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Bruce Everett Johnson
University of Nebraska Medical Center

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Bruce E. Johnson

Dr. Grissom

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Renewed interest has occurred in bacterial endocarditis during the past ten years, due to its occurrence as a serious complication following surgical procedures, especially cardiac surgery. The pathological process is changed with the presence of prosthetic valves in some cases, but not all. However, the clinical course of the disease appears to be changing even in cases not having artificial valves. Previously, the term "subacute bacterial endocarditis" was understood to include most cases of infective endocarditis. Presently, acute bacterial endocarditis is increasing in frequency and is more common than the subacute form in certain areas (1).

Reasons for this changing pattern are many, but two are of prime importance. First, patients undergoing cardiac surgery have an increased vulnerability, especially when a valve prosthesis is used, and second, infecting organisms are becoming more resistant to commonly used antibiotics. Diagnosis of endocarditis often is difficult in these patients, as few peripheral manifestations of the disease are present in the early stages of the disease. This makes the disease even more serious, as very early diagnosis and treatment are essential to recovery in the acute form.

This paper is a review of nine cases of bacterial endocarditis occurring in patients previously having some type of

surgical procedure done before the endocarditis occurred or at least before it was recognized, and one case apparently cured by surgery.

Four of the patients were hospitalized at Bishop Clarkson Hospital, and six at the University of Nebraska College of Medicine Hospital. Four of the patients had open heart surgery with insertion of valve prosthesis, three had closed heart surgery, two had cardiac catheterization and one had a ventriculo-atrial shunt prior to the diagnosis of bacterial endocarditis.

CASE HISTORY: L.F.

This 46 year old white male was first seen at the University of Nebraska Hospital in January, 1966 for evaluation of rheumatic heart disease. He was hospitalized in 1948 for 3½ months for acute rheumatic fever. Six months prior to this admission, he had increasing exertional dyspnea and palpitations. He was placed on diuril, potassium chloride and digoxin. He returned in February, 1966 when cardiac catheterization was performed, revealing aortic stenosis, aortic insufficiency, and probable mitral insufficiency.

In April, 1966, cardiac operation for aortic and mitral valve replacement using the Starr-Edwards prostheses was performed. Following the operation, a slight aortic regurgitant murmur was noted, believed to be due to slight leakage around the valve. The post-operative course was uneventful except for a low grade fever present up to one day prior to dismissal. Three blood cultures during that period were negative.

He was seen in late June, 1966, in the Cardiac Clinics for his first post-operative follow-up. At that time he was feeling fine, although a grade 2/6 intensity systolic murmur was present in addition to the slight aortic regurgitant murmur present earlier.

He was readmitted on July 25, 1966, because of a cough, productive of clear, white, foamy sputum, 1-2 cups per day for five weeks. These episodes lasted approximately one-half

hour. He noted some exertional dyspnea during this period of time. Two weeks prior to this admission he developed a low grade fever which his local doctor treated with tetracycline up to the time of admission. Two days prior to admission, he developed pedal edema.

On physical examination, he had a temperature of 38.5°C, questionable splinter hemorrhages, hepatomegaly to two fingerbreadths, but no splenomegaly. Auscultation revealed a grade 3/6 intensity systolic murmur heard best in the second right intercostal space and at the apex. A grade 1/6 intensity diastolic murmur was again heard along the lower left sternal border. Moderate pedal edema was present. His behavior seemed sluggish.

Laboratory work included a hemoglobin of 7.8 grams, white count 18,000, BUN of 22mg%. Blood cultures yielded hemolytic Staphylococcus aureus, coagulase negative. Antibiotic therapy was started immediately, using 12 grams methicillin intravenously and 30,000,000 units crystalline penicillin intravenously, daily. On July 30, the penicillin was discontinued when the organism showed in vitro resistance. The patient developed a gradual increase in the severity of the congestive heart failure, and a progressive increase in intensity of the diastolic murmur during the next two weeks. Atrial fibrillation appeared. He suffered several episodes of respiratory distress which responded to morphine and aminophyline. On August 13, he developed another episode of severe respiratory

distress and died.

Post-mortem examination revealed vegetations and abscess formation in the interatrial septum, around the aortic valve, with the aortic prosthesis hanging loose in the left ventricle. In addition, he had small bilateral subdural hematoma.

CASE HISTORY: W.J.

This 23 year old white male at age of eight years had rheumatic fever, and thereafter had rheumatic heart disease with aortic stenosis and insufficiency. He entered the hospital for aortic valve replacement on June 12, 1966. Admitting laboratory work: hemoglobin 14 grams, white cell count - 7,200; sedimentation rate - 18 mm/hr; normal BUN, urinalysis, and electrolytes. His temperature was 37.5°C..

Two days after admission splinter hemorrhages were noted in a couple fingers. This was felt to be insufficient evidence for bacterial endocarditis, as there were no other signs, and blood cultures were negative at 48 hours.

