Congenital Heart Disease with Septal Defects in which Paradoxic Bacterial Brain Abscess Causes Death

A Review of the Literature and Report of Two Cases

By Salvatore M. Sancetta, M.D., and Henry A. Zimmerman, M.D.

The presence of septal defects in congenital heart disease makes for a direct shunting of particulate matter from the venous to the arterial side of the circulation. In reviewing the literature we have been surprised to find that this phenomenon, with resultant brain abscess, has been second only to bacterial endocarditis as a septic cause of death. The subject deserves attention from the viewpoint of early diagnosis and cure, since the reported mortality has been almost 100 per cent.

Although brain abscess resulting from septic paradoxical embolization is well established the correct clinical diagnosis is rarely made. We here present an analysis of the 42 cases reported to date and add 2 of our own.

Historical

At this writing there are thirty articles in the literature concerned with 42 reported cases. In 1814 Farre discussed a case of tetralogy of Fallot in a boy aged 9 years who died of brain abscess. Lallemand, Louis, and Berthody described similar cases, and in 1880 Ballet reviewed the literature and added one case of his own.

By the end of the last century the entity of brain abscess due to septic paradoxical embolization was well known. In 1881, Peacock reported such a case, and in recording the 45 cases of tetralogy described to that time stated: "The death of the patients is in the largest proportion of cases, as in the present instance, caused by cerebral disease. Two of my previously reported cases died in attacks of convulsions." Abbott and her collaborators reported 2 cases in 1932 and reviewed the literature. Sutherland stated in 1929: "It is an old standing clinical observation that cases of congenital heart disease often suffered or died with signs of cerebral abscess or embolism." In 1932, Rabinowitz and associates were the first to report a case with a correct antemortem diagnosis. Wechsler and Kaplan described 2 cases in 1940 which were diagnosed correctly; both patients succumbed in spite of surgical drainage of the abscesses. Excellent discussions of the subject are given by Robbins, Hanna, and Gates and co-workers.

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Predisposing Factors

The presence of a septal defect with the chance shunting of organisms and infected material directly into the arterial system without the benefit of pulmonary filtering is the factor responsible for the brain abscess. It is interesting that in none of the patients were other secondary abscess sites found. There is a considerable polemic as to whether organisms alone by lodging in the brain tissue can produce an abscess without the benefit of previous trauma, local ischemia, or associated embolization with infected particulate matter. Two of Hanna's subjects showed unquestioned pathologic evidence of cerebral infarction preceding the formation of abscess. Collis gives a good discussion of the local factors involved.

Antecedent infection was found clinically or suspected and later verified post mortem in 15 of the reported cases. In 20 instances, including the cases herein reported, no primary source of infection was located (table 1). In none of the patients reported were any of the local head and face and intrathoracic sources of brain abscess found.

Bacterial endocarditis is not a factor. In 2 patients there was bacterial endocarditis of a stenotic pulmonic valve, but in these subjects the inclusion of the defect as part of the tetralogy of Fallot predicated the avoidance of pulmonary filtering by way of the septal defect.

Nature of the Abscesses

In forty-two instances it was possible to analyze the abscesses found. Thirty-seven
### Table 1.—Reported Cases of Brain Abscess Associated With Congenital Heart Disease

