. Contractions at 2 × 10⁻⁴ and 10⁻⁵ M PGF₂α were 61.2 ± 10.7% and 100% (1823 ± 213 mg, N = 6), respectively, in control preparations, and 106.7 ± 17.4% and 149.8 ± 20.0%, respectively, in aspirin (2 × 10⁻⁴ M)-treated preparations. Indomethacin (10⁻⁶ M) was also effective in potentiating the response to PGF₂α and E₂. Treatment with aspirin in concentrations of 5 × 10⁻⁵ and 2 × 10⁻⁴ failed to alter significantly the contractile response of cerebral arteries to 25 mM K⁺, but attenuated the response to serotonin in a dose-dependent manner (fig. 9).

Treatment with 2 × 10⁻⁴ M aspirin did not influence the relaxing effect of PGE₁ in cerebral and mesenteric arterial strips contracted with PGF₂α (fig. 10) or with K⁺.

Discussion

The addition of PGF₂α and E₂ caused a dose-related contraction of isolated dog basilar and middle
cerebral arteries, while PGE elicited relaxations. Similar results with PGE and E were observed in isolated dog coronary and mesenteric arteries.  

It has been demonstrated that cerebral vessels are constricted by PGF when applied intraarterially, intravenously or topically to basilar and pial arteries. However, there is conflicting evidence concerning the cerebrovascular effect of PGE and E. PGE injected intraarterially or intravenously causes cerebral vasodilatation in dogs and cats but when applied topically causes vasoconstriction in cats. Yamamoto et al. have demonstrated that PGE decreases cerebral blood flow in dogs, but Steiner et al. and Nakano et al. found the opposite in humans and dogs. Allen et al. have shown a PGE-induced contraction of isolated cerebral arterial segments from humans and dogs, while the present study demonstrated marked relaxation of dog as well as human cerebral arteries in response to PGE. Such an inconsistency in the response of cerebral vessels to PGE is not believed to be due to species difference but possibly to the ability of PGE to induce both contraction and relaxation. In approximately one-third of the cerebral arterial preparations, PGE in low concentrations induced slight but significant contractions. At the highest concentration used (10^-5 M), contractile

**Figure 5.** Inhibition by PPP of the contractile response of mesenteric arterial strips to PGF and E. Contractions induced by 10^-4 M PGF (left figure) or 10^-5 M PGE (right figure) in control media were taken as 100%; mean absolute values with PGF and E were 1636 ± 221 mg (N = 8) and 1417 ± 349 mg (N = 6), respectively.

**Figure 6.** Modification by PPP of the contractile response of dog cerebral arterial strips to 25 mM K+. The absolute contraction induced by 25 mM K in control media averaged 880 ± 190 mg (N = 6).
FIGURE 7. Modification by PPP of the relaxation of coronary and mesenteric arterial strips induced by PGE. Preparations were contracted with K+ (10 to 17 mM). Relaxation induced by 10^-4 M papaverine was taken as 100%; mean absolute values in control and PPP-treated preparations were 983 ± 195 mg (N = 4) and 1283 ± 217 mg (N = 4), respectively, in coronary arteries, and 661 ± 67 mg (N = 7) and 983 ± 119 mg (N = 7), respectively, in mesenteric arteries.

FIGURE 8. Potentiation by aspirin of the contractile response of dog cerebral arterial strips to PGF and E. Contractions induced by 10^-5 M PGF or 10^-4 M PGE (left figure) or 10^-5 M PGF or E (right figure) in control media were taken as 100%; mean absolute values with PGF and E were 1191 ± 279 mg (N = 7) and 871 ± 254 mg (N = 6), respectively. Preparations were exposed for 20 min to aspirin before the addition of PGF or E.
responses appear to be masked by marked relaxation, since treatment with PPP potentiated the relaxation.

