Congenital Cardiovascular Anomalies in Twins

By Lucille J. Ross, M.D.

An attempt was made to derive information about the types of mechanisms that can produce congenital cardiovascular anomalies from a study of twins. The presence or absence of a cardiovascular malformation in the twins and in their siblings, and the zygosity of each twin pair were determined.

GREAT advances have been made during the past 2 decades in methods of diagnosing congenital cardiovascular lesions, and in concepts and techniques of their surgical correction. There has been almost no progress, however, in the prevention of such defects because of the paucity of knowledge about their causes. The anomalies in humans appear to be genetically determined in certain instances and to be caused by an agent, such as the rubella virus, in the intrauterine environment on occasion; but in the majority of cases the etiologic factor is not known. It was hoped that a study of twins with congenital cardiovascular disease might clarify the cause of the anomalies, since twins are thought to be exposed to a relatively similar intrauterine environment, and monozygotic twins have an extremely similar genetic endowment.

A number of twins with congenital cardiovascular disease have been described. Unfortunately, at the time that some of the reports were written, the criteria for determining both the zygosity and the presence or absence of cardiovascular lesions were less rigid than currently. Table 1 summarizes the literature describing those pairs for which the diagnosis of zygosity seems valid. They have been divided into monozygotic pairs (those derived from 1 fertilized ovum) and dizygotic pairs (those derived from 2 fertilized ova). Table 1 also indicates which references describe twin pairs that were concordant for congenital cardiovascular disease (both co-twins affected), and which report discordant pairs (only 1 twin of the pairs had congenital heart disease).

Separate mention is made of twins having dextrocardia, either with45-47 or without48-56 another cardiac anomaly. Doolittle44 reported 2 opposite-sex pairs; all the others were same-sex pairs. Three pairs45, 49, 50 were concordant for dextrocardia.

Uchida and Rowe57 reported the first study of a series of twins with congenital heart disease. Following rigid criteria in determining zygosity, they observed 13 monozygotic and 13 dizygotic pairs. Only 1 member of each of their twin pairs was affected.

METHODS

A number of individuals associated with different health agencies throughout New York City suggested possible subjects for this investigation. Those twin pairs for which the zygosity could be determined and the presence or absence of a congenital cardiovascular anomaly could be established for each twin, were selected for inclusion in this study. The cases therefore do not represent a statistically random sample, and consequently the number of dizygotic pairs should not be compared with the number of monozygotic pairs, nor should the proportion of concordant pairs in each group be considered.

Insofar as possible, the investigation of each twin pair included the following data:

History

Family History. The family history was obtained from one or both parents, with particular inquiry about multiple births, congenital abnormalities in any relative, and consanguinity. The mother's gynecologic and obstetric history was elicited with emphasis on menstrual irregularities, abortions, prematurely born babies, and complications of pregnancies or deliveries. The mother was asked specifically whether she had, to her knowledge, any chronic anemia; pulmonary, renal, cardiovascular, thyroid, or psychiatric disease; and whether she had ever received radiotherapy. Only superficial inquiry was made about the father's health; we did not routinely ask about irradiation of the father.
TABLE 1.—Review of Literature on Twins with Congenital Cardiovascular Lesions

<table>
<thead>
<tr>
<th>Zygosity</th>
<th>Criteria upon which zygosity-determination was based</th>
<th>Bibliographic references to Probably concordant pairs</th>
<th>Probably discordant pairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dizygotic</td>
<td>Opposite-sex</td>
<td>2</td>
<td>1, 3, 4, 5 (3 pairs), 6</td>
</tr>
<tr>
<td></td>
<td>Physical differences or authors’ statement</td>
<td>5, 10, 11</td>
<td>7, 8, 9, 12-16</td>
</tr>
<tr>
<td>Monozygotic</td>
<td>Mono-chorionic</td>
<td>9, 19</td>
<td>17 (2 pairs), 18, 20</td>
</tr>
<tr>
<td></td>
<td>Similarity of many blood types and physical appearance</td>
<td>14 (2 pairs), 21, 22 (2 pairs), 23, 24, 25 (2 pairs)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Similarity of appearance</td>
<td>31, 32, 33</td>
<td>5 (7 pairs), 8, 26-30</td>
</tr>
<tr>
<td></td>
<td>Authors’ statement: “Identical”</td>
<td>34-39</td>
<td>14 (2 pairs), 38, 40, 41, 42</td>
</tr>
</tbody>
</table>

History of the Twin Gestation. Information about the twin pregnancy and delivery was obtained from the mother or hospital medical records. Mothers were questioned about excessive nausea or vomiting, vaginal bleeding, uterine cramps, medications (other than vitamins, calcium, or iron), surgery, any unusual psychogenic factors, infections, contact with the common contagious diseases, herpes simplex, immunization against poliomyelitis (in those pregnancies that occurred after the introduction of the Salk vaccine), and vaccination against smallpox. Medical records were examined for evidence of toxemia and the results of serologic tests. Information about the maternal blood types was available in only some instances, and about the hemoglobin in very few.

In the case reports, absence of a statement about any of the above facets of the history indicates that information was available and was negative. To avoid repetition, only positive information, or where appropriate, a comment that the information was incomplete, has been included.

Cardiac Evaluation

A physical examination of the cardiovascular system of the (living) twins and of their full siblings was performed by the author, unless a statement to the contrary appears in the case report. Electrocardiographic and roentgenographic findings and the descriptions of angioangiograms, the results of cardiac catheterization, surgical procedures, and postmortem examinations were usually obtained from hospital or clinic medical records.

The co-twins and siblings were examined for cyanosis and clubbing, and auscultation of their hearts was performed. Peripheral pulses were palpated in the lower extremities or the blood pressure was measured. The absence of a remark about a co-twin or sibling in a case report means that neither the history nor the physical examination suggested the presence of congenital cardiovascular disease. Findings on roentgenographic and electrocardiographic examinations, where available, have been included in the case reports.

Zygosity Determination

Two pairs consisting of like-sex co-twins with different blood types, and those having opposite-sex co-twins, were classified as dizygotic.