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Antecedent Infection</th>
<th>Cardiac Lesion</th>
<th>Location and Number of Abscesses</th>
<th>Microorganisms in Abscess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farre[4]</td>
<td>1814</td>
<td>9</td>
<td>M</td>
<td>Unknown</td>
<td>Tetralogy of Fallot</td>
<td>Rt. cerebral hemisphere (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Louis[24]</td>
<td>1838</td>
<td>25</td>
<td>M</td>
<td>Unknown</td>
<td>Basal ventricular septal defect</td>
<td>Rr. ant. corpus striatum (1); rt. optic tract (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Berthody[7]</td>
<td>1845</td>
<td>21</td>
<td>F</td>
<td>Unknown</td>
<td>Basal I.V. septal defect; hypoplasia pulmonary artery</td>
<td>Left occipital lobe (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Ballet[4]</td>
<td>1880</td>
<td>15</td>
<td>M</td>
<td>Unknown</td>
<td>Basal I.V. septal defect; aplastic rt. ventricle; tricuspid atresia; both atria open in left ventricle</td>
<td>Rt. frontal lobe (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Peacock[27]</td>
<td>1881</td>
<td>7</td>
<td>M</td>
<td>Unknown</td>
<td>Tetralogy of Fallot</td>
<td>Rt. ant. cerebrum (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Stone[35]</td>
<td>1881</td>
<td>19</td>
<td>F</td>
<td>Unknown</td>
<td>Basal I.V. septal defect as part of tetralogy of Fallot</td>
<td>Rt. occipital lobe (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Northrup[12]</td>
<td>1894</td>
<td>41</td>
<td>M</td>
<td>Unknown</td>
<td>Tetralogy of Fallot</td>
<td>Cerebral (1); location not given</td>
<td>Unknown</td>
</tr>
<tr>
<td>Acker[27]</td>
<td>1895</td>
<td>10</td>
<td>F</td>
<td>Unknown</td>
<td>Transposition of great vessels; basal I.V. septal defect; patent F.O. &amp; ductus arteriosus</td>
<td>Not given</td>
<td>Diplococcus lanceolatus</td>
</tr>
<tr>
<td>Jacobi[22]</td>
<td>1895</td>
<td>29</td>
<td>M</td>
<td>Unknown</td>
<td>Basal I.V. septal defect</td>
<td>Lt. temporal lobe (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Packard[16]</td>
<td>1895</td>
<td>?</td>
<td>M</td>
<td>Unknown</td>
<td>Basal I.V. septal defect; patent F.O.</td>
<td>Location unknown (1)</td>
<td>Unknown</td>
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<tr>
<td>Deneke[11]</td>
<td>1906</td>
<td>18</td>
<td>M</td>
<td>None</td>
<td>Tetralogy of Fallot; patent ductus arteriosus</td>
<td>Rt. cerebrum (1)</td>
<td>Streptococcus</td>
</tr>
<tr>
<td>Heigel[19]</td>
<td>1913</td>
<td>10</td>
<td>F</td>
<td>None</td>
<td>Ebstein’s disease with patent F.O.</td>
<td>Left cerebrum (1)</td>
<td>Gram-pos. cocci &amp; bacilli; gram-neg. bacilli</td>
</tr>
<tr>
<td>Abbott et al. [2]</td>
<td>1923</td>
<td>10</td>
<td>M</td>
<td>Phlegmon rt. arm</td>
<td>Tetralogy of Fallot</td>
<td>Brain not examined</td>
<td>Unknown</td>
</tr>
<tr>
<td>Abbott et al. [2]</td>
<td>1923</td>
<td>11</td>
<td>M</td>
<td>Acute appendicitis</td>
<td>Tetralogy of Fallot; patent ductus arteriosus</td>
<td>Lt. frontal lobe (1)</td>
<td>Streptococcus</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Age (years)</td>
<td>Sex</td>
<td>Antecedent Infection</td>
<td>Cardiac Lesion</td>
<td>Location and Number of Abscesss</td>
<td>Microorganisms in Abscess</td>
</tr>
<tr>
<td>-------------------</td>