The dose-response curve of PGF$_{2a}$ and E$_2$ in dog cerebral arteries is similar to the curves for coronary, mesenteric and femoral arteries. Similar dose-related contractions have been demonstrated by Strong and Bohr with isolated dog peripheral arteries. In contrast, PGE$_1$ induced relaxation relative to that induced by papaverine differed in different arteries. Relaxation of dog as well as human cerebral arteries by PGE$_1$ was less than for dog mesenteric arteries. It seems unlikely that the lower degrees of relaxation are associated with the ability of PGE$_1$ to contract cerebral arteries to a greater extent, since the relaxing effect of PGE$_1$ ($5 \times 10^{-7}$ to $2 \times 10^{-6}$ M) was not significantly influenced by treatment with aspirin or PPP. These were demonstrated in the present study to potentiate or attenuate the response to vasoconstricting PGs, respectively. Further, the difference in PGE$_1$-induced relaxation is not due to the relative unresponsiveness of cerebral arterial strips to vasodilating agents, since NaNO$_2$, adenosine and papaverine cause

![Dose-response curves to serotonin in dog cerebral arteries in the presence and absence of aspirin. Contraction induced by $2 \times 10^{-4}$ M serotonin in control media was taken as 100%; the mean absolute value was 1786 ± 261 mg ($N = 10$).](image)

![Modification by aspirin of the relaxing effect of PGE$_1$ in dog cerebral and mesenteric arteries. Preparations were contracted with PGF$_{2a}$ ($5 \times 10^{-7}$ to $2 \times 10^{-6}$ M) before the addition of PGE$_1$. Relaxation induced by $10^{-4}$ M papaverine was taken as 100%; mean absolute values in control preparations, in aspirin-treated preparations and after wash of preparations were 1000 ± 291 mg ($N = 6$), 1172 ± 247 mg ($N = 6$) and 1227 ± 235 mg ($N = 4$), respectively (left figure), and those in control and aspirin-treated preparations were 811 ± 129 mg ($N = 8$) and 931 ± 79 mg ($N = 8$), respectively (right figure).](image)
cerebroarterial relaxation to a similar or even greater extent than those of peripheral arteries. 19, 20

Contractile responses to PGFs and E2 were not reduced by phentolamine, methysergide and chlorpheniramine, suggesting that alpha-adrenergic, serotoninergic and histaminergic H1 mechanisms are not involved. These results are consistent with those of Strong and Bohr. 21 Relaxation induced by PGE2 was not attenuated by propanolol, atropine, cimetidine and aminophylline, suggesting that beta-adrenergic, cholinergic, histaminergic H2 and adenosine-related mechanisms are not involved. PPP suppressed the response to PGF2α and E2 in a dose-dependent manner, while this antagonist failed to alter the contractile effect of K+. Specific antagonism of PPP to actions of PGF2α and E2 has been demonstrated in isolated rabbit intestine, guinea pig, rat, rabbit and monkey uterus 22 23 and human bronchus. 24 However, the response of human umbilical cord to PGE2 is not specifically attenuated. 25 The findings obtained in the present study and studies with intestine, uterus and bronchus suggest that PGF2α and E2 share the site(s) of action with PPP. However, all mechanisms of action of these PGs on arterial contraction are not necessarily the same, because a PG derivative, 7-oxaprostynoic acid, in concentrations sufficient to reduce the response to PGE2 fails to alter the response to PGF2α. 26 On the other hand, relaxations induced by PGE2 were not influenced by PPP, except the relaxation at 10−4 M, which was potentiated, possibly due to an attenuation of the contractile response. It may be concluded that responses to vasoconstricting PGs (PGF2α, E2 and E1 except for the contraction induced by low concentrations of PGE1) are specifically antagonized by PPP but the response to vasodilating PGs is not influenced.

Aspirin and indomethacin, PG synthesis inhibitors, in concentrations sufficient to inhibit responses of isolated cerebral arteries to bradykinin 27 potentiated the contractile response to PGF2α and E2 but did not influence the relaxing effect of PGE2. Treatment with these concentrations of aspirin failed to alter the contraction induced by K+ but attenuated the contractile effect of serotonin. These findings indicate that aspirin and indomethacin specifically potentiate the action of vasoconstricting PGs but not the action of vasodilating PGE2. It has been postulated that probenecid, indomethacin and aspirin interfere with the active transport of PGs across cell membranes of kidney slices, 26 27 where PGs are metabolized. 28 The potentiation by aspirin as well as indomethacin may be associated with an interference with the metabolism of PGs in arterial smooth muscle cells. Whether the metabolism and the interference by these agents with the metabolism in arteries are observed only with PGF2α and E2 but not with PGE2 remains to be determined. Further, 15-hydroxyprostaglandin dehydrogenase, which inactivates PGs including E2, 29 is inhibited by aspirin and indomethacin. 30 However, the potentiation of contractile responses to PGF2α and E2 may not be related to the inhibition of the enzyme, since the response to PGE2 was unaffected.

