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CARDITIS IN POLIOMYELITIS
AN ANATOMIC STUDY OF THIRTY-FIVE CASES AND REVIEW OF THE LITERATURE *

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This investigation was undertaken because of the relative paucity of reports in the literature regarding cardiac lesions in cases of acute poliomyelitis and because we observed certain unusual cardiovascular lesions during the 1946 epidemic in Minnesota.

In 1910 Robertson and Chesley reported on the necropsies in 6 cases of acute poliomyelitis. In 5 the hearts were studied histologically and swelling of myocardial fibers and interstitial edema of the myocardium were noted. Even then these authors called attention to the lack of emphasis in the literature upon the changes in organs outside the nervous system.

Minimal myocardial inflammatory changes in cases of acute poliomyelitis were subsequently reported by Abramson, in 1918, and by Landon and Smith, in 1934. The latter authors stated that the observed lesions were similar to those occurring in diphtheria and scarlet fever, but apparently they did not feel that the changes were significant.

In 1934 Cowie, Parsons, and Lowenberg, reporting necropsy findings in 4 cases of acute poliomyelitis, included one case in which localized myocarditis of the right atrium, a mural thrombus at this site, and pulmonary emboli were observed.

Clark, in 1938, reported data on an interesting case of acute poliomyelitis in which severe diffuse interstitial myocarditis was found at necropsy. Since horse serum had been administered, with the subsequent development of typical signs of serum sensitivity, the myocarditis was attributed to horse serum.

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It remained for Saphir and Wile, in 1942, to point out that myocarditis is a feature of poliomyelitis. The histologic changes described by these authors in 6 of 7 cases included cellular exudate in the myocardium, consisting mainly of monocytes, adventitial cells, and lymphocytes, or of neutrophils and lymphocytes. Minimal degenerative changes also were described. Peale and Lucchesi, in 1943, reported the finding of essentially similar changes in 5 of 9 cases. In the same year Dublin and Larson reported the finding of 2 incidental cases of acute myocarditis among 12 cases of fatal acute poliomyelitis.

In 1945 Saphir published the results of a necropsy study on 17 additional cases of acute poliomyelitis, in 10 of which he found myocarditis. In 3 cases he noted histologic changes in the media of the aorta, consisting of separation of elastic lamellae by a substance which, he stated, had a fibrinoid appearance.

Luhan, in 1946, reported a series of 13 cases of fatal acute poliomyelitis, in one of which he found verrucous endocarditis involving the mitral valve. The heart was not further described.

Recently Gefter, Leaman, Lucchesi, Maher, and Dworin published a clinical and pathologic study of a group of 467 cases of acute poliomyelitis, in 6 of which necropsy was performed. Their investigation disclosed interesting facts concerning the incidence of cardiac murmurs, electrocardiographic changes, and other pertinent clinical findings related to the heart. Thirty-two (14.2 per cent) of 226 patients were found to have abnormal electrocardiograms. Myocarditis was found in 2 of the 6 cases in which necropsy was performed. Unfortunately, it had not been possible to take electrocardiographic tracings on these patients, because of the severity of their illnesses.

A survey of the literature on the pathology of poliomyelitis does not permit accurate determination of the incidence of significant cardiac changes, since the histopathologic findings in the heart are seldom described in the reports. After review of the few available studies in which the heart was specifically investigated, it would seem that cardiac lesions are common in cases of fatal acute poliomyelitis.

Material and Methods

The 35 cases used for the investigation herein reported represent all of the cases of poliomyelitis in which necropsy was performed at the Mayo Clinic, from August 2, 1925, to December 11, 1946, inclusive, and in which the hearts were available for this study. The specimens were sectioned for histologic investigation by the method used by Gross, Antopol, and Sacks in the study of rheumatic heart disease. Their method

was adopted primarily because it made possible, by simple standardized technics, the demonstration of most of the important anatomic structures of the heart. The hearts had all been fixed in 10 per cent formalin. Six blocks were cut from each specimen and embedded in paraffin. Sections were cut at 4 to 6 μ. Hematoxylin and eosin stains were used on sections from each block. Bodian's stain and Mallory's phosphotungstic acid hematoxylin stain were used in selected cases to demonstrate changes in muscle fibers. Where specifically indicated in order to evaluate changes in connective tissue, Verhoeff's elastic tissue stain counterstained with van Gieson's stain was employed. McCallum's Gram stain was used to demonstrate the presence or absence of bacteria. Blocks from selected specimens were stained with sudan III to determine whether fatty degeneration was present.