On June 16, 1966, the aortic valve was resected and a ball valve prosthesis was inserted. Numerous verrucous-appearing grayish-white areas were noted on the resected valve. The pathological diagnosis was fibrosis, hyalinization, and calcification of aortic valve, rheumatic valvulitis, and bacterial colonies of hyalinized fibrous tissue from aortic valve. Culture of these vegetations grew Staphylococcus albus. Blood cultures taken at admission also grew this strain after one week. It was highly sensitive to penicillin. He was placed on 22 million units potassium penicillin G intravenously daily.

On June 30, 1966 drainage of the chest wound was noted. Culture yielded Staphylococcus coagulase negative, resistant

to penicillin but sensitive to methicillin and oxacillin. He then was given sodium oxacillin, 2.0 grams daily.

Following the operation, the patient gradually developed splenomegaly, and the splinter hemorrhages became more prominent. On July 19, 1966, clubbing of the fingers was noted. By July 20, the surgical wound was well healed. On August 5, 1966, dental extraction was done to correct three carious molars. He was taking large doses of penicillin at this time. He received the penicillin G for a total of eight weeks. On August 10, 1966, he was discharged with phenoxymethyl penicillin, 500 milligrams, four times daily.

He was readmitted on September 19, 1966, with hematuria and right flank pain. He was receiving anticoagulant therapy and his prothrombin time was 35 seconds, with a control of 13 seconds. Anticoagulation was reduced and the urine cleared completely of red cells. There were no white cells in the urine. He became asymptomatic and was discharged on September 26, 1966. Blood cultures were negative. No splenomegaly was present, nor were splinter hemorrhages. He was afebrile.

CASE HISTORY: K.R.

This 27 year old white female, with congenital heart disease, was admitted on October 28, 1965, for cardiac catheterization. She had been seen three months earlier in mild congestive failure, for which she was treated and released. Three weeks prior to admission she developed increasing fatigue, exertional dyspnea, and a sensation of tightness in the chest. She lost consciousness, was taken to a local hospital, and treated with anticoagulants. Her prothrombia time was markedly prolonged, and this therapy was stopped.

Physical examination revealed a poorly developed woman with cyanosis of the lips and fingers. A systolic thrill was present at the lower left sternal border, associated with a harsh, crescendo, grade 3/4 intensity, systolic murmur heard best in the same area, with radiation to the carotids. The liver was enlarged two finger-breadths, but the spleen was not palpable. There was marked clubbing of the digits. Cardiac catheterization on November 1, 1965, demonstrated a tetralogy of Fallot with an atrial septal defect and tricuspid insufficiency. On November 3 and November 5, 1965, phlebotomies were done in an attempt to correct a hematocrit of 67%, 500 and 600 milliliters being taken on respective days. Thirty minutes following the second phlebotomy, the patient became hypotensive, but responded to oxygen and intravenous fluids.

During the period following the catheterization she had several episodes of respiratory distress which responded to oxygen. On November 10, 1965, she developed blurred vision, weakness, and lethargy. Blood cultures were drawn on November 11, 1965. The next day she suffered another episode of respiratory distress which did not respond to oxygen, and she died. During her hospital stay her temperature ranged from 37° to 38°C. The blood cultures taken yielded no growth in 10 days.

She had had urinary tract infections one year and seven years ago. Her BUN was 28 on admission and rose to 35.5. The 24-hour creatinine clearance was 27.6 milliliters. Her white cell count ranged from 11,000 to 13,000. Urinalysis showed 0-2 red cells, and 10-12 white cells per high powered fields on admission. The day before she died there were 50-75 red cells and 4-8 white cells per high powered field.

Autopsy revealed vegetations on the tricuspid valve, which cultured out (1) Alkaligenes fecalis, (2) Bacterium anitratum, and (3) a Bacillus species. Heart blood cultures yielded no growth.

CASE HISTORY: J.S.

This 25 year old white female was admitted on June 14, 1966, with complaints of chest pain and cough of one week's duration. This pain was constantly present, more intense at night, partially relieved by lying on the right side, but intensified by lying on the left side.

In December, 1964, she underwent a craniotomy and a small cystic hemangioendothelioma of the vermis was excised. The immediate post-operative period was complicated by Staphylococcal meningitis. In May, 1965, a ventriculo-atrial shunt with a Pudenz pump was inserted following the development of adhesive arachnoiditis of the posterior fossa with secondary hydrocephalus. Again the post-operative period was complicated with meningitis. She was readmitted on June 20, 1965, with chills and fever of 101.5°F. Although no murmur was audible, she was suspected of having endocarditis of the tricuspid valve. The initial blood cultures yielded coagulase negative micrococcus. She had no peripheral manifestation of endocarditis. She was treated with phenoxymethyl penicillin, 500 milligrams every four hours. Following administration of antibiotics, blood cultures were negative. She was dismissed afebrile on June 29, 1965, on phenoxymethyl penicillin, 750 milligrams every six hours, enough for a three week's course of therapy.

