Mechanism of cerebral arterial contraction induced by blood constituents

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In helically cut strips of cerebral, coronary, mesenteric, and renal arteries from dogs, a test solution containing hemoglobin (Hb) and soluble constituents, obtained by exposure of blood clot to distilled water, produced a dose-related contraction. The contraction of cerebral arteries was greater than that of the other arteries. Methemoglobin (metHb) caused only a slight contraction. The contractile response of cerebral arteries to the Hb-containing test solution was attenuated by aspirin (10⁻⁵ to 2 × 10⁻⁴ M), polyphloretin phosphate (PPP, 3 × 10⁻⁵ gm/ml), a prostaglandin (PG) antagonist, and cinanserin (10⁻⁷ M), a serotonin antagonist. Combined treatment with these antagonists suppressed the response to the test solution, but only slightly attenuated contractions induced by K⁺. Phentolamine was ineffective. Contractions of mesenteric arterial strips induced by the test solution were potentiated by aspirin, but were attenuated by PPP and cinanserin. Serum also produced contractions of cerebral and mesenteric arteries, which were attenuated by treatment with cinanserin or PPP. Contractile responses to Hb-containing solution and serum obtained from dogs pretreated with reserpine were weaker than those to the solutions obtained from control dogs. It may be concluded that the Hb-containing test solution releases vasoconstricting PG's from the cerebral arterial wall but vasodilating PG's from mesenteric arteries. The test solution appears to contain vasoconstricting PG's and serotonin. Serum-induced contractions appear to be mediated mainly by serotonin.

KEY WORDS • hemoglobin • arterial contraction • aspirin • prostaglandin • serotonin • blood • arterial spasm

Cerebral arterial spasm following subarachnoid hemorrhage is widely known to be related to blood within the subarachnoid space. The constriction persists when blood is allowed to clot around the artery. Humoral and neural causative mechanisms have been postulated for the blood-induced vasospasm. The contractile response of isolated cerebral arteries of dogs to norepinephrine is only slight as compared with the response to K⁺ and serotonin. Electrical stimulation of the adrenergic nerve innervating the arterial wall produces no or only a slight contraction, and alpha-adrenergic blocking agents do not reverse vasospasm. These findings indicate that the adrenergic mechanism does not appear to be mainly involved in the cerebral vasospasm. Cerebral arterial constrictors, including serotonin, norepinephrine, K⁺, oxyhemoglobin, and prostaglandins (PG's) are suggested as humoral factors; however, systematic analysis of the action of blood clot in relation to these substances has not been made.

Recent studies with humans have demonstrated that aspirin significantly prevents the occurrence of transient ischemic attack and cerebral infarction. Prostaglandins (PG's) may play a significant role in the disturbance of local cerebral circulation under pathological conditions. The present study was thus undertaken to clarify the mechanism of action of soluble constituents of blood on isolated cerebral arteries in the dog by the use of pharmacological antagonists, such as aspirin, polyphloretin phosphate (PPP), cinanserin, and phentolamine. These actions were also compared with those seen in dog mesenteric arteries.

Materials and Methods

Mongrel dogs of both sexes, weighing 7 to 16 kg, were anesthetized with sodium pentobarbital (50 mg/kg intraperitoneally) and sacrificed by bleeding from the common carotid arteries. The brain, heart, kidneys, and superior mesenteric artery were rapidly
removed. Basilar and middle cerebral arteries (0.6 to 0.8 mm in diameter) were isolated from the brain; ventr al interventricular branches of the left coronary artery (0.6 to 0.9 mm in diameter) were isolated from the heart; and intrarenal, interlobar branches of the renal artery (0.6 to 0.8 mm in diameter) were isolated from the kidneys. Distal portions of the mesenteric artery (0.6 to 0.8 mm in diameter) were also isolated.

The arteries were helically cut into strips, approximately 20 mm long. The strips were vertically fixed between hooks in the 20-ml muscle bath containing the nutrient solution, which was maintained at 37 ± 0.5°C and aerated with a mixture of 95% O₂ and 5% CO₂. The hook anchoring the upper end of the strips was connected to the lever of a force-displacement transducer.* The resting tension was adjusted to 1.5 gm, which was determined to be optimal for inducing the maximum contraction. 20 Constituents of the solution were as follows (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. Preparations were allowed to equilibrate for 90 to 120 minutes in the bathing media before the start of experiments.

