THE CONFLICT of data found in the literature suggests that more than one nervous mechanism with receptors in the lesser circulation may contribute to the control of systemic blood pressure. The experiments reported here are of interest because they describe a reflex which causes constriction of systemic arteries in response to changes of pressure in the pulmonary artery and its bifurcation.

Methods

Fifteen mongrel dogs, anesthetized with intravenous injections of either sodium pentobarbital (25 mg./Kg.) or chloralose (80 mg./Kg.), were subjected to a transverse, sternum-splitting thoracotomy at the fourth intercostal space. The animals were air-ventilated through a cuffed endotracheal tube by means of intermittent positive pressure from a Harvard respirator pump. Systemic arterial pressure was recorded by a Statham transducer (P23G) on a direct-writing oscillograph recorder. The animals were heparinized (1.5 mg./Kg.). Venous blood was diverted to a common blood reservoir from the three great veins, and the systemic circulation maintained by pumping oxygenated blood into a femoral artery (Kay-Cross oxygenator with roller pumps). Coronary venous blood was removed from the right heart, and pulmonary collateral blood from the left atrium, by drainage tubes inserted via the atrial appendages. Since the right ventricle was drained, coronary venous blood did not accumulate in it, and, for this reason, the pressure in the right ventricle remained below normal. A 30-ml. balloon-tipped Foley catheter was inserted through a stab wound in the right ventricle which was controlled by a purse-string and threaded into the desired position in the pulmonary artery. Separate perfusion of the greater and lesser circulation was performed in some experiments with a method described elsewhere. The pulmonary artery was distended by inflating the balloon with volumes of air ranging from 5 to 30 ml. Pressures in the balloon were measured when inflated with identical volumes of air before insertion (at 37 C.) and while in position in the pulmonary artery. The balloon was inflated during periods when the pulmonary blood flow was equal to the systemic flow (heart-lung machine) or to some fraction thereof. In five dogs, the position of the Foley catheter was varied; in three, the balloon was inflated first in the right ventricle and later in the main pulmonary artery. In two dogs, the balloon was inflated in the right or left pulmonary artery between control inflations in the main pulmonary trunk. In one dog, the balloon was inflated in the pulmonary artery before and after bilateral lung embolization with fine sand (average diameter of 300 /m).

Other balloons were inserted into the right atrium and left ventricle (three experiments) so that these chambers could be distended simultaneously with the pulmonary artery. Changes in the venous return were estimated by observations of the blood reservoir level during constant systemic blood flows. In two dogs, right ventricular pressure and heart rate were recorded by a cannula inserted via the azygos vein. Vagotomy was performed high in the neck in some experiments. Atropine (0.8 mg.) was used to block parasympathetic responses in two dogs, while phen tolamine (Regitine, 5 mg.) was used to block sympathetic responses in another dog. In two dogs, local injections of 2 per cent lidocaine (Xylocaine, 3 ml.) were used to block receptor sites in the wall of the main pulmonary artery.

In four additional experiments, snares were placed with a minimum of dissection around the right and left pulmonary arteries, and a cannula was tied into the main pulmonary artery so that the pulmonary artery and its bifurcation could be filled with blood at known pressures, recorded from a sidearm of the cannula. In two of these experiments, the snares that occluded the bifurcation were released periodically to allow injection of 6.0 Gm. of plastic microspheres (mesh sizes 40/50) in six equally divided doses.
Table 1

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Number of observations</th>
<th>Increase in SAP (mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>22</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>11</td>
<td>4</td>
<td>20</td>
</tr>
</tbody>
</table>

*Mean values given for systemic arterial pressure (SAP). Inflated balloon contained 18 to 28 ml. of air.

Results

At constant flow, the systemic arterial pressure increased 7 to 22 mm. Hg whenever the pulmonary artery was suddenly distended by balloon inflation (table 1, fig. 1). When the pulmonary balloon was deflated, the systemic arterial pressure returned to the control level. Changes in the systemic pressure were seen irrespective of the presence or absence of blood flow through the pulmonary circuit. Variations in pulmonary flow after distention of the balloon did not alter the rise of the systemic arterial pressure. This remained elevated as long as the balloon was inflated (maximum of six to seven minutes). The increase in systemic arterial pressure could not be elicited when the balloon was distended in either the right or left branches of the pulmonary artery or in the right ventricle. Extreme distention of the right atrium or moderate distention of the left ventricle (vis-

Figure 1

Effect of pulmonary-artery stretch upon systemic arterial pressure at constant systemic flow. Balloon positioned in main pulmonary artery. Note elevated systemic arterial pressure during balloon inflation; (PABP) outside dog's body = 310 mm. Hg. (SAP) = systemic arterial pressure, (PABP) = pulmonary-artery balloon pressure.

**Figure 1**

Effect of pulmonary-artery stretch upon systemic arterial pressure at constant systemic flow. Balloon positioned in main pulmonary artery. Note elevated systemic arterial pressure during balloon inflation; (PABP) outside dog's body = 310 mm. Hg. (SAP) = systemic arterial pressure, (PABP) = pulmonary-artery balloon pressure.
sence of pulmonary flow, suspensions of small emboli were rapidly injected into the lung vessels (three experiments); after embolization, the systemic arterial pressure fell progressively; distention of the pulmonary artery did not raise the systemic pressure after this had fallen below 60 mm. Hg mean pressure.