On this admission (June 16, 1966), she was afebrile,

without petechiae, clubbing, or splenomegaly, but she did have a grade 2/6 intensity, pan-systolic murmur at the tricuspid area and along the left sternal border extending to nearly the third intercostal space. Admitting chest X-ray revealed prominent increase in heart size compared to films in 1965. In addition, there was an area of segmental consolidation in the right middle lobe segments. Echocardiogram revealed an eleven millimeter pericardial effusion. Lung scan revealed multiple segmental avascular areas, most compatible with multiple areas of pulmonary embolism and infarction. Electrocardiogram was within normal limits. After obtaining the results of the lung scan, bacterial endocarditis was suspected even though the patient was afebrile. Blood cultures yielded coagulase negative micrococcus, sensitive to ampicillin, chloramphenicol, erythromycin, penicillin, nafcillin, and streptomyocin, but resistant to methicillin, oxacillin, and tetracycline. She was treated with phenoxymethyl penicillin 1.5 grams every six hours. Serum inhibition test demonstrated no bactericidal action in the undiluted state five hours after the antibiotic dose, so the regimen was changed to 1.0 gram every four hours. Serum inhibition tests at three hours following medication now revealed inhibition at a 1:4 dilution.

On July 6, 1966, the shunt and pump were removed, as

this was believed to be a contributing factor to the endocarditis. She required several lumbar punctures to relieve pressure immediately thereafter, but after two days, the site of the pump became soft and she continued to do well. Blood cultures became negative.

CASE HISTORY: H.K.

This 48 year old white male was admitted on May 31, 1962, with complaints of fever, chills, and pain in the chest. He had had a heart murmur since early childhood, but had never had any difficulty until March, 1962, when he developed a fever of 104°F., with chills. He thought he had the "flu" and was treated with "shots", following which he felt fine for a few days, then the fever and chills recurred, and again penicillin shots resolved the symptoms. These episodes of symptoms and treatment occurred six times. In April, 1962, he was admitted to his local hospital and treated heavily with penicillin for five days. Since then he received penicillin injections every other day, and took eight penicillin pills a day. He felt fine until one week prior to admission when he developed a "chalky" feeling in the throat. Two days prior to admission he developed chills and fever and sharp stabbing pain in the right side of the abdomen which moved into the right chest in the mid-axillary line. He was then referred to this hospital by his family doctor.

On physical examination, there was a loud "machinery" murmur heard throughout the precordium, continuous throughout systole into diastole, typical of patent ductus arteriosus. The heart was enlarged to percussion. The right lung base was dull to percussion, and breath sounds were

diminished in this area. No hepatosplenomegaly was present. There were no splinter hemorrhages, petechiae, or clubbing. Temperature on admission was 99.6°F. Blood cultures taken at his local hospital yielded Streptococcus viridans, but were all negative at this time. Chest X-ray revealed cardiomegaly, left ventricular in type, bilateral pulmonary vascular congestion, and right basilar pleural effussion.

On June 2, 1962, he was treated with streptomyocin, 1.0 gram intramuscularly daily, probenecid 1.0 gram four times daily orally, and 10 million units aqueous penicillin G, one ampule alidase, and 5 milliliters of 1% procaine in 1000 cc. 5% glucose and water, running deep intramuscularly, twice daily, over the 24-hour period. Two days later the alidase and procaine were discontinued and the fluid and penicillin were administered intravenously. At this time he developed nausea and anorexia and nausea, so the probenecid was reduced to 1.0 gram twice daily, and then changed to 0.5 grams four times daily. On June 10, 1962, the streptomyocin was discontinued. On June 15, 1962, a division and ligation of the patent ductus arteriosus was performed. Penicillin was discontinued on June 23, 1962. The patient was dismissed on June 26, 1962, with no evidence of endocarditis.

CASE HISTORY: Z.F.

This 42 year old white female was admitted on June 3, 1962, with a one week history of pain in her left leg, a low-grade fever, nausea and vomiting, and a temporary loss of memory. On the day prior to admission, she had numbness of the left side of her body, beginning in the left hand.

In 1958, she underwent a mitral commissurotomy for mitral stenosis, secondary to rheumatic heart disease, but unsatisfactory results were obtained because of pulmonary hypertension and inadequate valve opening. On April 4, 1962, a mitral valve prosthesis was inserted. Her post-operative condition was good, and her cardiac symptoms considerably improved.

On physical examination, she had a temperature of 38°C. No retinal petechiae were present. The heart was normal in size, but had an audible beat even without the use of a stethoscope. The first mitral sound was increased and there was a prominent opening snap. The liver was palpable two finger-breadths below the right costal margin, but this finding had been present prior to her last operation. A new finding of splenomegaly was noted. Laboratory results were within normal limits.

Blood cultures on the eve of admission and two days later yielded Staphylococcus, coagulase negative, resistant

to penicillin, sulfadiazine, and sulfisoxazale but sensitive to tetracycline, erythromycin, kanamycin, methicillin and oxacillin.

When the culture results were received, methicillin, 2 grams every four hours intravenously was begun. The next day, she suffered severe right upper quadrant abdominal pain, which gradually subsided after three to four days. Embolic phenomena were suspected as the cause of this pain, and of the apparent stroke. However the urinalysis failed to reveal any red cells. On June 13, 1962, a culture taken 3¼ hours following the intravenous methicillin showed four colonies at a one to two dilution but a heavy growth in all other dilutions. A culture taken immediately after the administration of methicillin was negative in all dilutions. It was during the period from June 12 to June 20 that the patient showed the most septic course and the highest degree of fever rising to 40°C. or 41°C. daily. On June 14, probenecid was added to the therapeutic regimen at 0.5 grams every eight hours, orally. On June 16, a culture taken four hours following methicillin produced a heavy growth at a one to two dilution. Again on June 18, cultures proved positive. On June 21, erythromycin was added to the regimen at 0.5 grams every six hours intravenously, which was changed to an oral dose of the same amount on June 25. On July 1, due to the lack

of veins for intravenous fluids, the methicillin was discontinued and replaced by oxacillin, one gram every four hours orally.