The pair of conjoined twins was considered monozygotic, as were also those same-sex pairs whose twin partners did not differ in blood types and who strongly resembled each other in general appearance and in the following characteristics: hair color, eye color, shape of external ear, attachment or absence of attachment of the ear lobe to the face, contour of the nose and of the chin in the profile view, and eyebrow shape. Fingerprints were taken of most of the monozygotic twins. In computing the total ridge counts, only the higher count of those fingers with whorl patterns was included. If the prints were not technically satisfactory for obtaining an accurate total ridge count, Brodhage and Wendt’s method of evaluating fingerprints was used.

It is extremely difficult to be certain that a pair of twins, other than conjoined twins, is monozygotic. Smith and Penrose have described in detail a method, which we followed, of “evaluating the relative chance that the twin pair is monozygotic.” In our computations, we have used the authors’ data for the “initial odds” that the pair is dizygotic, and their figures for blood group frequencies (regardless of the ethnic origin of our twins) and for intra-pair differences in fingerprint total ridge counts. In indicated instances, we have incorporated into the mathematical scheme of Smith and Penrose, Wendt’s findings on intra-pair differences in fingerprints or Steiner’s observations on the number of placentas present in monozygotic and dizygotic twin births. (The “relative chance in favor of a dizygotic pair” is 0.6197 if there is 1 placenta, and 1.931 if there are 2 placentas.) Since we consider that the data on “initial odds” and on blood groups are more reliable than those on fingerprints and placentas, in the case reports we have given one figure for the “relative chance that the twin pair is monozygotic” based on the former data, and have given a second estimate based on the inclusion of data dependent on the fingerprints or the number of placentas.
ANOMALIES IN TWINS

Findings

Twins

Thirty-seven pairs of twins were studied. Two of the 11 monozygotic pairs and 2 of the 26 dizygotic pairs were concordant for the presence of congenital cardiovascular anomalies; all the other pairs were discordant.

Type of Lesion. The precise nature of the anatomic lesions of the affected twins has been established in the following 9 instances. The children with patent ductus arteriosus were operated upon and were subsequently free of murmurs. The other diagnoses were made after postmortem examinations.

<table>
<thead>
<tr>
<th>Zygosity</th>
<th>Concordance</th>
<th>Case no.</th>
<th>Lesions of affected twins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monozygotic</td>
<td>Concordant</td>
<td>36</td>
<td>One twin had a ventricular septal defect, the other an atrial septal defect.</td>
</tr>
<tr>
<td></td>
<td>Discordant</td>
<td>37</td>
<td>Each twin had a patent ductus arteriosus.</td>
</tr>
<tr>
<td>Dizygotic</td>
<td>Discordant</td>
<td>6</td>
<td>Dextroposed heart; very small left ventricle; hypoplastic pulmonary artery; atrial pulmonary valve; ventricular septal defect.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10</td>
<td>Ventricular septal defect and pulmonary stenosis.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
<td>Tetralogy of Fallot.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13</td>
<td>Atrial and ventricular septal defects.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18</td>
<td>Patent ductus arteriosus.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24</td>
<td>Transposition of the great vessels.</td>
</tr>
</tbody>
</table>

Noncardiac Anomalies. Eighteen twins who had congenital cardiovascular anomalies and 7 twins without such lesions had at least 1 other congenital anatomic abnormality or were mentally retarded.

Birth Weight. The presence of congenital cardiovascular disease per se did not appear to have any significant or consistent effect on birth weight. The average birth weight of the affected members of the discordant monozygotic twin pairs was 5-4, and of their unaffected co-twins 5-2; the affected twin was the heavier at birth 3 times and the normal twin was the heavier 5 times. Among all discordant pairs of twins, the average birth weight of the affected twins was 5 pounds and of the unaffected co-twins was 5-8; in 10 instances the affected twin was the heavier at birth and in 22, he was the lighter.

Siblings

The twins were known to have had 74 liveborn, full siblings. Of the 60 whom we examined, 59 had no evidence of congenital cardiovascular disease and 1 had a murmur of undetermined significance. There were 7 living siblings whom we did not examine; their histories did not suggest a cardiovascular lesion. Five siblings had died. Four of them had been immature; postmortem examination of the fifth one showed no cardiovascular lesion. There was no available information about 2 of the siblings.

Families

Consanguinity. There was no consanguinity in any of the families.

Multiple Births. Fifty-two multiple births were reported to have occurred among the relatives of 23 twin pairs; they were approximately equally divided between the maternal and paternal lineages. The mothers of 3 of our sets of twins had had other twin pregnancies.

Congenital Anomalies. The parents were not aware of any other instances of congenital cardiovascular disease in their families. They reported the presence of the following congenital anomalies among the twins' relatives: syndactyly (1 aunt, 1 great grandmother); polydactyly (2 aunts); megacolon (cousin); harelip (uncle); harelip and cleft palate (cousin); and mongolism (distant cousin). A sister and 2 uncles were mentally deficient. A brother had pre-auricular papilloma.
Familial Disease. The following relatives of 7 pairs of twins were reported to be diabetic: a maternal aunt (case 35), a paternal grandmother (case 34), and 5 maternal grandmothers (cases 4, 19, 22, 25, 29). The mothers of these 7 pairs of twins had no stillbirths or neonatal losses, and only 1 spontaneous abortion. The average weight of these twins was 5-4, and of their siblings 7-11; the heaviest sibling weighed 9-8.

Parental Health. Nothing remarkable was noted with any degree of frequency or regularity in the histories of the health of the parents, other than that 4 mothers had had cholecystectomies. The maternal gynecologic histories were not, in general, unusual. One mother reported that as a baby she herself had received thymic irradiation; another mother had an intravenous pyelogram about a month prior to conception of the twins.

The maternal blood group was known in 23 instances. Ten mothers were group A, 3 were group B, 1 was group AB, and 9 were group O. Twenty-six mothers were Rh positive, and none was known to be Rh negative.

