FUNCTIONALLY significant intercoronary anastomoses, greater than 40 μ in diameter, are not present usually in normal human hearts according to several investigators. Other observers have concluded that intercoronary anastomoses may possess diameters ranging from 70 to 300 μ in normal hearts when there was no associated disease affecting the coronary arteries or the myocardium. Reiner and his associates stated that significant anastomoses were present in 78% of full-term neonates and further suggested that these collateral channels involute during childhood in the absence of stimuli known to further their development. In congenital heart disease the known stimuli of cardiac hypertrophy, anoxia, and anemia are present in various combinations. A group of congenital heart cases also offers some specimens that have been subjected to the trauma of surgical intervention—a factor which may also play a role in the development of intercoronary anastomoses but to date no reports considering it have been made. Thus, the present study comprises observations on cases of congenital heart disease with attention given to the possible influences of cardiac hypertrophy, anoxia, anemia, and operative trauma on the development of intercoronary anastomoses in the pediatric age group.

Methods

Thirty-five cases of congenital heart disease, ranging in age from one day to 19 years, were selected for investigation with the use of Pitt's method. Twenty cases, varying in age from 0 (3 stillbirths) to 14 years, were chosen randomly from the pediatric autopsy material to serve as controls.

Four wax-sphere suspensions were prepared by adding 3 mg of the appropriate sized spheres to 1 liter of normal saline. One milligram of Alcolox was added to each liter of solution to enhance the uniformity of suspensions. The range of sphere sizes in the four suspensions were 20 to 25 μ, 37 to 44 μ, 63 to 74 μ, and 100 to 120 μ.

The hearts were removed from the cadavers within 24 hours after death. The aorta was dissected free from the pulmonary artery, and ligatures were placed under the coronary arteries within a few millimeters of their ostia. Small polyethylene cannulas were inserted into the left and right coronary arteries via their aortic ostia and tied in place with the ligatures. The specimen was suspended on a perfusion board by means of a pin through the pulmonary veins. The injection apparatus was similar to that used by Pitt.

One coronary artery (right or left) was perfused with 100 ml of normal saline while the washings from the other coronary cannula were filtered through a layer of Seitz no. 50 filter paper. If necessary the direction of perfusion could be changed to ensure adequate flow.

After the coronary arteries were flushed with 100 ml of normal saline, alternate perfusions of 50 ml of wax-sphere suspension and normal saline into the coronary artery cannula were performed until all four wax-sphere suspensions had been perfused. The washings were collected on individually labeled filter papers. Perfusion pressure, monitored by a mercury manometer, was kept constant at 100 mm. The filter papers were next allowed to dry at room temperature and then were examined under a light microscope for the wax spheres. The presence of several spheres per low-power field was considered evidence for the existence of interarterial anastomoses of that minimum size. Statistical analysis, including the chi-square test, was carried out according to Bailey.

Results

Normal Hearts and Intercoronary Anastomoses

Criteria. In the 20 control cases a survey of

*Obtained from Dr. H. Emmenegger, Sandoz Inc., Basel, Switzerland.
the clinical histories and autopsy findings revealed the absence of such stimuli as cardiac hypertrophy, anemia, and hypoxia. Absence of the latter is confirmed by the absence of cyanosis or the presence of a normal arterial oxygen saturation or both. Also no cardiac or coronary artery disease was present at post-mortem examination.

Findings. In the 20 control hearts (table 1) the intercoronary anastomoses range in size from 20 to 74 μ. In only five cases, including one stillbirth, did the 63 to 74 μ spheres fail to pass whereas in no instance did the largest wax spheres, 100 to 120 μ, pass. In contrast to Reiner's observations, the size and frequency of the intercoronary anastomoses were the same in the first and second decades of our control group. Finally, the mean age of the control group, 4.2 ± 0.9 (SE) years, was not significantly different (p > 0.4) from that of the congenital heart group.

Congenital Heart Disease and Intercoronary Anastomoses

Criteria. The clinical histories and autopsy findings were surveyed for the presence or absence of such stimuli as hypoxia, cardiac hypertrophy, and anemia. Hypoxia was considered present if cyanosis was evident clinically or if the systemic arterial oxygen saturation was less than 85 per cent. Cardiac hypertrophy was based on total heart weight. If the specimen deviated more than 2 standard deviations from the normal mean values listed by Gruenwald and Minh or more than 20 per cent from the appropriate normal weights listed by Coppoletta and Wolbach, cardiac hypertrophy was considered to be present. The prosectors' observations confirmed the quantitative estimations in all instances. Anemia was considered present if the hemoglobin level was less than 10.2 Gm. per cent or the hematocrit level was 32 or less. This is in accordance with the criteria of Zoll and associates.