Under pentobarbital anesthesia, a cannula was inserted into the common carotid artery of the dogs, and blood was collected in a test tube. Blood was left at room temperature for 2 to 3 hours and centrifuged for 15 minutes at 3000 rpm. The supernatant serum was removed. The sediment was washed three times with distilled water, then distilled water of the same volume as that of serum was added. Blood clot in the water was mixed with an electric blender for approximately 5 minutes. After 10 minutes of centrifugation at 3000 rpm, the precipitate was discarded. The supernatant, containing hemoglobin (Hb) and soluble erythrocyte and platelet constituents, was used as a test solution, termed the "Hb-containing solution" in the remainder of this report. Unless otherwise mentioned, this solution and serum were used for the experiments with isolated arteries. The content of Hb was assayed by the hemoglobin-cyanide method 17 with a spectrophotometer at a wavelength of 541 nm. Following the method of Van Assendelft, 20 methemoglobin (metHb) was not detectable in the test solution. Concentrations of the test solution were expressed as final concentrations of Hb in the bathing medium. From some dogs, blood was collected into the test tube containing heparin sodium (10 U/ml blood) in order to prevent blood coagulation. The sediment of heparinized blood was also treated as described above. Hemolysate thus prepared, deprived of platelet constituents, was also used for comparison. Contents of Na⁺ and K⁺ in the Hb-containing solution and serum were assayed by a flame photometer, 4 and the content of Ca²⁺ was assayed by an atomic absorption spectrometer. 5 The osmotic pressure was measured by an osmometer. 6

Eleven dogs were pretreated for 20 to 24 hours with intraperitoneal injections of 0.5 mg/kg reserpine before the experiments were begun. This pretreatment depletes norepinephrine from arteries and abolishes or suppresses the response of mesenteric arteries to tyramine and adrenergic nerve stimulation. 18 As described above, helical strips of cerebral and mesenteric arteries were prepared, and test solutions of blood were obtained.

Isometric contractions were displayed on an ink-writing oscillograph.* Contractile responses to 30 mM K⁺ were first obtained, then preparations were washed three times with bathing medium and equilibrated for 40 to 50 minutes, during which time the solutions were replaced every 10 to 15 minutes. The Hb-containing solution or serum was added directly to the bathing medium in cumulative concentrations. Contractions relative to those induced by 30 mM K⁺ are presented. Preparations had been treated for 60 minutes with PPP and for 20 to 30 minutes with other antagonists before the dose-response relationship of Hb-containing solution or serum was obtained. Results are expressed as mean values ± standard error of the mean. Statistical analyses were made using the Student's t-test. Drugs used were methemoglobin prepared from crystallized dog Hb, 4 acetyl salicylic acid (aspirin), sodium PPP, cinanserin, reserpine, phentolamine mesylate, d-chlorpheniramine maleate, atropine sulfate, dl-propranolol hydrochloride, Sar¹, Ala²-angiotensin II, and hexamethonium bromide.

Results

Effects of Hb-Containing Solution and Serum on Different Arteries

In helically cut strips of cerebral (basilar and middle cerebral), coronary, mesenteric, and renal arteries, the addition of the Hb-containing test solution (0.01 to 1 gm/dl Hb as final concentrations in bathing medium) caused a dose-related contraction. The contraction of

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*Force-displacement transducer manufactured by Nihonkoden Kogyo Co., Tokyo, Japan.

Ink-writing oscillograph manufactured by Sanei Sokki Co., Tokyo, Japan.

Spectrophotometer (Model 100-10) manufactured by Hitachi Co., 2-Sakuragawa-cho, Shibamishikubo, Minato-ku, Tokyo 105, Japan.

\( ^4 \) Flame photometer (Type 775) manufactured by Hitachi Co., 2-Sakuragawa-cho, Shibamishikubo, Minato-ku, Tokyo 105, Japan.

\( ^5 \) Atomic absorption spectrometer (Model 1100) manufactured by Varian Associates Instruments, Palo Alto, California.

\( ^6 \) Osmometer (Model 5100) manufactured by Wescor Inc., Logan, Utah.

\( ^1 \) Crystallized dog hemoglobin obtained from Sigma Chemical Co., St. Louis, Missouri.