The patient improved subjectively very well by July 10, and was discharged on July 19, still receiving antibiotic therapy. She was advised to continue on her antibiotics for six months. She had no recurrence of the endocarditis. During the hospital course she developed a loud systolic murmur, which decreased in intensity considerably by the time of discharge.

CASE HISTORY: C.J.

This 10½ year old white girl with tetralogy of Fallot, had a Pott's procedure done elsewhere at age 19 months. For two months prior to her admission on June 23, 1963, she had intermittant fever, at times reaching 104°F., which responded to oral obenzathine penicillin G. There was increasing irritability, anorexia, and fatigue two weeks prior to admission, and three days prior to admission the fever increased and there was diaphoresis.

Physical examination revealed a grade 2/6 intensity continuous murmur below the left clavicle, and a grade 3/6 intensity pansystolic murmur along the left sternal border. The pulmonic second sound was increased. Hepatomegaly, two finger breadths, and splenomegaly, three finger breadths, were present. There was slight cyanosis of the nail beds.

Blood culture yielded alpha hemolytic Streptococcus, sensitive to penicillin, tetracycline, streptomyocin, novobiocin, and chloramphenicol. She was treated with 10 million units of aqueous penicillin daily. On the eighth day, probenecid, 0.5 grams, every eight hours orally was added, but discontinued seven days later when a hypersensitivity was suspected. The penicillin was increased to 20 million units daily two days prior to the cessation of

probenecid. At the time of discontinuance of probenecid (July 12, 1963), the temperature ceased spiking and she remained afebrile thereafter.

During the hospital course her hemoglobin was 10.9 grams %, and her white count varied between 9,000 and 12,000. Her chest X-ray showed moderate cardiac enlargement with moderate increase in pulmonary vasculature. Electrocardiogram showed sinus tachycardia (125/min.), extreme right axis deviation, and biventricular hypertrophy.

She was discharged on July 21, 1963, afebrile and improved. She was seen in clinics on September 5, 1963, at which time no hepato-splenomegaly was present. She was again seen on August 23, 1966, for cardiac catheterization. No evidence of bacterial endocarditis was present.

CASE HISTORY: W.J.O.

In August, 1963, at the age of 10 months, this white male infant had cardiac catheterization elsewhere, where the diagnosis of truncus arteriosus was made. He had had cyanosis and a cough since birth. In addition, he was mentally retarded. He was first seen at the University of Nebraska Hospital in the cardiac clinics in February, 1964. A grade 4/6 intensity holosystolic, ejection murmur was present over the entire precordium, heard best at the left sternal border. Moderate cyanosis and clubbing were present. Chest X-ray revealed a moderately enlarged heart with moderate pulmonary overcirculation. Thereafter, he developed frequent upper respiratory infections.

At the age of 2½ years he was hospitalized at the University of Nebraska Hospital in July, 1965, for a fever of three week's duration, which daily spiked to 38.5° to to 39°C. and returned to normal. He was treated with penicillin, methicillin, and finally kanamycin consecutively, with no alteration of the temperature pattern. Blood cultures at that time yielded a Bacillus species, which was thought to possibly be a contaminant. Four weeks after admission his temperature returned to normal and he was discharged. He suffered repeat episodes of fever thereafter, which seemed to respond to penicillin. Repeat blood

cultures taken in clinics yielded Listeria monocytogenes in October, 1965, sensitive by the disc method to tetracycline, chloramphenicol, erythomyocin, novobiocin, heomycin, cephalothin, and lincomycin, with partial sensitivity to penicillin, streptomyocin, and methicillin. He was admitted and treated with penicillin, chloramphenicol, kanamycin, erythromycin, tetracycline, and oxacillin, with no alteration in the temperature pattern. Finally, ampicillin suppositories, 0.4 grams, four times daily, were followed by a return of the temperature to normal. He was discharged on that medication.

He returned one week later in January, 1966, with recurring spiking temperatures, despite the continuation of ampicillin. He was then treated with lincomycin and methicillin for six weeks which brought the temperature down to normal. One week after cessation of the antibiotics, the fever recurred. Renewal of lincomycin and methicillin failed to alter the fever and were discontinued after two week's trial. Then kanamycin was tried which also was unsuccessful. This was followed by ampicillin, 0.25 grams, every six hours for two weeks on which he was discharged. Blood cultures during this hospital stay while the patient was off of all antibiotics were negative.

He was readmitted in July, 1966, for further blood

cultures after not having antibiotics for five days. Two blood cultures daily for seven days and a bone marrow culture were negative at six weeks.

At the time of this writing, the patient is continuing to have intermittent, spiking fevers.

CASE HISTORY: W.H.