**Discussion**

Reflexes from the pulmonary blood vessels to the systemic circulation have been studied since 1935 and were reviewed in 1955. Some authors found peripheral vasodilation after experimental maneuvers that increased pulmonary-artery pressure. Systemic vasodilation was followed by systemic vasoconstriction in the embolization experiments of Binet and Burstein. Williams observed no change of systemic resistance after pulmonary emboli. Parhofer et al. injected large clots of autogenous blood into the pulmonary system and attributed the resultant systemic vasoconstriction to anoxia. Baroceptors localized in the region of the pulmonary bifurcation have been discovered in dogs by Coleridge and Kidd and in cats by Bianconi and Green. The literature does not contain unequivocal evidence that systemic vasoconstriction can be elicited by reflexes from the lesser circulation.

The experimental arrangement described here permitted us to distinguish reflexes that arise in the main pulmonary artery and its bifurcation from those in the rest of the pulmonary vascular tree. Since the systemic flow was kept constant, any variation of the systemic arterial pressure must have been caused by changes of systemic arterial vasomotor tonus.

The balloon was inflated in the main pulmonary artery with volumes of air ranging from 18 to 28 ml. When similar volumes of air were injected into the balloon outside the body, pressures of 250 to 350 mm. Hg were recorded in it. Measurement or evaluation of the forces applied to the pulmonary artery was not attempted because the vessel was not stretched uniformly by the balloon: the applied forces were maximal at the "equator" of the balloon and minimal at the "poles."

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>Number of observations</th>
<th>PAP (mm. Hg)</th>
<th>Increase in SAP (mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>5</td>
<td>150</td>
<td>15</td>
</tr>
<tr>
<td>13</td>
<td>1</td>
<td>250</td>
<td>25</td>
</tr>
<tr>
<td>14</td>
<td>12</td>
<td>80-100</td>
<td>15</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>90</td>
<td>7</td>
</tr>
</tbody>
</table>

*Placing of snares had caused previous increases of systemic arterial pressure (SAP) amounting to 10 to 20 mm. Hg. Note additional increments of SAP after pulmonary-artery distention.

For this reason, we cannot claim that pulmonary-artery stretch is a physiological mechanism that contributes to the reflex regulation of blood pressure. Neither can a physiological role of the "pulmonary-artery—stretch reflex" be postulated from our experiments that distended the vessel with blood. The act of tightening the pulmonary-artery snares had already caused marked increases in the systemic arterial pressure even when the pulmonary vessels were empty; further increases of the systemic arterial pressure became evident only when the pressure in the isolated pulmonary-artery segment was grossly unphysiological (80 to 200 mm. Hg). Reflexes originating from the "pulmonary-artery receptors" at more physiological pressure levels may well have been masked by vasomotion, which occurred during the preliminary tightening of the snares.

The effect of local anesthesia of the pulmonary-artery wall is evidence of receptor sites in this area. Peripheral vasoconstriction was not seen after stretching vessels beyond the bifurcation, which confirms the finding of Coleridge and Kidd, who did not observe baroceptors beyond the bifurcation. The vagus was identified as the pathway for the reflex described here and the effect of phentolamine argues for its transmission to the effector sites by sympathetic pathways.

In our experiments, systemic vasodilation (fall of systemic arterial pressure with constant systemic flow) was seen after injecting small particles into the lung vessels. The complex pattern of interdependent reflexes that
regulate blood pressure may embody the new phenomenon described here, since it is able to overcome opposing reflexes from baroceptor regions but, in turn, appears to be superseded by reflexes from small pulmonary vessels.

Summary

In open-chest dogs, the greater and lesser circulations were perfused by a system of pumps and oxygenator. All blood was drained from the right heart and from the left atrium. In most experiments, there was no dissection around the pulmonary hila, the aorta, or the pulmonary artery. A 30-ml. balloon (Foley catheter) was inserted into the pulmonary artery through a stab wound in the wall of the right ventricle. Pressures were recorded in the pulmonary-artery balloon and in a femoral artery. In other experiments, the main pulmonary artery was distended with blood at known pressures after hydraulic isolation with ligatures and snares.

When the main pulmonary artery was distended proximal to its bifurcation, constriction of the systemic arteries occurred. This phenomenon was abolished by local anesthesia of the wall of the main pulmonary artery, by interrupting conduction in the vagi, by a sympatholytic drug, and by reflex systemic hypotension elicited by multiple small pulmonary emboli. The pressor reflex from the pulmonary artery to the systemic circulation was not influenced by changes of pulmonary blood flow or by inflation of other balloons in various chambers of the heart. Limitations inherent in the experimental procedure did not permit us to assign physiological significance to the phenomenon.

References

Stretch Reflexes from the Main Pulmonary Artery to the Systemic Circulation
RICHARD J. LEWIN, CECIL E. CROSS, P. ANDRE RIEBEN and PETER F. SALISBURY

Circ Res. 1961;9:585-588
doi: 10.1161/01.RES.9.3.585

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1961 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/9/3/585

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/