Obstetrical Histories. The obstetrical histories of the 36 mothers indicated that 12 of them had a total of 17 spontaneous abortions, 2 had stillborn babies, 1 had an ectopic gestation, and 1 had a hydatidiform mole. They had given birth to 74 living full siblings of the twins. These included 41 male children, 31 females, and 2 children whose sex was not known to us. There were 2 pairs of immature twins who died very shortly after birth. The average birth weight of the sisters of the twins (based on information furnished by the mothers and only sometimes verified) was 7-7, and of the brothers 7-11. There was no consistently long childless interval prior to the conceptions of the twins. The average maternal age at the birth of the twins was 29 years, with a range of 18 to 39 years.

Twin Pregnanancies

Twelve mothers reported having had excessive nausea or vomiting during the twin gestations; it occurred during the first trimester in 6 of them, during the latter part of the pregnancy in 2 cases, and throughout pregnancy in 4 instances. Vaginal bleeding was reported in 10 instances. Nine mothers had toxemia.

One mother had rubella in the first month of her pregnancy, 1 had thrombophlebitis in the sixth month, 1 had a renal tract infection in the fourth month, and 1 had pertussis in the fifth month. A cervical polyp was removed from 1 mother 6 weeks after her last menstrual period. Eight mothers appeared to have been under quite severe and protracted nervous tension during the twin pregnancy.

In only 3 instances, were the pregnancies considered normal in retrospect.

The duration of pregnancy was thought to be 38 weeks or less in 22 instances, full-term in 12 cases, and 42 weeks in 2 instances. Thirty-two of the twins weighed less than 5 pounds at birth and 42 weighed 5 pounds or more.

The probable month of conception was calculated from the estimated duration of pregnancy and the date of birth. Conception apparently occurred in November, December, or January in 15 instances; in February, March, or April 8 times; in May, June, or July 7 times; and in August, September, or October 6 times.

The noncardiac aspects of the cases have been summarized in tables 2 and 3. Cases 1 through 14, 25, and 26 represent opposite-sex pairs of twins. The case reports of the monogygotic twin pairs are given in the appendix. Detailed case reports of the dizygotic twins have been deposited with the American Documentation Institute.*

*Document number 5905 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting $3.75 for photoprints, or $2.00 for 35 mm. microfilm. Advance payment is required. Make checks payable to: Chief, Photoduplication Service, Library of Congress.
### Table 2.—Family and Gestational Histories: Dizygotic Twin Pairs

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diabetes</th>
<th>Gestational Anomalies</th>
<th>Vaginal bleeding</th>
<th>Nausea tension</th>
<th>Toxemia</th>
<th>Miscarriages</th>
<th>Premature</th>
<th>In twin with cardiovascular anomaly</th>
<th>In noncardiac co-twin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discordant twin pairs</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>Cervical ribs</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td>Pelvic inflammatory disease; sterility</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>(+)</td>
<td>3 abortions</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>+ (++)</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5.</td>
<td></td>
<td>Many abortions and stillbirths</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>6.</td>
<td></td>
<td></td>
<td>+</td>
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<td></td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td></td>
<td>Thrombophlebitis: 6th month</td>
<td>+</td>
<td>Situs inversus; myopia; mental retardation; nonfunctioning kidney; ? Hand-Schuller-Christian; triplet</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>8.</td>
<td></td>
<td></td>
<td>Thrombophlebitis: 6th month</td>
<td>+</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td></td>
<td>2 abortions</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>10.</td>
<td></td>
<td></td>
<td>Rubella: 1st month*</td>
<td>+</td>
<td>Bilateral cataracts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td></td>
<td></td>
<td>Pertussis: 5th month</td>
<td>+</td>
<td>Congenital deafness; marked freckling of skin; very light-colored irides; external ears protrude</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.</td>
<td></td>
<td>1 abortion; a Montgomery-Simpson suspension; salpingo-oophorectomy Sterility</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td></td>
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<tr>
<td>14.</td>
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<tr>
<td>15.</td>
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</tr>
</tbody>
</table>

(Continued on next page)
## Table 2.—Family and Gestational Histories: Dizygotic Twin Pairs (Continued)

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diabetes</th>
<th>Congenital Anomalies</th>
<th>Vaginal bleeding</th>
<th>Nervous tension</th>
<th>Toxemia</th>
<th>Miscarriage</th>
<th>Premature</th>
<th>In twin with cardiovascular anomaly</th>
<th>Other known anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.</td>
<td>(+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17.</td>
<td>(+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.</td>
<td>1 abortion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19.</td>
<td>+</td>
<td>1 abortion; sterility</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20.</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>21.</td>
<td>1 abortion</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>22.</td>
<td>+</td>
<td>1 abortion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23.</td>
<td>+</td>
<td>Rheumatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24.</td>
<td>(+)</td>
<td>Hydatid mole; cholecystectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Concordant twin pairs**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis</th>
<th>Other known anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.</td>
<td>Choledectomy +</td>
<td>A. — B. Mental retardation; hypospadias; cryptorchidism; short 5th fingers; protruding ears</td>
</tr>
<tr>
<td>26.</td>
<td>3 abortions; sterility +</td>
<td>A. Hare-lip; cleft palate; colobomas; microphalmas; macrocephaly; abnormal vertebrae B. —</td>
</tr>
</tbody>
</table>

**Note:** + in the congenital anomalies column indicates that one of the twins’ siblings had an anomaly; (+) that some other relative had an anomaly.

## Discussion

It is reasonable to suppose that there are various mechanisms causing human congenital cardiovascular lesions. Like older individuals, the newborn baby doubtless is as he is because of the interaction of his genetic endowment and his previous environment. Yet we postulate that either a hereditary or an environmental factor was the more influential (or at times, possibly, the sole) mechanism in the production of an anomaly in any particular baby. An indication of the relative etiologic importance of the genetic and environmental factors may be gained if we can explain the discordance of the twin pairs.

Although discordance of dizygotic twin pairs is certainly compatible with the idea of a primarily genetic etiologic mechanism, the discordant monozygotic pairs (consisting of individuals with similar genetic endowment) militate against this postulate.