This white female infant was first seen at the University of Nebraska Hospital in February, 1961. She had a grade 4/6 intensity, rough, blowing, systolic murmur present over the entire precordium, and loudest at the left fourth interspace. Her liver was descended 7 centimeters. Chest X-ray and electrocardiogram were within normal limits. She was followed and treated with digoxin to correct failure for the next two years, and in November, 1962, cardiac catheterization was done. Results were compatible with tetralogy of Fallot.

In December, 1962, a Blalock end-to-side subclavian to pulmonary artery anastomosis was performed. The day before the operation and eight days afterward, she was given procaine penicillin G, 600,000 units twice daily. The post-operative course was uneventful.

During the next four years she received intermittent prophylactic benzathine penicillin G.

In April, 1966, she was admitted to the University of Nebraska Hospital following eight days of intermittent fever up to 103°F., and increasing cyanosis and fatigue, which was treated by her family doctor with chloramphenicol and triple sulfa. Blood cultures taken after admission grew microaerophilic, alpha hemolytic Streptococcus, sensitive to penicillin, tetracycline, chloramphenicol,

erythromycin, and novobiocin. She was treated with phenoxymethyl penicillin, 0.5 grams every four hours and tetracycline, 0.125 grams every six hours for five weeks. At that time the diagnosis of bacterial endocarditis was made in view of positive blood cultures, and increasing symptoms of cardiac decompensation. Follow-up blood cultures have remained negative to the present time.

CASE HISTORY: D.L.

This 47 year old white male with rheumatic heart disease, aortic stenosis and insufficiency, was operated on elsewhere, where the aortic valve was excised and replaced with a Starr-Edwards valve prosthesis in November, 1963. Following this operation, he suffered a Streptococcus faecalis septicemia which responded slowly to penicillin therapy. Cardiac catheterization was also done at that time for evaluation of the mitral valve which was found to be normal. He was dismissed with the prosthesis in place and with a residual diastolic murmur. Since that dismissal he reported not feeling well.

He was admitted to Bishop Clarkson Hospital on January 6, 1964, with complaints of increasing exertional dyspnea, extreme fatigability and orthopnea during the past three weeks. He also has had moderate swelling of his ankles. Auscultation of the heart revealed a pansystolic murmur and a short diastolic murmur heard greatest in the second right intercostal space. He also had hepatomegaly, three centimeters, and a palpable and tender spleen.

It was felt that he had endocarditis involving the prosthetic valve attachment with loosening of the valve. On January 11, 1964, he was operated on again and the valve was resutured in place. He died early the next morning.

Post-mortem examination revealed subacute bacterial

endocarditis due to Streptococcus faecalis with focal myocardial necrosis and fibrosis. In addition he had passive congestion of viscera.

TABLE 1.

CLINICAL COURSE OF DISEASE

Patient	Predisposing heart disease	Delay from surgery to onset of BE	Age at onset	Duration of disease	Survival
L.F.	RHD	0-2 months	46	2 months	No
W.J.	RHD	0*	23	2 months	Yes
K.R.	CHD	0**	27	11 days	No
J.S.	None	1 month	23	14 months	Yes
H.K.	CHD	0***	48	3 months	Yes
Z.F.	RHD	2 months	42	2 months	Yes
C.G.	CHD	9 years	10	3 months	Yes
W.O.	CHD	2 years	3	16 months+	Yes
N.H.	CHD	1¼ years	5	1 month	Yes
D.L.	RHD	less than 1 month	47	2 months	No

RHD: Rheumatic heart disease
CHD: Congenital heart disease
* : Endocarditis diagnosed at time of surgery
** : Either developed endocarditis at the time of cardiac catheterization or had it for an undetermined length of time before catheterization.
***: Endocarditis was present for 3 months prior to surgery.
\+ : Patient still living and still suffering from endocarditis at the time of this article.

TABLE 2

CAUSATIVE ORGANISMS AND EFFECTIVE ANTIBIOTICS

Organisms	Cases	Effective Antibiotics
Staphylococcus aureus, Coagulase-negative	3 L.F. J.S. Z.F.	Tetracycline Erythromycin Ampicillin Kanamycin Chloramphenicol Methicillin Oxacillin Penicillin
Staphylococcus albus	1 W.J.	Penicillin Streptomyocin Chloramphenicol Tetracycline Erythromyocin
Streptococcus viridanz	3 H.K.* C.G. N.H.	Penicillin Streptomycin Chloramphenicol Tetracycline Erythromyocin Novobiocin
Listeria monocytogenes	1 W.O.	Tetracycline Chloramphenicol Erythromyocin Novobiocin Neomycin Cephalothin Lincomycin **Penicillin **Methicillin **Streptomyocin
Alkaligenes faecalie Bacterium anitratum A Bacillus species	1 K.R.	Sensitivity studies not done

* : Sensitivity reports were not available for H.K.
** : Organisms demonstrated partial sensitivity to these antibiotics