Findings. There was an association (χ² = 14.27; p < 0.001) between the large anastomoses and the congenital heart group with 19 of the 35 congenital hearts possessing intercoronary anastomoses which were at least 100 to 120 μ in diameter (table 1). Of the remaining 16 cases, only four did not pass the 63 to 74 μ spheres.

Effects of Hypoxia (Table 2)

Even though the mean age of the acyanotic group, 6.3 ± 1.9 (SE) years, was significantly greater (p < 0.01) than that of the cyanotic group, 1.5 ± 0.5 (SE) years, no significant difference (χ² = 0.004; p > 0.9) in the size and frequency of the anastomoses was noted between the cyanotic and acyanotic cases. Eleven of 21 (53 per cent) cyanotic cases and 8 of the 14 (57 per cent) acyanotic cases had anastomoses greater than 100 μ in diameter.

Effects of Cardiac Hypertrophy and Anemia

The effects of cardiac hypertrophy on intercoronary anastomoses in congenital heart disease can not be evaluated, since 32 of the 35 (92 per cent) congenital hearts had cardiac hypertrophy. In the three cases in which cardiac hypertrophy was absent the intercoronary anastomoses were at least 100 μ in diameter.

Table 1

<table>
<thead>
<tr>
<th>Incidence and Size of Intercoronary Anastomoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Congenital hearts</td>
</tr>
<tr>
<td>Control hearts</td>
</tr>
</tbody>
</table>

*The largest anastomoses in this category were at least 100 μ in diameter, since the largest wax spheres perfused were 100 to 120 μ in diameter.
†The youngest cases were 1 day of age in the congenital heart group; the controls included three stillbirths.
INTERCORONARY ANASTOMOSES

Table 2

Effects of Hypoxia on the Size and Frequency of Intercoronary Anastomoses in Congenital Hearts

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cases</th>
<th>Size of intercoronary anastomoses</th>
<th>Age (in years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>20-74 μ</td>
<td>20-120 μ</td>
</tr>
<tr>
<td>Cyanotic</td>
<td>21</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Acyanotic</td>
<td>14</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

Only two cases, in which cardiac hypertrophy was also present, showed the presence of anemia. The intercoronary anastomoses in these two hearts range in size from 20 to 74 μ.

Effects of Surgical Intervention (Table 3)

Fifteen of the congenital heart cases had never been subjected to any surgical procedure while the remaining 20 cases had undergone some form of definitive open or closed-heart surgical repair. There was an association (x² = 14.97; p < 0.001) between the presence of large anastomoses, greater than 100 μ, and the operated group. However, the duration of postoperative survival does not appear to influence the size of intercoronary anastomoses, for in the three cases having anastomoses less than 100 μ in diameter, two died within 48 hours of the operative procedure while the third survived for 5 months. In 17 cases having interarterial anastomoses greater than 100 μ in diameter, eight died within 48 hours of the surgical procedure; the other nine survived for periods ranging from 5 weeks to 3 years. It is also unlikely that age may be influencing these results, since the higher mean age of the operated group, 5.1 ± 1.4 (SE) years, was not significantly different (p > 0.1) from that of the nonoperated group, 1.9 ± 1.3 (SE) years.

Effects of Age (Table 4)

In table 4 the size and frequency of intercoronary anastomoses have been tabulated for the various ages of the congenital heart group in a manner similar to the one used by Reiner et al.9 The frequency of the largest anastomoses, greater than 100 μ, is similar in the 0-1 year and the 1-5 years groups (x² = 0.042; p > 0.9). However, the presence of the large anastomoses in all congenital heart cases greater than 5 years of age suggests that the intercoronary anastomoses in congenital hearts increase in size with increasing age. This hypothesis, when tested, is of significance (x² = 8.97; p < 0.02).