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<td>-------------------------------------------------------------------------------</td>
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<td>---------------------------</td>
</tr>
<tr>
<td>Raab²³</td>
<td>1923</td>
<td>15</td>
<td>M</td>
<td>Unknown</td>
<td>Tetralogy of Fallot; patent F.O.</td>
<td>Rt. cerebrum (1)</td>
<td>Gram-neg. rods</td>
</tr>
<tr>
<td>Bach⁶</td>
<td>1928</td>
<td>30</td>
<td>M</td>
<td>Removal of 6 carious teeth</td>
<td>Tetralogy of Fallot; patent F.O.</td>
<td>Rt. postero-temporal (1)</td>
<td>Gram-pos. rods</td>
</tr>
<tr>
<td>Baumgartner &amp; Rabinowitz et al.²⁹</td>
<td>1929</td>
<td>21</td>
<td>M</td>
<td>None</td>
<td>Eisenmenger's complex Tetralogy of Fallot</td>
<td>Rt. frontoparietal (1)</td>
<td>Hemolytic streptococcus</td>
</tr>
<tr>
<td>Drey et al.¹²</td>
<td>1932</td>
<td>16</td>
<td>F</td>
<td>None</td>
<td>Tetralogy of Fallot</td>
<td>Cerebellar (1)</td>
<td>B. coli</td>
</tr>
<tr>
<td>Ingham⁶. ²¹</td>
<td>1938</td>
<td>14</td>
<td>F</td>
<td>Acute upper respiratory infection</td>
<td>Cor diastium triloculare Patent foramen ovale</td>
<td>Intraventricular cerebral (1)</td>
<td>Not done</td>
</tr>
<tr>
<td>Wechaler &amp; Kaplan⁷. ²⁷</td>
<td>1940</td>
<td>14</td>
<td>M</td>
<td>None</td>
<td>Tetralogy of Fallot</td>
<td>Rt. frontoparietal (1)</td>
<td>Gram-neg. rods</td>
</tr>
<tr>
<td>Wechaler &amp; Kaplan⁷. ²⁷</td>
<td>1940</td>
<td>114</td>
<td>F</td>
<td>Acute upper respiratory infection</td>
<td>Tetralogy of Fallot</td>
<td>Rt. frontal lobe (1)</td>
<td>Streptococcus viridans</td>
</tr>
<tr>
<td>Hanna¹⁸</td>
<td>1941</td>
<td>18</td>
<td>F</td>
<td>Unknown</td>
<td>Basal I.V. septal defect</td>
<td>Lt. internal capsule &amp; thalamus (1)</td>
<td>Streptococcus</td>
</tr>
<tr>
<td>Hanna¹⁸</td>
<td>1941</td>
<td>34</td>
<td>F</td>
<td>Unknown</td>
<td>Basal I.V. septal defect</td>
<td>Lt. frontal lobe (1)</td>
<td>H. influenzae</td>
</tr>
<tr>
<td>Hanna¹⁸</td>
<td>1941</td>
<td>10</td>
<td>F</td>
<td>Unknown</td>
<td>Tetralogy of Fallot</td>
<td>Lt. thalamus (1)</td>
<td>H. influenzae</td>
</tr>
<tr>
<td>Hanna¹⁸</td>
<td>1941</td>
<td>3</td>
<td>M</td>
<td>Unknown</td>
<td>Tetralogy of Fallot; bicuspid pulmonic valve</td>
<td>Rt. temporal lobe (1)</td>
<td>No organisms found</td>
</tr>
<tr>
<td>Hanna¹⁸</td>
<td>1941</td>
<td>19</td>
<td>M</td>
<td>Acute upper respiratory infection</td>
<td>Muscular I.V. septal defect; subpulmonic stenosis; pulmonary atresia</td>
<td>Rt. occipital lobe lobe (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Hanna¹⁸</td>
<td>1941</td>
<td>46</td>
<td>F</td>
<td>Pain in knee, fever, 7 days</td>
<td>Atrial septal defect</td>
<td>Multiple infarcts &amp; abscesses, rt. frontal lobe</td>
<td>Unknown</td>
</tr>
<tr>
<td>Ruhberg³¹</td>
<td>1942</td>
<td>6</td>
<td>F</td>
<td>Acute upper respiratory infection</td>
<td>Basal I.V. septal defect; pulmonary stenosis</td>
<td>Multiple abscesses, rt. occipital lobe</td>
<td>B. coli, Staphylococcus albus, hemolytic streptococcus</td>
</tr>
<tr>
<td>Vann &amp; Miller³¹²</td>
<td>1944</td>
<td>8</td>
<td>M</td>
<td>Pharyngeal abscess</td>
<td>Pseudomonoventricular heart; transposition great vessels; pulmonary stenosis</td>
<td>Rt. frontal lobe (1); lt. frontal lobe (1)</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
### Table 1.—Continued