TABLE 3

CLINICAL MANIFESTATIONS OF BACTERIAL ENDOCARDITIS

	Temperature (Degrees C.)	Hemoglobin (Gm. %)	WBC	Changes in Murmurs	Increase in Congestive Failure	Positive Blood Cultures
L.F.	38.5	7.8	18,000	Yes	Yes	Yes
W.J.	37.5	14.0	7,000	No	No	Yes
K.R.	37-38	16.3	12,000	No	Yes	No
J.S.	38.5	9.5	9,000	Yes	No	Yes
H.K.	38.0	12.4	8,000	No	No	Yes
Z.F.	38-41	13.8	11,000	No	No	Yes
C.G.	40	10.9	10,000	No	No	Yes
W.O.	38-39	13.0	9,500	No	No	Yes
N.H.	39.5	13.0	8,500	No	Yes	Yes
D.L.*				Yes	Yes	

	Splenomegaly	Splinter Hemorrhages	Petechial Hemorrhages	Embolic Phenomena	Abdominal or Chest Pain
L.F.	No	Yes	Yes	No	No
W.J.	Yes (late)	Yes	No	No	No
K.R.	No	No	No	Yes	No
J.S.	No	No	No	Yes	No
H.K.	No	No	No	Yes	Yes
Z.F.	Yes	No	No	Yes	No
C.G.	Yes	No	No	No	No
W.O.	No	No	No	No	No
N.H.	No	No	No	No	No
D.L.	No	No	No	No	No

*: Complete records not available.

TABLE 4

SENSITIVE ANTIBIOTICS

	L.F.	W.J.	K.R.	J.S.	H.K.	Z.F.	C.G.	W.C.	N.H.
1. Penicillin	-	+	0	+	+	-	+	±	+
2. Ampicillin	+	0	0	+	0	0	0	0	0
3. Methicillin	+	0	0	-	0	+	0	±	0
4. Oxacillin	0	0	0	-	0	+	0	0	0
5. Tetracycline	+	0	0	-	0	+	+	+	+
6. Erythromyocin	+	0	0	-	0	+	0	+	+
7. Chloramphenicol	0	+	0	+	0	0	+	+	+
8. Streptomyocin	0	+	0	+	+	0	+	±	0
9. Kanamycin	+	0	0	0	0	+	0	0	0
10. Novobiocin	0	0	0	0	0	0	+	+	+

\+ : Antibiotic positive on disc sensitivity on cultures
\- : Antibiotic negative on disc sensitivity on cultures
± : Partial sensitivity
0 : Antibiotic not tested on cultures

RESULTS AND DISCUSSION:

In reviewing the time delay from the surgical procedure to the onset of the infection, we find that five of the ten patients developed bacterial endocarditis within three months following surgery (L.F., J.S., Z.F., D.L., and K.R.) (Table 1). It is not possible to rule out the possibility that K.R. may have had endocarditis before the catheterization, since the diagnosis was made at autopsy, blood cultures were always negative, and since her clinical course had deteriorated before the catheterization was done. Although no information is available concerning the time period required for the development of vegetations on valve leaflets, it would appear questionably if they could have developed in the eleven day period between the catheterization and her death.

Three of these cases had undergone open-heart surgery with extra-corporeal circulation and insertion of a ball-valve prosthesis, the aortic valve being affected in two, and the mitral in the other. One patient developing endocarditis in this post-operative period had a ventriculo-atrial shunt with a Pudenz pump inserted to correct a hydrocephalus secondary to adhesions following a craniotomy.

Thus, four of the five patients who developed the endocarditis in this time period had a "foreign body" present in the heart, which acted as a focus of increased suscepti-

bility to infection. In addition to the presence of this foreign body, extra-corporeal circulation increases the possibility of bacterial contamination during the operative procedure itself. Thus, the open-heart technique carries an increased risk of infection compared to closed-heart methods. In 250 patients managed with extra-corporeal circulation, 2.4 per cent developed an infection, whereas in 345 patients not having extra-corporeal circulation, only one, or 0.28 per cent developed an infection (2).

The seriousness of this complication is manifested by the fact that two of these patients with valve replacements died in less than three months following the surgery. Both of these had had aortic valve replacements, and the infection had dislodged the valves from their original positions.

The nature of the heart lesion is important with respect to the possibility of development of bacterial endocarditis. In one series, aortic valve surgery was complicated by endocarditis in 3.8 per cent of the cases while only 4.0 per cent of the cases of mitral valve surgery developed the infection (3).

In addition to an increased incidence of endocarditis with aortic valve surgery, there also is an increased mortality in those patients with endocarditis involving the aortic valve in comparison to mitral valve endocarditis, when a prosthetic valve is in place. At the National

Heart Institute, over 200 aortic and mitral valve replacements were done with no endocarditis occurring in the immediate post-operative period. However, three patients later developed endocarditis, between three and nineteen months following surgery, and all died. All three had had an aortic valve replacement (4). These authors stated that endocarditis involving the site of a prosthetic aortic valve rarely could be eradicated by any antibiotics.

Littlefield, et al, reported a case of Pseudomonas septicemia following an aortic valve replacement, presumably endocarditis, with survival after appropriate antibiotic treatment (5). In this series, W.J. underwent aortic valve replacement, was found to have bacterial endocarditis of the excised aortic valve, and became quite symptomatic following the operation, although he had been asymptomatic prior to surgery. Massive antibiotic therapy led to an apparent cure, at least for six months at the time of this article.