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References

Cerebral Arterial Lesions Resulting from Inflammatory Emboli

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SUMMARY  In order to study the effects of septic embolism on the brain, silicone rubber emboli of various types were injected into the carotid arteries of 35 dogs. Pathologic and angiographic studies were performed to assess the resultant arterial and parenchymal lesions.

Pure silicone rubber emboli (14 dogs) produced occasional intra-arterial thrombosis but no arteritis. Sterile and bacterially contaminated emboli containing a lead-chrome pigment (similar to those used in previous studies of septic embolism) (11 dogs) and pure silicone rubber emboli with transversely oriented canals (10 dogs), after brief placement in a bacterial suspension, were associated with intense inflammatory arteritis. This was accompanied by focal meningitis, subarachnoid hemorrhage, thrombosis, and cerebritis of the underlying cortex. The findings resembled those found in mycotic aneurysm. Aneurysmal dilatation was observed in one postmortem angiogram.

In previous models of mycotic aneurysm, the inflammation attributed to bacterial contamination was probably due to the lead-chrome pigment used.

INJECTION of artificial emboli into the cerebral circulation has often been utilized as a means of producing experimental cerebral infarction. Emboli used have included autologous blood clots,1 steel ball bearings,2 psyllium seeds, pigmented silicone rubber compounds with and without a coating of bacteria,3,4 barium-impregnated silicone spheres,5 and others. These studies usually have reported examinations of the resultant parenchymal lesions but little attention has been given to examination of the arterial lesions produced by the emboli. Molinari and associates,6 in their report describing experimentally produced cerebral mycotic aneurysms, injected pigmented silicone rubber cylinders coated with Staphylococcus aureus into the cerebral circulation. They noted polymorphonuclear leukocyte invasion of the vasa vasorum which they theorized preceded inflammatory infiltration of the arterial wall followed by dilatation and formation of aneurysms. No controls

were used with nonpigmented emboli to rule out the possibility of arteritis secondary to the pigment.

The purpose of this study was to evaluate the arterial lesions produced by 3 different types of artificial emboli with or without bacterial contamination.

Methods

Adult mongrel dogs weighing 11.2 to 16.2 kg were anesthetized with intravenous injections of pentobarbital (32 mg/kg of body weight) and, similarly to Molinari's technique, were premedicated with intramuscular injections of 10,000 μg of procaine and benzathine penicillin G. Under sterile conditions, a longitudinal incision was made in the anterolateral portion of the neck and the common carotid and internal carotid arteries were identified. The internal carotid artery was ligated at its origin and a 16-gauge catheter was introduced into it via a transverse arteriotomy. An embolus was then flushed through the catheter with approximately 5 ml of sterile normal saline solution, after which the artery was ligated distally and the catheter was removed.

Emboli were of 3 types: microfil emboli, solid elastic emboli, and canalated Silastic emboli (fig. 1). These emboli were produced as follows:

1. Elastic emboli were produced as follows:

   1. Elastic emboli were produced by using a Silastic catheter (1-2 mm) and introducing microfil. The catheter was then removed, and the microfil was allowed to polymerize and form a solid mass.

   2. Solid elastic emboli were produced by using a Silastic catheter (1-2 mm) and introducing a mixture of silicone rubber and barium sulfate. The catheter was then removed, and the mixture was allowed to polymerize and form a solid mass.

   3. Canalated Silastic emboli were produced by using a Silastic catheter (1-2 mm) and introducing a mixture of silicone rubber and barium sulfate. The catheter was then removed, and the mixture was allowed to polymerize and form a solid mass. The catheter was then reintroduced, and a transverse incision was made in the catheter to create anastomotic canals.

2. Microfil emboli were produced as follows:

   1. Microfil emboli were produced by using a Silastic catheter (1-2 mm) and introducing microfil. The catheter was then removed, and the microfil was allowed to polymerize and form a solid mass.

   2. Microfil emboli were also produced by using a Silastic catheter (1-2 mm) and introducing a mixture of silicone rubber and barium sulfate. The catheter was then removed, and the mixture was allowed to polymerize and form a solid mass.
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