An environmental teratologic factor could affect a fetus in one of 2 general ways—via the maternal circulation, or locally at a site very close to the ovofetus. In the former
### Table 3.—Family and Gestational Histories: Monozygotic Twin Pairs

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Family history</th>
<th>Maternal history</th>
<th>Twin gestation</th>
<th>Other known anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Vaginal bleeding</td>
<td>Nausea</td>
</tr>
<tr>
<td>Discordant twin pairs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>27. (+)</td>
<td>Thymic irradiation as baby; menstrual irregularities; 1 abortion</td>
<td>+</td>
<td>Syndactyly</td>
<td>Syndactyly; abnormal incisor</td>
</tr>
<tr>
<td>28. +</td>
<td>Cholecystectomy</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>29. +</td>
<td>1 abortion during prior marriage</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>30. +</td>
<td>Urinary tract infections: 4 and 7½ months</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>31. +</td>
<td>1 abortion</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>32. +</td>
<td>Menstrual irregularities; infan-tile uterus; I.V.P. 2½ weeks before last menstrual period</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>33. +</td>
<td>Cholecystectomy</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>34. +</td>
<td>Ptotic eyelid</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>35. +</td>
<td>A. Mongol B. Mongol</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Concordant twin pairs

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Family history</th>
<th>Maternal history</th>
<th>Twin gestation</th>
<th>Other known anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td>36. +</td>
<td>1 stillbirth; 2 cesarean sections</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>37. +</td>
<td>Ectopic gestation and salpingectomy; 2 abortions during prior marriage</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Notation same as table 1.**

Event, the fetus could be damaged (1) by an excessively high concentration in the maternal blood of a substance, such as a hormone or nutrient, which is normally present; (2) by maternal deficiency of some substance, such as a hormone, or a nutrient, or an enzyme, or oxygen; or (3) by the abnormal presence of an injurious chemical or infectious agent.

The discordant monozygotic twin pairs make it very difficult to accept the concept of an etiologic factor transported by the maternal circulation, since genetically similar embryos would be expected to react in a similar fashion to the same environmental stimulus. Although discordance of dizygotic pairs would be a somewhat surprising finding were the teratologic agent blood-borne, there could be at least 2 explanations for such discordance. Either the co-twins could differ genetically in their susceptibility to the environmental factor, or the co-twins could have reached slightly different stages of development at the time of the insult, with only 1 twin at the critically susceptible period for the production of the anomaly.

A more satisfactory explanation of the discordance of the monozygotic twin pairs
appears to us to be that of an environmental factor acting in close proximity to the zygote, embryo, or fetus, so localized that it can affect 1 twin and leave his co-twin unscathed. The insult may occur in the uterins, for instance, in one of the following ways described by Javert:44 "When one recalls the physiologic anemia which characterizes the early development of the ovotet us, it does not take much more than a simple twist of the cord, or a small area of decidual hemorrhage, or avascularity of the villi, or a faulty implantation, to compromise normal oxygenation and nourishment of the ovotet us, and its subsequent faulty development." Or the damage may be inflicted in or by the ovum. Or the responsible agent may be in the cytoplasm of the ovum. If such locally operative factors can, indeed, constitute a type of teratologic mechanism, the problems of delineating their nature and of determining what produces them are posed.

SUMMARY

Twenty-six pairs of dizygotic twins and 11 pairs of monozygotic twins were studied. In 2 of the former and 2 of the latter, both twin partners had congenital cardiovascular anomalies. Only 1 member of each of the remaining pairs had a congenital cardiovascular lesion. The problem of the etiology of the malformations is discussed in the light of these findings.

ACKNOWLEDGMENT

This study could not have been carried out without the generous cooperation of many individuals, hospitals, and organizations to which we are indebted and very grateful. Acknowledgment is made, in particular, to Miss Gladys V. Haber, Bacteriologist-in-Chief of the Bureau of Laboratories of the City of New York Department of Health, for typing the blood specimens; to Mr. Herbert Rich, Senior Statistician of the Bureau of Records and Statistics of the City of New York Department of Health; and to the following who suggested cases for, or permitted inclusion of their patients in, this study:

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APPENDIX

In the following case reports, each twin is designated by 3 letters. The first indicates whether he did (C) or did not (N) have congenital cardiovascular disease; the second indicates whether the individual was male (M) or female (F); the third refers to his having been born first (A) or second (B).

**Monozigotic Pairs Discordant for Cardiovascular Anomalies**

*Case 27.* The paternal greatgrandmother and a daughter of the maternal grandmother's sister were thought to have syndactyly. When the twins' mother was a baby, her thymus was irradiated. She had had menstrual irregularities from the time she was 18 years old until after the birth of the twins. Her first pregnancy ended in a missed abortion at about 4½ months. A son was born the next year, following which she had intermittent pyrexia of unknown etiology for 2 to 3 months. About 3½ years later, she was considered well enough to have more children, and promptly conceived.

The mother was given some type of injections to preserve the twin pregnancy. Albuminuria and ankle edema were present during the last week; on the day of delivery and on the following day, her blood pressure varied between 135-170/90-100. The duration of pregnancy was not definitely known, but it was thought probably to have been full-term. The twins were born when their mother was 24 and their father 25 years old. NMA weighed 5-13 at birth, and CMB 4-13.

A systolic murmur was noted when CMB was 1 week old. He had noisy breathing and occasional coughing and choking spells as a baby; these symptoms gradually subsided. He always weighed less than his co-twin. His mother felt that he was asymptomatic and that he tired a little less easily than, and was physically stronger than his normal co-twin.

At 6½ years of age, the patient weighed 48 pounds. The proximal phalanges of his second and third toes were fused bilaterally. There was mild bilateral parasternal prominence. He had a grade III, harsh, systolic murmur, loudest at the lower left sternal border; the murmur was transmitted laterally and up the left sternal border. An esophagram at age 3 years and a chest x-ray and an electrocardiogram at 6 years of age were within normal limits. The only finding of possible significance was an R' wave, 1 mm. in amplitude, in lead V1; the intrinsiceoid deflection in this lead was 0.05 second. Cardiac catheterization, performed when CMB was 6 years old, was suggestive, although not definitely diagnostic, of an interventricular septal defect, the presumptive clinical diagnosis.

The co-twin weighed 10 pounds more than and was 2½ inches taller than the patient. He had the same abnormality of the toes as did CMB. A right lateral incisor, a temporary tooth, was about twice as wide as normal. The non-twin brother did not have syndactyly.