Three patients developed bacterial endocarditis between 1½ to 9 years following a surgical procedure. Two of these had Tetralogy of Fallot. C.G. developed endocarditis nine years after undergoing a Pott's procedure, while N.H. developed an infection 18 months after a Blalock procedure was done. While these infections are probably not secondary to contamination during the operation, the resultant anatomy of the heart and its vessels predisposes to endo-

carditis. In a series of 500 patients with tetralogy who underwent a Blalock-Taussig anastomosia, 6.0 per cent developed endocarditis within five years (6). The third patient had a truncus arteriosus, and developed endocarditis two years following cardiac catheterization. In this patient, the congenital abnormality is the predisposing cause and it is doubtful that the catheterization could be implicated.

This patient (W.O.) represents an unusual clinical course of endocarditis. The offending organism is Listeria monocytogenes. Despite treatment with a variety of different antimicrobial agents, both singly and in combination, the infection has not been eradicated after sixteen months. The patient is alive presently with the antibiotics acting only to suppress the symptomatology of the endocarditis with a recurrence of symptoms whenever the drugs are withdrawn.

H.K. had patent ductus arteriosus, and developed bacterial endocarditis which could be suppressed but not eradicated by antibiotics. After three months of unsuccessful medical management, ligation and division of the lesion was done. In less than two weeks following surgery he became asymptomatic with a continuation of the antibiotic therapy. Surgical correction of this congenital anomaly is the best known method of both prevention and correction of bacterial

endocarditis. This defect has a very high incidence of endocarditis - up to 42 per cent in some studies - but after surgical correction the incidence is almost that of a person with a normal heart (7).

Other congenital anomalies which have a high incidence of endocarditis are Tetralogy of Fallot as already mentioned, and ventricular septal defects. Whereas surgical correction of the patent ductus arteriosus markedly reduces the incidence of bacterial endocarditis, hopes of prevention of this infection is not an indication for surgical correction of the ventricular septal defect. These patients are vulnerable to infection after surgery has occurred (8).

Whereas Streptococcus viridans is the most common pathogen usually in bacterial endocarditis, Staphylococcus aureus and albus are the most common offenders when the infection is associated with surgical procedures involving the heart, the coagulase-negative strains being more common than the coagulase-positive forms (9, 10, 11). In this series, coagulase-negative Staphylococcus aureus caused three of the cases and Staphylococcus albus one (Table 2). They were the offending pathogen in three of the four valve replacements. The fourth Staphylococcal infection occurred in the patient with the ventriculo-atrial shunt. It would thus appear that the presence of foreign materials may play a leading role in the predisposition to Staphylococcal

endocarditis, although they are not a "sine qua non."

The alpha-hemolytic Streptococcus caused three cases of endocarditis, one in a patient receiving a valve replacement, and the other in cases with surgical procedures modifying a Tetrology of Fallot.

Listeria monocytogenes caused one case in this series, and the infection continues despite repeated trials of various antibiotics, as already discussed.

One patient had negative blood cultures, the organisms not being identified until post-mortem when cultures of the valve leaflets yielded three organisms, Alkaligenes faecalis, Bacterium anitratum, and a Bacillus species.

Blood cultures play a very important role both in the diagnosis and in the treatment of bacterial endocarditis. A positive blood culture is a major criteria in the diagnosis of endocarditis, although it is not essential. The importance of antibiotic sensitivity tests on the culture are obvious. This is the best means by which to choose the best therapeutic regimen.

In this series, one patient had consistently negative blood cultures, and as a result the recognition of the presence of this disease was delayed, with a fatal outcome.

During the past 15 years, most series report negative blood cultures in 7 to 28 per cent of the cases of endocarditis (12, 13, 14, 15, 16, 17, 18, 19). This is not

always recognized because many reports include only those cases with positive blood cultures, using this as an essential criteria for diagnosis.

The first blood culture was positive in 82 per cent of patients with bacterial endocarditis in a series reported by Wedgewood (20). Five blood cultures are the maximum number usually required, more cultures rarely increasing the possibility of the diagnosis of a bacteremia (21, 22).

The clinical manifestation of bacterial endocarditis includes fever, murmur, petechiae, subungual splinter hemorrhages, Osler's nodes, splenomegaly, clubbed fingers, embolic phenomena, congestive failure, and anemia. Clinical manifestations in this series is summarized in Table 3.

Fever is the single most frequent sign of bacterial endocarditis. In this series, temperatures ranged from 37°C. to 41°C. In one-half of the cases the temperature never was above 38.5°C. In one patient, the temperature did not rise above 37.5°C. throughout most of the hospital course.

Only three patients had anemia with a hemoglobin below 12.0 gm.%. However, this may be masked in those patients having extracorporeal circulation, with large amounts of blood exchanged during the procedure.

Moderate leukocytosis was present in only three of the patients, the remainder of the patients having normal leukocyte counts. This is compatible with previous reports,

which have shown that this is often within normal values.