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FIG. 1. Dose-response curves for hemoglobin (Hb)-containing test solution (left) and serum (right) in cerebral, mesenteric, coronary, and renal arterial strips. Contractions induced by 30 mM K⁺ were taken as 100%; mean absolute values in these arteries in response to the test solution were 1692 ± 137 mg for 37 cerebral artery specimens, 3099 ± 250 mg for 26 mesenteric artery specimens, 2441 ± 309 mg for 10 coronary artery specimens, and 3068 ± 517 mg for five renal artery specimens; those with serum were 1633 ± 178 mg for 25 cerebral artery specimens, 2511 ± 232 mg for 21 mesenteric artery specimens, 2754 ± 418 mg for five coronary artery specimens, and 2710 ± 481 mg for four renal artery specimens. Vertical bars represent standard error of the mean. Figures in parentheses indicate the number of preparations used.

Cerebral arteries was appreciably greater than that of the other arteries (Fig. 1 left). Responses of basilar and middle cerebral arteries did not significantly differ; mean values of contractions at 1 gm/dl Hb were 154 ± 21.0 for 20 specimens and 110 ± 7.9% for 17 specimens, respectively. The contraction developed shortly after the addition of the solution and stabilized within 1 to 3 minutes. The tension developed by high concentration (1 gm/dl) of Hb-containing solution gradually declined. The median effective dose (ED₉₀) values of the Hb-containing solution in cerebral, coronary, mesenteric, and renal arteries were (gm/dl): 0.22 ± 0.012 (37 specimens), 0.13 ± 0.028 (10 specimens), 0.28 ± 0.006 (26 specimens), and 0.25 ± 0.038 (five specimens), respectively.

Hemolysate obtained from heparinized blood also contracted cerebral arteries; mean values for six specimens at 0.01, 0.1, and 1 gm/dl Hb were 9.0 ± 4.1, 17.2 ± 4.3, and 98.8 ± 4.8%, respectively, relative to contractions induced by 30 mM K⁺. These values were appreciably less than those shown in Fig. 1 left.

Contractile responses of cerebral arteries to dog metHb in concentrations of 0.1 and 1 gm/dl were markedly less than the responses to the Hb-containing solution; in four dogs, contractions at 0.1 and 1 gm/dl metHb were 13.0 ± 3.5 and 19.5 ± 5.1% of contractions induced by the Hb-containing solution in the same concentrations.

The Hb-containing solutions included a mean of: K⁺ 2.99 ± 0.34 mEq/liter, and Na⁺ 51.9 ± 7.6 mEq/liter in four animals; Ca²⁺ was not detectable. Osmotic pressure was 168 ± 23 mOsm/liter. The addition of bathing medium made hypotonic by the addition of distilled water (150 mOsm/liter) in a volume of 2 ml, which was the volume of the Hb-containing solution applied to make the final Hb concentration 1 gm/dl, produced a slight contraction of cerebral arteries (6.3 ± 2.5% in nine specimens, relative to contractions induced by 30 mM K⁺).

The addition of serum (1 to 100 µl/ml) contracted cerebral, coronary, mesenteric, and renal arterial strips in a dose-dependent manner; the contractions of cerebral arteries were significantly greater (Fig. 1 right). Contractions of basilar and middle cerebral arteries did not significantly differ; mean values at 100 µl/ml were 93.2 ± 11.4 in 10 specimens, and 103 ± 9.8% in 15, respectively. The ED₉₀ values of serum in cerebral, coronary, mesenteric, and renal arteries were...
Blood-induced cerebral arterial contraction

**Mechanism of Action of Hb-Containing Solution and Serum**

Cerebral Arteries. The contractile response of cerebral arteries to Hb-containing solution was attenuated by treatment with aspirin (10⁻⁵ and 5 × 10⁻⁶ M) in a dose-dependent manner. Further increases in the concentration to 2 × 10⁻⁴ M did not produce additional attenuation (Fig. 2 left). Similar results were obtained with hemolysate prepared from heparinized blood (three specimens). The effect of aspirin was reversed by repeated washing of preparations. On the other hand, the response to serum was not influenced by aspirin (Fig. 2 right).

Dose-response curves for Hb-containing solution and serum were shifted to the right and downward following treatment for 60 minutes with 3 × 10⁻⁸ gm/ml PPP (Fig. 3).

Treatment with cinanserin (10⁻⁷ M) in a concentration sufficient to suppress the contraction induced by serotonin attenuated the response of cerebral arteries to Hb-containing solution and serum (Fig. 4).

Contractions of cerebral arteries induced by the Hb-containing test solution obtained from the blood of reserpine-pretreated dogs were significantly smaller than those induced by the test solution obtained from control dogs. Cerebral arteries isolated from reserpine-treated dogs responded to the Hb-containing solution obtained from control dogs with similar contractions to those seen in the arteries from control dogs. The results are summarized in Table 1. Greater attenuation was obtained by reserpine pretreatment of the response to serum.