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Antecedent Infection</th>
<th>Cardiac Lesion</th>
<th>Location and Number of Abscess</th>
<th>Microorganisms in Abscess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robbins&lt;sup&gt;30&lt;/sup&gt;</td>
<td>1945</td>
<td>10 F</td>
<td></td>
<td>Unknown</td>
<td>Tetralogy of Fallot</td>
<td>Lt. parieto-occipital (1)</td>
<td>Hemolytic streptococcus</td>
</tr>
<tr>
<td>Robbins&lt;sup&gt;30&lt;/sup&gt;</td>
<td>1945</td>
<td>19 F</td>
<td></td>
<td>Severe pyorrhea, stomatitis</td>
<td>Tetralogy of Fallot; patent ductus arteriosus</td>
<td>Rt. parieto-occipital (1)</td>
<td>No growth (sulfonamide therapy)</td>
</tr>
<tr>
<td>Robbins&lt;sup&gt;30&lt;/sup&gt;</td>
<td>1945</td>
<td>20 F</td>
<td></td>
<td>Unknown</td>
<td>Tetralogy of Fallot; patent ductus arteriosus</td>
<td>Left temporal lobe</td>
<td>No organisms on smear &amp; culture</td>
</tr>
<tr>
<td>Sidenburg et al.&lt;sup&gt;31&lt;/sup&gt;</td>
<td>1946</td>
<td>6 M</td>
<td></td>
<td>Severe stomatitis &amp; gingivitis</td>
<td>Tetralogy of Fallot</td>
<td>Lt. parietal lobe (1)</td>
<td>B. pyocyaneus, Staph. aureus, B. coli</td>
</tr>
<tr>
<td>Smolik et al.&lt;sup&gt;12&lt;/sup&gt;</td>
<td>1946</td>
<td>9 F</td>
<td></td>
<td>P.U.O. 2 wks. prior to onset abscess symptoms</td>
<td>Prob. I.V. septal defect with patent ductus arteriosus</td>
<td>Lt. frontal lobe (1)</td>
<td>H. influenzae</td>
</tr>
<tr>
<td>Gates et al.&lt;sup&gt;16&lt;/sup&gt;</td>
<td>1947</td>
<td>6 M</td>
<td></td>
<td>Tonsillectomy</td>
<td>Cor biaatriatum triloculare; patent F.O.</td>
<td>Lt. temporoooccipital (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Gates et al.&lt;sup&gt;11&lt;/sup&gt;</td>
<td>1947</td>
<td>8 M</td>
<td></td>
<td>Unknown</td>
<td>Tetralogy of Fallot; patent F.O.</td>
<td>Rt. frontal lobe, posteroinferior (1)</td>
<td>Gram-neg. anaerobic rods</td>
</tr>
<tr>
<td>Gates et al.&lt;sup&gt;4&lt;/sup&gt;</td>
<td>1947</td>
<td>5 M</td>
<td></td>
<td>Unknown</td>
<td>Tetralogy of Fallot</td>
<td>Lt. frontoparietal (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>Gates et al.&lt;sup&gt;16&lt;/sup&gt;</td>
<td>1947</td>
<td>26 F</td>
<td></td>
<td>Acute upper respiratory infection</td>
<td>Atrial septal defect</td>
<td>Rt. occipito-parietal (1)</td>
<td>Actinomyces bovis</td>
</tr>
<tr>
<td>Hand&lt;sup&gt;17&lt;/sup&gt;</td>
<td>1947</td>
<td>54 F</td>
<td></td>
<td>Acute upper respiratory infection</td>
<td>Tetralogy of Fallot</td>
<td>Lt. temporal (1); lt. occipital (1); lt. parietal (1)</td>
<td>Gram-pos. diplococci</td>
</tr>
<tr>
<td>Hand&lt;sup&gt;27&lt;/sup&gt;</td>
<td>1947</td>
<td>8 F</td>
<td></td>
<td>Unknown</td>
<td>Tetralogy of Fallot</td>
<td>Rt. temporal lobe (1)</td>
<td>Unknown</td>
</tr>
<tr>
<td>This report&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1949</td>
<td>9 M</td>
<td>None</td>
<td></td>
<td>Tetralogy of Fallot</td>
<td>Probably lt. parietal occipital</td>
<td>? Gram-pos. diplococci</td>
</tr>
<tr>
<td>This report&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1949</td>
<td>35 F</td>
<td>None</td>
<td></td>
<td>Basal L.V. septal defect; patent ductus arteriosus</td>
<td>Lt. temporal lobe (1)</td>
<td>Hemolytic Staphylococcus albus</td>
</tr>
</tbody>
</table>