Discussion

Although Schlesinger and associates9, 3 and Pitt4 concur in the view that intercoronary anastomoses in normal hearts are not usually greater than 40 μ in diameter when there is no associated disease affecting either the coronary arteries or the myocardium, contrary evidence exists. Prinzmetal and associates,8 using calibrated glass beads, concluded that intercoronary anastomoses in normal hearts may have diameters ranging from 70 to 180 μ. Baroldi and others,6 Bellman and Frank,6 and Laurie and Woods7 stated that interarterial anastomoses in normal human hearts may

Table 3

Effects of Surgical Intervention on the Size and Frequency of Intercoronary Anastomoses in Congenital Hearts

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cases</th>
<th>Size of intercoronary anastomoses</th>
<th>Age (in years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>20-74 μ</td>
<td>20-120 μ</td>
</tr>
<tr>
<td>Nonoperated</td>
<td>15</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Operated</td>
<td>20</td>
<td>3</td>
<td>17</td>
</tr>
</tbody>
</table>

Circulation, Volume XXXIII, February 1966
have diameters as large as 300 μ. In view of these findings along with those of Reiner and colleagues⁹ and our observations with Pitt's method⁹ on neonate and infant hearts not subjected to the stimuli of hypoxia, anemia, or cardiac hypertrophy, it seems likely, as James¹⁶ and Bloor and Liebow¹⁷ concluded, that the arbitrary designation of 40 μ as the upper limit of size for normal intercoronary anastomoses is probably too conservative. Our findings in the control hearts, however, did not support Reiner's contention⁹ that "good intercoronary anastomoses" involute during the first decade and reappear during the second decade. Instead, the size of the intercoronary anastomoses in the controls remains constant throughout childhood.

In those congenital hearts not subjected to surgical procedures, no marked difference was noted from the control group with respect to the size and frequency of intercoronary anastomoses. Despite the presence of known stimuli for the expansion of interarterial coronary anastomoses, namely, hypoxia,¹⁰ cardiac hypertrophy,¹⁰ and anemia,¹⁰–¹² only two cases had anastomoses greater than 100 μ in diameter. The low mean age of this group, 1.9 ± 1.3 (SE) years, suggests that the known stimuli require a minimum duration of action before their effects, namely, an increase in the size and frequency of the anastomoses, can be observed. The fact that only the largest anastomoses, at least 100 μ in size, were observed in those congenital hearts greater than 5 years of age also supports this contention.

The marked increase in frequency of the largest intercoronary anastomoses in the operated group is interesting. Cardiac hypertrophy is present in each case of this group and may be a sufficient stimulus. However, surgical trauma warrants consideration as a possible stimulus. The fact that there is little difference in the size and frequency of the anastomoses observed in those cases dying within 48 hours of operation when compared to those living for more than 5 weeks after operation suggests that operative trauma alone has little effect on collateral expansion. Thus the increased incidence of large anastomoses in the operated group and the higher mean age of this group may be additional evidence that intercoronary anastomoses in congenital heart disease increase in size with increasing age. Large intercoronary anastomoses are certainly present at birth in some cases of congenital heart disease, whereas in those cases lacking large anastomoses at birth, the presence of known stimuli for collateral expansion may result in the appearance of these large anastomoses at older ages.

**Summary**

Thirty-five cases of congenital heart disease were investigated for the frequency and size of intercoronary anastomoses. Studies of control hearts showed normal intercoronary anastomoses to range to 74 μ in diameter. In those congenital hearts not subjected to surgical procedures, the anastomoses did not differ in size from the control group, even in the presence of anemia, cardiac hypertrophy, and cyanosis. However, the mean age of the cyanotic group was significantly less than the acyanotic group. Even though the size and frequency of the anastomoses were significantly increased in the operated group, surgical trauma alone was an unlikely stimulus, since the size and frequency of anastomoses in those dying within 48 hours of operation and in those surviving for more than 5 weeks were similar. There was also a significant increase in the frequency and size of the intercoronary anastomoses in cases greater than 5 years of age, implying that intercoronary communications in congenital heart disease increase in size with increasing age.

**References**


*Circulation, Volume XXXIII, February 1966*
To sum up, as the natural foundation of experimental medicine, experimental physiology cannot suppress observation of the sick or lessen its importance. Moreover, physiological knowledge is not only indispensable in explaining disease, but is also necessary to good clinical observation. For example, I have seen observers surprised into describing as accidents certain thermal phenomena which occasionally result from nerve lesions; if they had been physiologists, they would have known how to evaluate morbid symptoms which are really nothing but physiological phenomena.—Claude Bernard: An Introduction to the Study of Experimental Medicine. New York: The Macmillan Company, 1927, p. 200. Centenary of First Publication, 1865.
Intercoronary Anastomoses in Congenital Heart Disease
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