Combined treatment of cerebral arteries with aspirin + PPP, aspirin + cinanserin, or PPP + cinanserin moderately attenuated contractions induced by Hb-containing solutions (Figs. 5 and 6 left). Further attenuation of the contractions was obtained following combined treatment with the three antagonists, aspirin, PPP, and cinanserin (Fig. 6 right), which, however, reduced only slightly the response to 25 mM K⁺ (10.1 ± 3.6% reduction, 10 specimens).

The contractile response of cerebral arteries to the...
Fig. 3. Modification by polyphloretin phosphate (PPP) of the response of cerebral arteries to hemoglobin (Hb)-containing solution (left) and serum (right). Contractions induced by 1 gm/dl Hb and 100 μl/ml serum in control media were taken as 100%; mean absolute values were 1494 ± 289 mg (eight specimens) and 1957 ± 507 mg (seven specimens), respectively.

Fig. 4. Modification by cinanserin of the response of cerebral arteries to hemoglobin (Hb)-containing solution (left) and serum (right). Contractions induced by 1 gm/dl Hb and 100 μl/ml serum in control media were taken as 100%; mean absolute values were 2490 ± 400 mg (six specimens), and 1950 ± 339 mg (six specimens), respectively.
Blood-induced cerebral arterial contraction

**FIG. 5.** Modification by aspirin (2 × 10⁻⁴ M) + cinanserin (10⁻⁷ M) (left) and polyphloretin phosphate (PPP, 3 × 10⁻⁴ gm/ml) + aspirin (right) of the response of cerebral arteries to hemoglobin (Hb)-containing solution. Contractions induced by 1 gm/dl Hb in control media were taken as 100%; mean absolute values were 3069 ± 580 mg for eight specimens (left), and 2857 ± 250 mg for six specimens (right).

**FIG. 6.** Modification by polyphloretin phosphate (PPP, 3 × 10⁻⁴ gm/ml) + cinanserin (10⁻⁷ M) (left) and PPP + cinanserin + aspirin (2 × 10⁻⁴ M) (right) of the response of cerebral arteries to hemoglobin (Hb)-containing solution. Contractions induced by 1 gm/dl Hb in control media were taken as 100%; mean absolute values were 2232 ± 300 mg for six specimens (left), and 2919 ± 538 mg for eight specimens (right).
TABLE 1
Contractile responses of cerebral arterial strips isolated from control and reserpine-pretreated dogs*

<table>
<thead>
<tr>
<th>Groups Studied (artery and blood)</th>
<th>No. of Specimens</th>
<th>Responses (%) to Hb-Containing Solution</th>
<th>K+ (mg)</th>
<th>No. of Specimens</th>
<th>Responses (%) to Serum</th>
<th>K+ (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0.01 gm/dl</td>
<td>0.1 gm/dl</td>
<td>1 gm/dl</td>
<td></td>
<td>1 µl/ml</td>
</tr>
<tr>
<td>control dog artery vs. control dog blood</td>
<td>37</td>
<td>11.9 ± 3.2</td>
<td>35.3 ± 6.2</td>
<td>134 ± 12.3</td>
<td>1692 ± 137</td>
<td>25</td>
</tr>
<tr>
<td>control dog artery vs. reserpinized dog blood</td>
<td>7</td>
<td>4.8 ± 2.6</td>
<td>11.3 ± 5.7</td>
<td>53.9 ± 13.5</td>
<td>1819 ± 224</td>
<td>7</td>
</tr>
<tr>
<td>reserpinized dog artery vs. control dog blood</td>
<td>18</td>
<td>11.0 ± 2.1</td>
<td>20.7 ± 3.5</td>
<td>75.9 ± 6.2</td>
<td>1876 ± 211</td>
<td>18</td>
</tr>
</tbody>
</table>

*Responses to Hb-containing solution and serum obtained from blood of control and reserpinized dogs.
†Mean values of contractions induced by 30 mM K+, which were taken as 100%.
‡Significantly different from values with artery and blood from control dogs, p < 0.001.
§Significantly different from values with artery and blood from control dogs, p < 0.01.