Anatomic Observations

GROSS FINDINGS

The hearts usually were moderately increased in weight, as shown in Table I. No significant changes in color or consistency at the time of necropsy were recorded.

Slight to moderate dilatation of the ventricles was found in 24 hearts. Usually only the right ventricle was dilated, but left ventricular dilatation accompanied the more severe degrees of right ventricular dilatation. Significant ventricular hypertrophy was found in only 3 hearts.

There were unusual gross findings in 3 cases in which myocarditis was demonstrated microscopically. One heart (case 1) presented a perforation of the posterior wall of the right atrium. The defect measured about 3 by 4 mm., was oval, and had slightly irregular borders (Fig. 1). There was hemorrhage into the surrounding tissue and there were about 100 cc. of bloody fluid in the pericardial sac.

Verrucous endocarditis of the mitral valve was found in another heart (case 12). There were firm, grayish red, slightly irregular vegetations situated along the line of closure of the mitral leaflets (Fig. 2). No old rheumatic stigmas were found.

There was verrucous endarteritis of a patent ductus arteriosus in a third case (no. 13). The vegetations were friable, brownish red, elevated lesions protruding from the pulmonary end of the ductus arteriosus (Fig. 3).

HISTOLOGIC FINDINGS

Myocarditis

Histologic evidence of myocarditis was found in 14 hearts. The myocardial changes varied considerably in extent and severity. Lesions were

somewhat more frequent in the left posterior papillary muscle and the ventricular septum than in other parts of the heart.

In 3 hearts (cases 1, 2, and 3) minimal acute myocarditis was present. Degenerative changes included irregular affinity of the cytoplasm of

TABLE I

*Heart Weights: Comparison with Normal Standards**

Case	Age	Sex	Estimated body weight	Heart weight	Normal heart weight according to sex and age, or sex and body weight
	years		*lbs.*	*gm.*	*gm.*
1	7	M		120	93.3
2	9	M		165	108.3
3	15	M		330	200.6
4	21	M		335	303.5
5	22	M		228	311.1
6	26	M	150	300	294.0
7	36	F	165	222	297.0
8	21	F		235	250.6
9	31	M	140	295	274.0
10	32	F	150	340	272.0
11	44	M	185	383	363.0
12	34	M	165	340	297.0
13	7	F		140	81.4
14	17	M		336	250.9
15	17	M		250	250.9
16	31	F	120	163	215.0
17	3	M		70	64.5
18	3	M		85	64.5
19	4	M		75	74.7
20	5	M		109	83.7
21	5	M		96	83.7
22	10	M		173	130.9
23	10	M		130	130.9
24	12	M		143	157.0†
25	13	F		253	142.5
26	14	M		267	216.1
27	14	F		161	173.8
28	17	M		353	250.9
29	17	M		315	250.9
30	20	M		355	305.3
31	22	M		382	311.1
32	22	M		310	311.1
33	23	F		220	258.5
34	29	M	155	290	304.0
35	30	M	170	370	333.0

* Normal heart weights from Vierordt and Smith.
† Mean normal heart weight.

muscle fibers for eosin, swelling of muscle fibers, loss of striations, cytoplasmic vacuolation, and occasional fragmentation of muscle fibers. Cellular exudate was not prominent, consisting mainly of small, scattered, perivascular collections of large mononuclear cells with occasional plasma cells and lymphocytes. There was moderate congestion and edema of the interstitial connective tissue. The significance of the appar-

ently minimal changes in these specimens is indicated by the heart in case 1, in which a perforation of the right atrium was present. Except near the site of perforation, where there was severe necrosis (Fig. 4), myocardial alterations were minimal.

In 4 hearts (cases 4, 5, 6, and 7) there was acute myocarditis of moderate severity. The predominant finding was the presence of cellular infiltrate, consisting of large mononuclear cells, situated usually around vessels and in the wider bands of interstitial connective tissue. Neutrophils were present in regions of more severe muscular degeneration (Fig. 5). In one heart a few multinucleated cells were seen. Degenerative changes were similar to those described in the preceding group.