Zygosity: The twins resembled each other very much. The blood typing of the family was as follows:

<table>
<thead>
<tr>
<th>Blood group</th>
<th>Rh</th>
<th>rh'</th>
<th>hr'</th>
<th>Kell</th>
<th>Duffy</th>
<th>MN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father</td>
<td>0</td>
<td>Pos.</td>
<td>Pos.</td>
<td>Neg.</td>
<td>Pos.</td>
<td>Pos.</td>
</tr>
<tr>
<td>Brother</td>
<td>0</td>
<td>Pos.</td>
<td>Neg.</td>
<td>Pos.</td>
<td>Pos.</td>
<td>Pos.</td>
</tr>
</tbody>
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The difference in the fingerprint total ridge counts was 1. The relative chance that this pair of twins was monozigotic was 0.9322; it was 0.9836 if the fingerprint data were included.

*Case 28.* The paternal grandmother and a paternal aunt had twins. The mother's blood group was A, type Rh positive. The twins were born during the first year of the parents' marriage; the mother was 19 and the father 26 years old at the time. Another daughter was born a year later, and a fourth one 4 years after that.

The mother reported that she had excessive nausea and vomiting during the last few months of her pregnancy. Her blood pressure was elevated from the beginning of the second trimester; the highest pressure, 180/100, was noted 2 days before the twins were born, at which time she also had 3+ edema of the extremities. The duration of pregnancy was 7 months. NFA weighed 4-10 and the patient weighed 4-6 at birth. There was a single placenta and 2 umbilical cords.

The presence of a murmur was recorded when CFB was 5 years old. She was less active than her twin, but it was difficult to determine whether this was the result of diminished exercise tolerance or of greater mental retardation. Her I.Q. was 38; NFA's was 52. CFB was always the smaller twin. When 7 years old, she weighed 44 pounds and was 45 inches tall; her co-twin weighed 55 pounds and was 50 inches tall.

At 9 years of age, CFB weighed 54 pounds and was 50 inches tall. The point of maximal cardiac impulse was palpable in the sixth intercostal space, medial to the midediaphragmatic line. The second sound at the pulmonary area was of normal intensity and was split. There was a grade IV, harsh, systolic murmur, maximally intense at the left sternal border in the second intercostal space, transmitted
down the left sternal border, and audible posteriorly. There was also a short, grade III, diastolic murmur along the left sternal border. Moderately marked transverse enlargement of the heart, with enlargement of both the right and left ventricles, was noted on fluoroscopic examination. The electrocardiogram was suggestive of right ventricular hypertrophy. It was thought that the child had more than one anatomic lesion, but the diagnosis was not clear.

NFA weighed 69 pounds and was 56 inches tall. Physical, electrocardiographic (including precordial leads), and fluoroscopic examinations showed no abnormalities. (Neither twin had any findings in the facies or hands suggestive of mongolism.)

Zygosity: The twins were Negro children who resembled each other, but could be differentiated because of their difference in size. Both twins were group A, type MNss, Rh-rh, Duffy negative, Kell negative, P negative. All the fingerpints of both girls were similar loops. The difference in total ridge counts was 6. The relative chance that they were monozygotic was 0.9533: it was 0.9931 if the single placenta and fingerprints were considered.

Case 29. The maternal grandfather's brother's daughter and the paternal aunt had twins. A daughter of the same paternal aunt had a pair of opposite-sex twins. The maternal grandmother died in diabetic coma. The twins' mother had a cholecystectomy when she was 52 years old, and their father had a similar operation when he was 54 years old. At about the same time, he was discovered to have polycythemia.

Two and a half years after the parents were married, they had a daughter. A son was born 5 years after that, and another one 3 years later. Four years subsequently, after a 5-months' gestation, twin sons were born and died almost immediately. CFB and NFA were born 2 years later; their mother was 36 years old then and their father 38.

The mother was hospitalized prior to the birth of the twins for treatment of toxemia. Her average blood pressure was about 150/90 mm. Hg, she had 3+ albuminuria, and gained 12½ pounds during the final month of pregnancy. The twins were born after a 36-week gestation; NFA weighed 4-2 and CFB weighed 6-5. There was a single placenta.

At 4 months of age, CFB developed cyanosis which lasted for a few months. She always tired somewhat more easily than NFA; she teenedh and walked a little later than her co-twin, and had to study more intensively than her sister in order to achieve the same marks in school. The mother reported that CFB had frequent upper respiratory infections, and whooping cough, scarlet fever and measles which her normal twin did not contract. However, CFB always weighed more than NFA and her menarche occurred at 12 years of age, 6 months prior to NFA's.

At 17½ years of age, CFB weighed 110 pounds and was 5 feet 2 inches tall. She was right-handed. She had a grade IV, harsh, systolic murmur, which was maximally intense at the left sternal border in the fifth intercostal space, and was widely transmitted. The fluoroscopic and electrocardiographic (including precordial leads) findings were within normal limits. The girl was thought to have a ventricular septal defect.

Her co-twin weighed 98 pounds and was 5 feet 2 inches tall. She was left-handed. Both she and the older brother were said to have had strabismus which had been surgically corrected.

Zygosity: Both girls were blood group A, type Rh,Rh1, Mss, Duffy positive, P negative, Kell negative. There were 3 fingerprint pattern differences; the difference between their fingerprint counts (by the method of Brodhage and Wendt) was 2. The relative chance that this pair of twins was monozygotic was 0.9750; it was 0.9956 if the data for the placenta and fingerprints were included.

Case 30. These conjoined twins were the products of their mother's first pregnancy, and were conceived a few weeks after her marriage. The father was 23 years old when they were born and the mother was 25. The parents were Negroes. Another daughter was born 1 year after the twins.

The mother had excessive vomiting during the first trimester, with a weight loss of 15 pounds during the early part of the pregnancy. When 3½ months pregnant, she had 9.2 Gm. Hb per 100 ml and 3,600,000 red blood cells per mm.3 The twins were born after a 36-week gestation. CFA weighed about 3-10. The conjoined co-twin was stillborn and weighed about 2-2. There was a single, large placenta and a single umbilical cord. The twins were surgically separated soon after birth. CFA died at 8 hours of age.