Mesenteric Arteries. Contractions of mesenteric arterial strips induced by Hb-containing solution and serum were potentiated by aspirin in concentrations ranging from 2 × 10⁻⁴ to 5 × 10⁻⁵ M in a dose-dependent manner (Fig. 7). The contractile response to Hb-containing solution (1 gm/dl) and serum (100 µl/ml) was significantly attenuated by treatment with PPP (p < 0.05) (Fig. 8), and suppressed by cinanserin (Fig. 9). Pretreatment of dogs with reserpine abolished almost completely the responses to the Hb-containing solution and serum (Fig. 10). Phentolamine (10⁻⁷ M) and chlorpheniramine (10⁻⁶ M) did not reduce the response of mesenteric arteries to the Hb-containing solution and serum.

Discussion
The present study revealed that the Hb-containing test solution obtained by exposure of blood clot to distilled water caused a greater contraction in dog cerebral arteries than in the other arteries tested. The test solution was hypo-osmotic; however, the effect of osmolarity was only minimal. K⁺ and Ca²⁺ are not involved, because the amount of K⁺ and Ca²⁺ contained in the test solution was less than that contained in the bathing medium. Dog metHb produced only a slight contraction, and the test solution did not contain measurable amounts of metHb. These findings indicate that contractions induced by the Hb-containing solution are mainly ascribed to actions of oxyhemoglobin and other soluble erythrocyte and platelet constituents.

The influence of antagonists on the contractile response of cerebral and mesenteric arteries to the Hb-containing solution and serum is summarized in Table 2. The contractile response of cerebral arteries to Hb-containing solutions was attenuated by aspirin, a cyclooxygenase inhibitor, and by PPP, a PG antagonist, in a concentration that does not significantly inhibit the contraction induced by K⁺. Aspirin potentiates contractile responses of dog cerebral arteries to exogenously applied PG's F₂α and E₂, and PPP suppresses contractions induced by PG's F₂α, E₂, and H₂, but does not affect dilations induced by PG's E₁ and I₁. These findings may indicate that Hb-containing solutions stimulate the synthesis of vasoconstricting PG's in the cerebral artery wall, which are released to contract the arterial smooth muscle. Heme-containing substances, such as Hb and hematin, function as co-enzymes of PG endoperoxide synthetase and promote the synthesis of PG's. Hagen, et al., have actually demonstrated the synthesis of PG's F₂α and E₂ from arachidonic acid in the cerebral arteries of pigs, and concluded that cerebral vessels can be a source of vasoconstricting PG's, which may be important in the pathogenesis of cerebral vasospasm. On the other hand, contractions of cerebral arteries induced by serum were not influenced by aspirin but were attenuated by PPP, suggesting that serum does not possess the ability of stimulating the synthesis of PG's, but contains vasoconstricting PG's.

Cerebral artery contractions induced by the Hb-containing test solution and serum were attenuated or suppressed by cinanserin in this study or by methysergide in concentrations sufficient to suppress the response to serotonin, a powerful cerebral artery...
Blood-induced cerebral arterial contraction

**Fig. 7.** Modification by aspirin of the response of mesenteric arterial strips to hemoglobin (Hb)-containing solution (left) and serum (right). Contractions induced by 1 gm/dl Hb and 100 μl/ml serum in control media were taken as 100%; mean absolute values were 1053 ± 276 mg (18 specimens) and 1352 ± 280 mg (16 specimens), respectively. The following were significantly different from control: at 1 gm/dl Hb in the presence of 2 × 10⁻⁶, 10⁻⁵, and 5 × 10⁻⁵ M aspirin, p < 0.001; at 100 μl/ml serum in the presence of 10⁻⁵ and 5 × 10⁻⁵ M aspirin, p < 0.001.

**Fig. 8.** Modification by polyphloretin phosphate (PPP) of the response of mesenteric arteries to hemoglobin (Hb)-containing solution (left) and serum (right). Contractions induced by 1 gm/dl Hb and 100 μl/ml serum in control media were taken as 100%; mean absolute values were 1772 ± 236 mg (eight specimens), and 2380 ± 496 mg (seven specimens), respectively.
FIG. 9. Modification by cinanserin of the response of mesenteric arteries to hemoglobin (Hb)-containing solution (left) and serum (right). Contractions induced by 1 gm/dl Hb and 100 μl/ml serum in control media were 2332 ± 418 mg (six specimens) and 1950 ± 339 mg (six specimens), respectively.