F.O. = foramen ovale; I.V. = interventricular; ant. = anterior

<sup>a</sup> Clinical diagnosis; necropsy limited to thorax.
<sup>b</sup> Acute endocarditis of lower pulmonary conus orifice.
<sup>c</sup> Correct clinical diagnosis.
<sup>d</sup> Correct clinical diagnosis; left temporoparietal decompression; death thirteen days postoperatively.
<sup>e</sup> Clinical diagnosis; abscess trephined; death in fifty days; no necropsy.
<sup>f</sup> Clinical diagnosis; abscess trephined; sulfapyridine therapy; death in forty-three days.
<sup>g</sup> Acute bacterial endocarditis on pulmonary valve (H. influenzae).
<sup>h</sup> Correct clinical diagnosis.
<sup>i</sup> Correct clinical diagnosis; surgical aspiration of abscess; complete recovery in two months.
<sup>j</sup> Correct clinical diagnosis; surgical drainage; death in twenty-nine days.
<sup>k</sup> Correct clinical diagnosis; death before localization of abscess.
<sup>l</sup> Correct clinical diagnosis; evacuation of abscess with apparent recovery; recurrence and death. Bacterial endocarditis of aortic valve.
<sup>m</sup> Clinical diagnoses; permission for necropsy denied.
were solitary whereas 5 patients had multiple abscesses. In 21 patients the abscesses were in the right hemisphere, in 15 they were left sided, and in one patient a cerebellar abscess was found. In 25 of the patients, a postmortem bacteriologic study of the abscess was attempted. Micro-organisms were identified on smear or cultured in 15 of these. The species were wide in range (table 1). Chronicity of the abscess occurred in the few patients who had benefit of chemotherapy or surgical intervention.1

**Diagnosis**

In only 9 patients was the correct clinical diagnosis made. In 6, surgical drainage or decompression was performed, but only one patient survived.

**Table 2.** Age and Sex Distribution in Forty-three cases of Congenital Heart Disease with Paradoxic Brain Abscess

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>No. of Cases</th>
<th>Sex Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>14</td>
<td>Age Range: 3 to 57 years</td>
</tr>
<tr>
<td>10-19</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>6</td>
<td>Average Age: 16.6 years</td>
</tr>
<tr>
<td>30-39</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>1</td>
<td>Male Distribution:</td>
</tr>
<tr>
<td>50-59</td>
<td>1</td>
<td>Males 22</td>
</tr>
<tr>
<td>Age Unknown</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>Females 22</td>
</tr>
</tbody>
</table>

The diagnosis should be suspected in all patients with known congenital septal defects who have symptoms of central nervous system involvement. It should be especially suspected in young subjects. Although the age range of the patients included in this report varied from 3 to 57 years, the average age was 16.6 years (table 2). An overwhelming number of patients have a history of acute onset of fever, headache, and lethargy, often associated with nausea or vomiting. The lumbar puncture often reveals an increase in pressure and a slight to moderate increase in cells. It is this early predominant lymphocytosis, or even the complete initial absence of pleocytosis, so characteristic of early developing brain abscess, which often leads to a mistaken diagnosis of encephalitis or tuberculous meningitis. Blood and spinal fluid cultures should be made but diagnostic dependance upon them is to be decried. In the 44 cases reported, blood culture, when made, was consistently negative. Spinal fluid culture was attempted in 17 instances, and in the 5 patients in whom it was positive the abscess had ruptured with a resultant terminal meningitis.