The twins were fused from below the xiphoid to the pubis; there was a cartilaginous bridge in the xiphoid region. They had one large liver, a single biliary tract, and a large, bifid gallbladder. The gastrointestinal tracts were continuous at the upper jejunal level. Each baby had her individual stomach, large intestine, and genitourinary tract. CFA's spleen was on the right side.

CFA had a cor triloculare. The tricuspid valve and the right ventricle were absent; the pulmonary artery was atrophic. The ductus arteriosus and the foramen ovale were patent. The heart weighed 30 Gm. The stillborn baby's heart weighed 4 Gm., and appeared anatomically normal. Her ductus
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arterosus and foramen ovale were also patent; these findings were considered "physiological." She had marked bilateral pulmonary atelectasis and severe left dorsolumbar scoliosis. Their younger sister was examined when she was 21 months old.

Of interest in connection with this case, are other conjoined twins discordant for congenital heart disease and a pair who were probably concordant for it.68

Case 31. The family history was incomplete. During the mother's first marriage, she had seven pregnancies, productive of 5 full-term babies, one premature baby who weighed 3 1/2 pounds at birth, and one spontaneous abortion of a 6-month fetus. The son of a half-sibling of the twins had a club foot. The only pregnancy during the mother's second marriage was that productive of the twins who were born 9 years after their youngest half-sibling. Both parents were 36 years old at the time of the twins' birth.

The mother had labor-like abdominal pains during the second month of the twin gestation; she was treated with stilbestrol. The duration of the pregnancy was 8 months. Both umbilical cords prolapsed late in labor. The onset of respiration was delayed in both twins, and they required tracheal aspiration. NMA weighed 5-3 and the patient weighed 4-13 at birth. There was one placenta.

CMB was noted to have a murmur when he was 10 months old. He seemed to tire a little more easily than his co-twin, and reached his landmarks slightly later than did NMA. His I.Q. was 49 and his co-twin's was 47.

At 9 years of age, CMB weighed 49 pounds and was 49 inches tall. He had a grade III to IV, harsh, systolic murmur which was loudest at the left sternal border in the fourth intercostal space and was transmitted laterally and up the left sternal border. The second sound at the pulmonary area was accentuated and split. An electrocardiogram, which included precordial leads, was recorded when he was 7 1/2 years old, and was normal. Roentgenographic examination at that time showed increased bronchovascular markings and questionable lifting of the apex. He was thought to have a ventricular septal defect.

The co-twin weighed 53 pounds and was 50 inches tall. Physical, electrocardiographic (including precordial leads), and fluoroscopic examinations at 9 years of age revealed no cardiovascular abnormalities. He had a Simian crease on the right hand; CMB had one on the left hand. Neither twin had any facial findings suggestive of mongolism.

Zygosity: The color of the normal twin's skin was a little darker than that of the affected twin; they were Negroes. Both twins were group O, type Rhnull, Mns, P positive, Duffy negative, Kell negative. The difference in their fingerprint total ridge counts was 3. The relative chance that they were monozygotic was 0.9417; it was 0.9913 if the placenta and fingerprints were considered too.

Case 32. The mother's paternal grandmother had twins. The father developed an inguinal hernia at 12 years of age. The twins had 2 brothers, the first of whom was born 2 years after the parents' marriage. The twins were born 2 1/2 years later; both parents were then 25 years old. The youngest child was born 16 months after the twins.

The mother's last menstrual period prior to the twin pregnancy began on April 17. On August 14, she developed a urinary tract infection for which she was treated with gantrisin and penicillin. Her hemoglobin at the time was 9.4 Gm. per 100 ml. A month before delivery, the mother probably had a recurrence of the infection, and was treated with gantrisin and aureomycin. At this time, her hemoglobin was 8.4 Gm. per 100 ml. and her red blood count was 2,790,000 per mm.3. The twins were born on December 28. NMA weighed 5-14 and CMB 6-0. There were two completely separate placentas.

The 2 babies developed adequately and in a similar fashion for approximately 3 months. Then CMB's appetite diminished and he failed to gain well. He developed respiratory difficulties (frequent coughing, wheezing, and labored breathing), became seriously ill, and was hospitalized on 4 occasions during the first 2 years of his life. Marked enlargement of his heart, especially of the left ventricle, was noted when he was 4 months old. The baby was treated with digitalis until the age of 4 1/2 years. At 1 year, he weighed 17 pounds and his co-twin weighed 23 pounds. CMB began to improve at about 2 1/2 years of age, and within half a year, he was the equal of his co-twin in weight, height, and physical activity, according to his mother. There were no significant murmurs at the beginning of his illness, but by the time he was 4 years old, an organic-sounding systolic murmur was present, and when he was 6 years old, a diastolic murmur was also noted. Angiocardiography (at 6 1/2 years of age) revealed a tremendous left ventricle with thick walls; there was minimal increase in the size of the left atrium. There was electrocardiographic evidence of left ventricular hypertrophy.

At 7 years of age, both twins weighed 52 pounds and were 4 feet tall. CMB had a slight precordial bulge. The point of maximal impulse was palpable at the midclavicular line in the sixth intercostal space. There was a grade III,
harsh, systolic murmur, maximally intense at the apex, and transmitted up the left sternal border and to the axilla. There was an inconstant, grade II, apical diastolic "thud." The nature of the cardiac disease was not definitely established, but it was considered most likely that the boy had "cured" fibroelastosis.

Zygosity: The boys resembled each other very, very much. Both were group O, type Rh\textsubscript{b}Rh\textsubscript{b}, Mss, P positive, Duffy positive, Kell positive. The difference between their fingerprint total ridge counts was 13. The relative chance that they were monozygotic was 0.9420; it was 0.9590 if the placentas and fingerprints were taken into consideration.

Ullrich\textsuperscript{9} reported endocardial fibrosis in the 2 monozygotic brothers of a set of triplets, and Greaves et al.\textsuperscript{33} described endocardial fibroelastosis in both of a pair of "identical" twins.

Case 33. The family history was incomplete and unreliable. The mother's blood was group O, type Rh positive. The twins had a brother of 20 years who was not examined by us, but who was considered free of heart disease on 2 Service examinations, and a 16-year-old brother. The mother had a spontaneous abortion of the products of a 3 months' gestation about a year after the birth of her first child.