FIG. 10. Dose-response curves for hemoglobin (Hb)-containing solution (left) and serum (right) obtained from blood of control and reserpine-pretreated dogs in mesenteric arteries isolated from control and reserpinized dogs, respectively. Contractions induced by 30 mM K⁺ were taken as 100%; mean absolute values with Hb-containing solution obtained from control and reserpinized dogs were 3009 ± 250 mg (26 specimens) and 2690 ± 362 mg (13 specimens), respectively, and those with serum from control and reserpinized dogs were 2511 ± 232 mg (21 specimens) and 2581 ± 376 mg (12 specimens), respectively.
Blood-induced cerebral arterial contraction

TABLE 2
Effects of antagonists on the response to blood constituents of dog cerebral and mesenteric arteries*

<table>
<thead>
<tr>
<th>Antagonist &amp; Concentration</th>
<th>Response of Cerebral Artery</th>
<th>Response of Mesenteric Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hb Serum</td>
<td>Hb Serum</td>
</tr>
<tr>
<td>cinanserin (10^-7 M) PPP</td>
<td>(-) (-)</td>
<td>(-) (-)</td>
</tr>
<tr>
<td>aspirin (2 X 10^-4 M) + PPP</td>
<td>(-) (-)</td>
<td>(-) (-)</td>
</tr>
<tr>
<td>reserpine + cinanserin</td>
<td>(-) (-)</td>
<td>(-) (-)</td>
</tr>
<tr>
<td>mechanism involved</td>
<td>sero. sero. sero. sero.</td>
<td>sero. sero. sero. sero.</td>
</tr>
<tr>
<td>release from artery PG's</td>
<td>PG's PG's PG's PG's</td>
<td>PG's PG's PG's PG's</td>
</tr>
</tbody>
</table>

*PPP = polyphloretin phosphate; reserpine = blood from reserpine-pretreated dogs; Hb = hemoglobin-containing test solution; I = 11% to 40% inhibition; II = 41% to 70% inhibition; III = 71% to 100% inhibition; (-) = no change; I = potentiation; sero. = serotonin; V-const. = vasoconstricting; V-dil. = vasodilating; PG's = prostaglandins. Inhibition of contractions induced by Hb-containing solution and serum at ED50 was calculated.

Combined treatment with aspirin, PPP, and cinanserin suppressed the contractile response of the cerebral arteries to the Hb-containing solution, but attenuated only slightly the response to K+. These results again support the hypothesis that vasoconstricting PG's and serotonin are mainly involved in the genesis of contractions induced by Hb-containing solution. Histamine and angiotensin II produce contractions in cerebral arteries. Chlorpheniramine, Sar1, Ala6-angiotensin II were ineffective in attenuating the response to Hb-containing solution, suggesting that histaminergic H1 and angiotensin-related mechanisms are not involved.

The contractile response of mesenteric arteries to the Hb-containing solution was potentiated by treatment with aspirin but attenuated by PPP. The contractions induced by the addition of PG's F2α and E2 are potentiated by aspirin but are inhibited by PPP. These findings suggest that the Hb-containing solution includes vasoconstricting PG's and releases vasodilating PG's synthesized in the vascular wall. The involvement of synthesized PG's is postulated from the contrast effects of aspirin on cerebral and mesenteric arteries. Heterogeneity in the response of a variety of arteries to the Hb-containing solution (Fig. 1 left) may be associated with the ability of the solution to release vasodilating (mesenteric arteries) or vasoconstricting PG's (cerebral arteries) from the arterial wall. Results with cinanserin, phenolamine, and reserpine pretreatment indicate that contractions of the mesenteric arteries induced by Hb-containing solution and serum are due partly to serotonin, but are not related to the alpha-adrenergic mechanism.

In summary, it is postulated that the Hb-containing solution elicits contractions in the cerebral arteries mainly by the release of vasoconstricting PG's from the arterial wall and by the action of vasoconstricting PG's and serotonin contained in the solution (Table 2). Vasoconstrictor actions of the latter two on mesenteric arteries appear to be counteracted by the release of vasodilating PG's. Vasodilating PG1α and vasoconstricting PG's F2α and E2 are synthesized in the arterial wall. Possible conversion from PGH2 to PG1α, and the relaxant effects of PG1α, are appreciably less in cerebral arteries than in mesenteric arteries. PGD2 contracts dog cerebral arteries but, in contrast, relaxes mesenteric arteries (unpublished data). Serum-induced contractions appear to be due mainly to serotonin present in the serum (Table 2). Heterogeneity in the response of dog arteries to serum (Fig. 1 right) may be explained by the fact that contractions induced by serotonin are greater in dog cerebral arteries than in the other arteries.

References

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