**Report of Cases**

**Case 1.**—The patient, A. W., a 9 year old white boy, cyanotic since birth, was admitted to the Contagious Division, Cleveland City Hospital, on June 5, 1946. The admission diagnosis was “acute encephalitis.” He had been treated since May 13 at another hospital with penicillin and sulfadiazine for an alleged “streptococcus infection” characterized by headache, fatigueability, and fever. Eighteen days prior to admission into this hospital the boy developed right facial weakness. No history of antecedent infection could be elicited.

The patient was acutely and chronically ill. The physical and roentgenologic findings were characteristic of the tetralogy of Fallot. Brunziński's sign was questionably present bilaterally, there was weakness in the muscles supplied by the right facial nerve, and the speech was thick.

**Laboratory Studies:** The hemogram revealed a hemoglobin of more than 17 grams, and a red blood cell count of 9,000,000, with 10,000 white cells, predominantly polymorphonuclear leukocytes. On lumbar puncture the spinal fluid pressure was 300 mm. of water, the protein value was 55 mg. per 100 cc. of fluid, the chloride value 445 mg. per 100 cc. (as Cl), and the cell count 18 per cubic millimeter. Organisms could not be demonstrated in the blood and spinal fluid by culture or smear.

**Hospital Course:** The boy was given penicillin and sulfadiazine. The temperature throughout the hospital stay fluctuated between 36.8 and 39.8 C. On the second day, weakness of the right arm and leg developed. Sulfadiazine was discontinued because of gross hematuria, which did not recur. He seemed to be improving and the temperature became normal, but on the eighth day the temperature rose to 38.5 C., and the patient became confused. There was marked nuchal rigidity and sustained ankle clonus on the right. Lumbar puncture revealed 11,200 cells per cu. mm. of fluid, almost all of them being polymorphonuclear leukocytes. Gram-positive diplococci were seen on smear and grown on culture. On the nineteenth day the optic disc became fuzzy, right facial weakness was more pronounced, and there was tremor, oculogyresis, and paraparesis of the right arm and leg. The diagnosis of brain abscess in the left parieto-occipital area with rupture and secondary meningitis was suggested. The patient failed to respond to continued chemotherapy and died on the thirty-third hospital day.
Comment: Although necropsy was not permitted, it was obvious that this patient suffered from a veno-arterial shunt, which most likely was part of the tetralogy of Fallot. The course and findings were characteristic of a brain abscess producing a local, surface meningitis, followed by rupture into a lateral ventricle and flooding of the cerebrospinal fluid with pus. The correct diagnosis was made too late to be of benefit to the patient. A diagnosis was made initially of bacterial endocarditis with cerebral embolism, which was adhered to in spite of persistently negative blood culture (a common occurrence in brain abscess). Moreover, there were no clinical findings to substantiate the diagnosis other than the presence of congenital heart disease of a type in which bacterial endocarditis is of low incidence.1 In retrospect the circumstances were such that, coupled with the signs of early localization, a correct diagnosis could have been attained in two days following admission to this hospital.

Case 2.—The patient, J. D., a 35 year old Negro woman, known to have an interventricular septal defect, was first admitted to the Tuberculosis Division, Cleveland City Hospital, in 1937, because of far advanced pulmonary tuberculosis without cavitation. After two years' bed rest, she was followed in the Outpatient Department and continued to remain asymptomatic until March 22, 1947, when she complained of sudden onset of nausea, intermittent vomiting, severe headache, and fever, which continued unabated until March 30, when she became stuporous. She was seen by a physician, and admitted to the Contagious Division, Cleveland City Hospital, on April 1, 1947, with the diagnosis of acute encephalitis or tuberculous meningitis.

On admission the patient was semicomatose. The right optic disc showed slight papilledema. There was definite nuchal rigidity. The heart was not enlarged, and the murmur heard previously apparently had not changed. The lungs were clear to percussion and auscultation. The Kernig and Brudzinski signs were present, and the deep tendon reflexes were hyperactive on the left side.