The twins were born 7 years after their younger brother, when the mother was 33 and the father 38 years old. The mother was bothered throughout the twin pregnancy by "spitting up water." The twins were born 3 weeks prematurely. CMA weighed 4.12 and his co-twin 5.2. There was 1 placenta; the presence of 1 chorion and 2 amnions was reported on the basis of gross examination.

A murmur was detected when CMA was 3 years old. He was slightly more dyspneic than the average child after climbing 3 flights of stairs, but otherwise asymptomatic. His mother considered him mentally more alert and physically stronger and more pugnacious than NMB.

At 8 years of age, CMA, a Negro boy, weighed 57 pounds and was 50\(\frac{1}{2}\) inches tall. He had a grade II, blowing, systolic murmur, loudest at the left sternal border in the third intercostal space and transmitted locally. Fluoroscopic examination revealed a full pulmonary artery segment and mild left ventricular enlargement. There was an RSR' pattern in precordial leads V\textsubscript{1} and V\textsubscript{2} of the electrocardiogram; the intrinsicoid deflection was 0.05 second in V\textsubscript{1}. The presumptive clinical diagnosis was an atrial septal defect.

The co-twin was the same height as CMA and weighed 9 pounds more. Physical, electrocardiographic (including precordial leads), and fluoroscopic examinations showed no cardiovascular abnormality. The 16-year-old brother had a soft, blowing, systolic murmur at the left sternal border in the second and third intercostal spaces; it was not transmitted and was audible in the supine, but not in the erect position. The clinical impression was that the murmur was innocent; however, since electrocardiographic and fluoroscopic examinations could not be made, the boy was considered to have an undiagnosed manifestation.

Zygosity: The twins looked very much alike, except that the face of the heavier one was rounder than his brother's and that there was some difference in the shapes of their eyebrows. The presence of a single chorion indicated that the twins were monozygotic. In case the clinical impression of a single chorion may have been in error, the following information is included. Both twins were group O, type Rh\textsubscript{b}rh, Nss, P positive, Duffy negative, Kell negative, Kidd negative. The difference between their fingerprint total ridge counts was 9. The relative chance that they were monozygotic was 0.9556, or 0.9926 if the single placenta and the fingerprints were taken into consideration.

Case 34. The paternal grandfather's sister and the paternal grandmother's cousin's daughter had twins. The paternal grandmother had diabetes. Prior to her marriage, the mother had severe dysmenorrhea and menstruated at 4- to 6-week intervals. She was told that she had an infantile uterus. At about the time of her marriage her basal metabolic rate was \(-18\). The twins were the parents' first children and were born when the mother was 25 and the father 35 years old. Two years later they had a son, born after a 41-week gestation. A second son was born 1\(\frac{1}{2}\) years after the first.

Seven weeks after her marriage, the mother had acute cystitis; \textit{Bacillus pyocyaneus} was cultured from the urine. She was treated with aureomycin. Excretory urography was performed and was normal. Her last menstrual period prior to the twin gestation began 18 days after the urography. The mother vomited excessively during the first 2 or 3 weeks of the pregnancy, and had vaginal staining for 2 days at the time of her fourth and fifth missed menstrual periods. The twins were born 5 weeks prematurely; CFA weighed 5.5 and NFB weighed 4.2.

CFA was noted to have a murmur at birth. She was asymptomatic and the twins' growth and development were very similar. The mother considered the affected twin to be physically more
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active than her sister. CFA was 4 pounds heavier than her sister until they were 6 years old.

At 7 years of age, both twins weighed 50 pounds and were 43½ inches tall. CFA had several black nevi about 2 mm. in diameter on the anterior and posterior chest. She had a systolic thrill and a grade VI, coarse, systolic murmur at the left sternal border in the third intercostal space; the murmur was widely transmitted and was audible posteriorly. The second sound at the pulmonary area was inaudible. Cardiac catheterization demonstrated the presence of pulmonary stenosis; the pressure in the right ventricle was 144/10. The catheter could be passed from the right to the left atrium, probably through a patent foramen ovale, since there was no significant increase in the oxygen content of the blood at the atrial level. Valvulotomy and dilatation of the stenotic pulmonary valve were performed when the child was 8 years old.

Zygosity: There was a striking resemblance between the twins. Both were blood group A, type Rh1Rh2, Ns, P negative, Kell negative, Duffy negative. The difference between their fingerprints as evaluated by the method of Brodhage and Wendt was 3. The relative chance that they were monozygotic was 0.9578; it was 0.9783 if the fingerprint data were considered also.

Case 35. The father's brother's son had a pair of opposite-sex twins. The mother's sister had asthma, diabetes, and severely impaired vision and hearing. The mother became hard-of-hearing when she was about 47 years old, and had a cholecystectomy at about the same age. A year after their marriage, the parents had a daughter. The twins were born 4 years later, after a full-term, uncomplicated pregnancy, according to the history obtained from the mother. (No medical records were available and the serology was not known.) The mother recalled that she ate no meat during the pregnancy, and that she ate very many pumpkin seeds. At birth, CMB weighed 5-7 and NMA weighed 6-3. There was one "afterbirth."

Ptosis of CMB's left upper eyelid was present from birth. During the first 3 years of his life, he, unlike his co-twin, had a poor appetite and very many upper respiratory infections.

Coarctation of the aorta was discovered when CMB was 16 years old, and was confirmed the following year on angiography. Between the ages of 16 and 23 years, CMB had progressive increase in blood pressure, some dizziness, some blurring of vision, and mild girdling pains of the lower rib cage. Roentgenographic evidence of notching of the ribs was present when he was 20 years old. Surgery was performed when he was 22½ years old. The narrowed area of the aorta was located at the level of the ligamentum arteriosum, distal to the origin of the left subclavian artery. The outer diameter of the coarcted region was 11 mm. and the inner diameter was 3 mm. There was post-stenotic dilatation of the aorta; just distal to the coarctation the outer diameter of the aorta was 25 mm., whereas above the coarctation it was 16 mm. A segment of the aorta 2 cm. in length was removed and an end-to-end anastomosis was performed.