The development of or change in a murmur is an important sign in bacterial endocarditis, and signifies the involvement of a valve. Murmurs were present in all but one patient prior to the onset of the infection. In the patient without a pre-existing murmur (J.S.), no murmur occurred in the first episode of endocarditis, but a tricuspid insufficiency murmur did develop when the endocarditis recurred. A change in murmurs occurred in two patients (L.F., D.L.), both of whom had aortic valve prosthesis which became dislodged.

Four patients had a progression of their congestive failure as a prominent manifestation of bacterial endocarditis. This usually occurs late in the course of subacute bacterial endocarditis and carries a poor prognosis. Three of these died in congestive failure.

Splenomegaly was present initially in two patients and occurred later in another. The remainder of the patients never developed an enlarged spleen.

Splinter hemorrhages were present in two patients and petechiae in only one. Frequency of occurrence of these cutaneous manifestations varies in the literature. Lerner and Weinstein found petechiae in 26 per cent of their patients. They question the importance of splinter hemorrhages, as they are found in 10 to 66 per cent of persons

with no apparent infection (23).

Embolic phenomena are a cardinal feature of bacterial endocarditis, usually occurring late in the course of the disease, but occurring initially in about one-third of the cases (23). Four patients in this series had manifestation of emboli: Z.F. suffered an apparent stroke, J.S. suffered multiple pulmonary emboli and infarctions, H.K. had apparent pulmonary emboli, and K.R. was found at autopsy to have multiple septic emboli in the cerebrum and meninges, which could account for her mental confusion, lethargy, and diplopia.

Other manifestation of the emboli are hematuria secondary to renal emboli and infarction. This has been reported to be present in 37 to 93 per cent of cases of bacterial endocarditis (23).

Treatment of bacterial endocarditis requires massive antibiotic therapy, with penicillin the drug of choice if sensitive organisms are present. This is given in doses in the range of 24 million units daily. Methicillin is important in treating penicillin-resistant Staphylococci. Choice of antibiotics is best done with the aid of blood cultures and sensitivity tests (Table 4).

Prophylactic antibiotic therapy for the prevention of bacterial endocarditis in patients undergoing the open heart type of cardiac surgery offers an opportunity for

reduction of the frequency with which this disease complicates the post-operative period. Incidences of this complication range from 0.0 to 10 per cent (24, 25, 26, 27, 28, 29). The goal in the prophylactic treatment is the prevention of endocarditis primarily due to Staphylococcus, the most frequent organism causing this disease in the post-operative period. Common treatment includes the use of methicillin, 4-8 grams intravenously daily, the day before surgery and thereafter until oral oxacillin, 2 grams daily can be taken. This is carried out for a total of ten days (27). Some investigators use penicillin and streptomyocin in place of the methicillin, but it would appear that this might not be as effective against all strains of Staphylococcus (24).

Use of prophylactic antibiotics is not universally accepted. Some feel that it would be more advantageous to take frequent blood cultures the first three days and then administer appropriate antibiotics if a septicemia is present (23). In theory, this probably is the more acceptible method. However, the time lag between drawing blood and the report of the culture and sensitivity is several days, during which time the course of the infection may be irreversible. The presence of an artificial valve makes these patients extremely vulnerable, and prevention of an infection is much more important than having

cultures available after an infection has occurred.

The final alternative in antimicrobial therapy would be to take blood cultures on the first one or two post-operative days, and then begin antibiotic therapy immediately if infection is suspected. After culture and sensitivity studies are completed, the regimen can then be altered. This method has the advantage of bacterial diagnosis, and fairly early initiation of antibiotic therapy. However, one must remember that prevention should remain as the goal in this disease, as well as the other afflictions of mankind.

SUMMARY:

The cases of ten patients who had bacterial endocarditis in association with a surgical procedure on the cardiovascular system are reviewed.

Five of these patients developed the infection within a three month period following the surgery, and the operation was considered to be a probable source of the infecting organism. Two of these patients died following the dislodging of prosthetic aortic valves from their original sites by the erosive lesions of the infection.

One patient with an aortic valve prosthesis was found to have endocarditis at the time of surgery. Biopsies of the diseased valve revealed bacteria and yielded positive cultures. He was treated and recovered.

Another patient developed the infection following placement of a mitral valve prosthesis. She suffered multiple emboli, but recovered with treatment. A patient with hydrocephalus and a ventriculo-atrial shunt developed endocarditis shortly after insertion of this bypass. She apparently recovered with antibiotic treatment, but had a recurrence a year later which responded only after the shunt was removed.

A patient with patent ductus arteriosus developed bacterial endocarditis which could not be eradicated with antibiotics was operated on and a division and ligation of the

patent ductus arteriosus was followed shortly with resolution of the symptoms of the endocarditis.

Two patients with Tetralogy of Fallot developed endocarditis one and nine years following Potts and Blalock procedures. The surgery itself was not a source of contamination, but the resultant shunts make the individual more susceptible to endocarditis.

The last patient has truncus arteriosus and developed endocarditis due to Listeria monocytogenes, which has been resistant to all antibiotic therapy. The patient continues to have symptoms sixteen months after the diagnosis was made.

A review of the literature is discussed with emphasis on infecting organisms, prophylactic antibiotics, symptomatology, and predisposing causes of endocarditis.

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