Laboratory Studies: The red blood cell count was 6,400,000, the hemoglobin value 20 grams, and the white blood cell count 16,900; 90 per cent of the white cells were polymorphonuclear leukocytes. This picture may have been partially modified by the patient's extreme dehydration. The spinal fluid (lumbar puncture) was under 54 mm. of water pressure; there were 80 cells per cu. mm. of fluid, all of them being mononuclear leukocytes. Twenty-four hours later the spinal fluid contained 100 cells per cu. mm., 90 per cent of which were mononuclear cells; the protein value was 180 mg. and the chloride (as Cl) value 436 mg. per 100 cc. of fluid. Cultures of the spinal fluid and of the blood showed no growth.

Hospital Course: The patient remained unconscious, often moving aimlessly the left arm and leg, both of which showed marked increase in extensor tonus. She failed to regain consciousness and expired after forty-eight hours.

Necropsy: The heart weighed 350 grams. Both right and left ventricular walls measured 1 cm. in thickness. All valves were normal and no endocarditis was present. There was a basal interventricular septal defect which was oval and measured 1.5 cm. in the greatest diameter. The ductus arteriosus was patent, but the lumen was only 2 mm. in diameter. At the tip of the right temporal lobe was an acute globular abscess measuring 5 cm. in diameter, from which 60 cc. of foul-smelling pus were evacuated. Smears of this abscess showed many gram-positive cocci, and on culture a hemolytic Staphylococcus albus was grown. The mastoid air cells and accessory paranasal sinuses were normal. The leg veins were not thrombosed. In the lungs there was moderately extensive fibrosis and nodulation consistent with healed tuberculosis. No primary source of the acute infection was found.

Comment: This patient was practically moribund on admission, and there was little that could have been done diagnostically or therapeutically. As is common in patients with brain abscess, the blood culture, and spinal fluid smear and culture were all negative. Cognizance of the not infrequent complication of congenital heart disease with septal defects by brain abscess, coupled with the pointing history of sudden onset of symptoms and the suggestion of localization (extensor rigidity of the left sided extremities, right papilledema), might have led to immediate consideration of a diagnosis which was not even suspected.

Physiologic Considerations

For many years it has been speculated, partly on the basis of paradoxical embolization, that a right-to-left shunt must occur sometime during the cardiac cycle in the presence of septal defects. Physiologic studies on living patients by means of cardiac catheterization have now shown this to be true beyond dispute. In Fallot's tetrad the shunt is obvious, and Bing and associates have shown that this shunting from right to left occurs in the absence of failure, owing to the overriding of
the aorta. This direct shunt is again obvious on anatomic grounds alone in the instances of complete transposition of the great vessels and of monoventricular hearts.

Until now it has been assumed that in the presence of a functionally patent foramen ovale or of an atrial septal defect the shunt is entirely from left to right until such time as failure supervenes, when a reversal of flow is said to occur, favoring paradoxical embolization. In instances in which failure was not demonstrable, chance interplay of blood currents at the orificial margin has been held responsible. Courand and colleagues have studied this problem. By direct catheterization of right and left auricles in three young subjects with no evidence of failure, they demonstrated the overall preponderance of left-to-right flow. They likewise showed that reciprocal admixture is distinctly possible. Simultaneous recording of pressures with a double-lumen catheter, however, is needed to prove this point definitely. Additional evidence is afforded by lower oxygen saturation of peripheral arterial blood during periods of exercise as compared to blood from the pulmonary vein.

In solitary ventricular septal defects it has not been demonstrated that a right-to-left shunt occurs in the presence of a totally unembarrassed right ventricle, but exercise tolerance tests have shown a decrease in peripheral arterial oxygen saturation in patients who at rest showed no evidence of failure.

In the cases analyzed in this report, there were 9 instances of ventricular septal defect (table 3). Of these, one was not proved by necropsy. In 4 instances the defect was associated with pulmonary stenosis or hypoplasia, a factor which would enhance the load on the right ventricle and lead to increased opportunity for reciprocal blood admixture.