At 27 years of age, CMB was 5 feet 4 inches tall and weighed 145 pounds. Partial ptosis of the left upper eyelid was present. His blood pressure was 128/68 and the pulsation of the dorsalis pedis artery was palpable. A grade III, harsh, systolic murmur was present. It was loudest at the left sternal border in the second intercostal space when CMB was in the erect position, and at the lower left sternal border when he lay down; the murmur was widely transmitted in both positions.

NMA was the same height as his twin, and weighed about 12 pounds less. He had neither ptosis nor clinical evidence of cardiovascular disease. His blood pressure was 118/78.

Zygosity: We were not able to see the men together. Through high school age, the twins were often confused; their mother has considered them "identical." Their hair color, eye color, and ear lobes were similar. Both were group O, type Rh1Rh2, M, S positive, P positive, Duffy positive, Kell negative. The difference in their fingerprint total ridge counts was 15. The relative chance that they were monozygotic was 0.8979; it was 0.9752 if the placental and fingerprint data were taken into consideration also.

Monozygotic Pairs Concordant for Cardiovascular Anomalies

Case 36. The mother's first pregnancy was productive of a stillborn, macerated baby girl who weighed 9-14 and was born 2 years after the parents' marriage. No fetal heart sounds had been heard for 2 days prior to her birth. At the time of delivery, the mother had an upper respiratory infection; her husband had had a viral infection shortly before that. At postmortem examination of the stillborn baby, both the foramen ovale and the ductus arteriosus were observed to be patent; these findings were not considered pathologic. There were multiple, small, white, infarcted areas in the placenta.

Since the mother's pelvis had a contracted outlet, her next baby, born a year later, was delivered by elective cesarean section performed after 38 weeks' gestation. The boy weighed 7-8;
he had a pre-auricular papilloma. There were extensive calcified deposits in the placenta. Two years later, another son was delivered by elective cesarean section a week before term; he weighed 8-10. Neither of these 2 boys was examined by us; their pediatrician reported them free of congenital heart disease at 7 and 5 years of age.

The twins were born a year and a half after their younger brother. The father was then 42 years old, and the mother at least 38 years old. The pregnancy lasted 38 weeks. A cesarean section was performed after the mother went into labor. There was a single placenta. The first-delivered twin weighed 4-11 and the second 5-8. Both babies were considered mongoloid from birth.

CMA had a murmur from birth, and died at 2½ months of age, weighing 9 pounds. He had blue eyes and brown hair. Postmortem examination of the heart showed that there was a 4 by 3 cm. defect in the ventricular septum "about 3 mm. below the aortic ring and underneath the anterior cusp." The foramen ovale was closed.

A systolic murmur was intermittently heard in the second twin. He died of bronchopneumonia at 5 months of age; he weighed 8-5 at the time. He, too, had blue eyes and brown hair. At postmortem examination, an open foramen ovale was noted; as this term is used by the pathologist who examined the heart, it indicated that there was an anatomic defect of at least 1/3 of the area of the atrial septum.

Zygosity: Both twins were group A, type Rh positive. Allen and Baroff\textsuperscript{89} considered the maximal concordance rate for mongolism among dizygotic twins to be 2.7 per cent. The probability that the twins were monozygotic, calculated from this figure as well as those based on our knowledge of the "initial odds," blood types, and placenta was 0.9887.

The following reports of twin pairs concordant for mongolism are of interest in connection with this case. Both members of the pair described by Rosanoff and Handy\textsuperscript{70} were considered to have congenital heart disease. It is difficult to judge whether the "systolic murmur" heard in both co-twins reported by Lund\textsuperscript{71} was caused by congenital heart disease. A pair apparently discordant for congenital cardiac disease was described by Jervis;\textsuperscript{72} the question of their zygosity was later discussed by Allen and Baroff.\textsuperscript{69} Young\textsuperscript{73} reported a pair of twins, one of whom showed no evidence of heart disease during the first seven weeks of life, although his co-twin was definitely affected.

Case 37. The mother was receiving psychiatric therapy on an ambulatory basis at the time of our interview. She gave a history of having been married twice. During her first marriage, and beginning at 16 years of age, she had 4 pregnancies, productive of 2 full-term children (one of whom was examined by us), an abortion of twins, and an abortion of a single fetus. The mother was pregnant 6 times during her second marriage. A daughter was born 15 months before the twins. Nine months before their birth, the mother had a salpingectomy for a ruptured ectopic pregnancy. The twins were born when the mother was 23 years old. A girl was born 3 years after them; during this pregnancy, the mother took an overdose of sleeping tablets. A boy was born the following year, and another one 14 months later. During the final pregnancy, the mother voluntarily entered a mental hospital for 10 days. She was sterilized after the birth of this, her eighth living child.

During the twin gestation, the mother "spotted" for 4 days in the second month, and again in the fourth month. The twins were born after a 33-week gestation; CFA weighed 3-15 and CFB weighed 3-11. There was a single, large placenta.

Both children underwent cardiovascular surgery when they were 1½ years old. Each had a patent ductus arteriosus, which was about 5 mm. in diameter. The attachment of the pericardium to the pulmonary artery and the ductus arteriosus was firmer and more extensive than usual. CFA's ductus was ligated, and her sister's was divided.

The twins had no clinical evidence of cardiovascular disease when examined at 6 years of age. Each weighed 42 pounds. CFA was 42 inches tall and CFB was 44½ inches tall. CFA had a very small umbilical hernia not present in CFB.

Zygosity: The little girls resembled each other very, very much. Both were group O, type Rh\textsubscript{0}, MN, S positive, P positive. The difference in their fingerprint total ridge counts was 10. The relative chance that they were monozygotic was 0.8874; it was 0.9923 if the data on the placenta and the fingerprints were included.

McAleese,\textsuperscript{36} Holman et al.,\textsuperscript{37} and Starer\textsuperscript{38} have also described "identical" twin pairs concordant for patent ductus arteriosus. However, several probably monozygotic twin pairs discordant for a patent ductus have also been reported.\textsuperscript{14, 22, 38, 41}
Congenital Cardiovascular Anomalies in Twins
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