There were 5 instances of isolated defects in the atrial septum. In one, further embarrassment was caused by associated pulmonary stenosis, in the other by a displaced, insufficient tricuspid valve (Ebstein's disease).

There is no clear evidence in the 4 patients with solitary ventricular defects and in the 3 with atrial defects that early failure was not present. In all instances there was anatomic evidence of right-sided enlargement. None of these patients were younger than 18 years of age, which would point to a prolonged period of stress on the right side of the heart before failure becomes manifest.

**Discussion**

Robbins has been quoted before, but it may not be amiss to cite him again: “In all probability, this apparent obscurity and paucity of reported cases represents the failure either of their recognition or of their publication, rather than the rarity of their occurrence.” Maude Abbott found 98 instances of bacterial endocarditis and endarteritis (17.6 per cent) in 555 autopsied congenital hearts. Gates and co-workers reviewed 115 fatal cases of congenital heart disease. They found 5 instances of brain abscess (4.3 per cent) and 8 of bacterial endocarditis (7 per cent). Robbins reviewed the records of 53 autopsy subjects who had congenital heart disease and found 3 instances of paradoxical abscess (5.6 per cent). Hanna described 6 cases in a series of 160 autopsy subjects with congenital heart disease, an incidence of 3.8 per cent. This indicates that the condition is probably one-fourth as common as bacterial endocarditis, yet mention of this fact is rare; the diagnosis is usually missed, and many cases are probably not reported. The relative frequency of the condition is magnified when one studies the breakdown of Maude Abbott’s cases. In 59 instances of transposition of the great vessels, bacterial endocarditis occurred in 6 patients (10 per cent); in 21 patients with cor bilocular and triloculare, none; in 31 patients with patent foramen ovale, none. The incidence was con-

**Table 3.—Cardiac Lesions Encountered (Forty-four Cases)**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetralogy of Fallot</td>
<td>23</td>
</tr>
<tr>
<td>Basal interventricular septal defect</td>
<td>8</td>
</tr>
<tr>
<td>Patent foramen ovale and atrial septal defect</td>
<td>5</td>
</tr>
<tr>
<td>Cor biatrimum triloculare</td>
<td>2</td>
</tr>
<tr>
<td>Complete transposition of great vessels</td>
<td>1</td>
</tr>
<tr>
<td>Eisenmenger's complex</td>
<td>1</td>
</tr>
<tr>
<td>Muscular interventricular septal defect</td>
<td>1</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>1</td>
</tr>
</tbody>
</table>
CONGENITAL HEART DISEASE WITH SEPTAL DEFECTS

considerably higher in patients with atrial septal and basal interventricular septal defects. This is in accordance with her explanation that “juxtaposition of the defect to the valvular endocardium and the attainment of a moderately advanced age are two factors that definitely increase the rate of frequency.”

The great prevalence of solitary abscesses offers inducement to early diagnosis, as does the improved outlook for patients with the tetralogy because of the successful results of the Blalock-Taussig operation. In addition, Selzer and associates²¹ have recently suggested remedial surgery in patients with pulmonary stenosis associated with patent foramen ovale. In one of our collected cases this combination of anomalies was presented.

CONCLUSIONS

1. Two cases of paradoxical brain abscess due to crossed septic emboli in patients with congenital septal defects of the heart are presented, and the literature is reviewed.

2. The incidence of this complication is probably much higher than is reported. As a specific bacterial cause of death in patients with congenital heart disease, paradoxical brain abscess stands second only to bacterial endocarditis.

3. Brain abscess should be suspected in all patients with congenital heart disease with septal defects presenting symptoms of central nervous system involvement.

4. Improvements in cardiac surgery, and the relative longevity of patients with isolated septal defects, particularly with the present availability of antibiotics, further justify all attempts to improve the poor therapeutic results reported to date.

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Circulation. 1950;1:593-601
doi: 10.1161/01.CIR.1.4.593

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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