In 6 hearts (cases 8, 9, 10, 11, 12, and 13) there was severe acute myocarditis. The most conspicuous findings were complete focal necrosis of muscle fibers and fairly abundant cellular infiltration (Figs. 6 to 12). Usually, severe necrosis of muscle involved only one or two adjacent muscle fibers. These muscle fibers were completely replaced by irregularly staining, disorganized masses of coagulated cytoplasm. Less marked degenerative changes, including vacuolation, fragmentation, and coalescence of the cytoplasm of muscle fibers, and karyolysis, were found to involve wide regions of myocardium. In the foci of severe muscular degeneration neutrophils usually were abundant. Fairly frequently, however, regions of severe necrosis were found with very little cellular infiltration in their immediate vicinity. In general, the cellular exudate was most prominent around the smaller vessels and in the wider bands of interstitial connective tissue. In these regions large mononuclear cells were numerous. Plasma cells and lymphocytes were less abundant. Congestion and edema of the interstitial connective tissue usually were conspicuous. Frequently the collagenous fibers of the interstitial connective tissue showed an increased affinity for eosin. There was straightening of collagen fibers and a tendency of fibers to form small clumps. This change was most marked around medium-sized vessels.

One heart (case 14) was classified separately as healed myocarditis. The outstanding change was the presence of large regions in the posterior wall of the left ventricle containing practically no muscle fibers (Figs. 13 and 14). In these regions the cellular components consisted mainly of large mononuclear cells situated in a rather delicate lacework of connective tissue fibers, suggesting that extensive complete necrosis and absorption of muscle fibers had occurred, leaving the myocardial stroma and a few macrophages. No vascular lesions were found in association. The remainder of the cardiac muscle showed minimal changes, including

vacuolation and hyaline droplet degeneration of cytoplasm, marked variations in cytoplasmic affinity for eosin, and karyolysis. There were a few scattered plasma cells and lymphocytes.

Selected hearts from each of the groups discussed previously, in which cytoplasmic vacuolation was present, showed only minimal deposition of lipid when stained with sudan III.

Endocarditis

Minimal valvular changes were found almost constantly, with and without associated myocarditis. These changes included separation of valvular stroma as if by edema, and foci of highly eosinophilic bundles of collagen (Fig. 15). These findings were somewhat more marked in the aortic and mitral valves than in other valves and were most prominent in hearts showing myocardial changes.

As mentioned previously, in one patient (case 12) there was acute vegetative endocarditis of the mitral valve. The entire valvular stroma was infiltrated with numerous cells, mainly neutrophils and, to a lesser degree, lymphocytes (Fig. 16). The vegetations consisted of irregular deposits of fibrin which were undergoing organization (Fig. 17). No bacteria were seen. Within the valve leaflets there were scattered thin-walled vessels the size of arterioles, indicating previous vascularization of the valve and possibly, therefore, previous inflammation.

In one heart there was a subendothelial circumscribed mass, about 2 mm. in diameter, situated on the inferior aspect of the mitral valve. This lesion consisted of fibroblasts, budding capillaries, deposits of hemosiderin, and recent hemorrhage. Atypical for a healing vegetation, it may have represented a resolving hematoma.

The mural endocardium frequently showed changes in those hearts in which myocarditis was found. These changes included endothelial proliferation, subendothelial edema, and the presence of cellular infiltration, the cell types corresponding to those in the myocardium. There were no significant endocardial changes in those hearts not showing myocardial inflammation.

Endarteritis of a Patent Ductus Arteriosus

As already mentioned, in one case (case 13) acute vegetative endarteritis of a patent ductus arteriosus was observed. The vegetations, consisting mainly of fibrin and leukocytes, were apparently of recent origin, although beginning organization was noted (Figs. 18 and 19). No bacteria were seen. There was moderately severe arteritis at the site of the vegetations, indicated by marked subintimal edema, many neutro-

phils, and slight endothelial proliferation. The left pulmonary artery was uninvolved. There was associated severe acute myocarditis (Fig. 20).

Pericarditis

In one case (case 14) there were left pleuropericardial adhesions and obliterative pericarditis, raising the question of primary pleuritis with secondary pericarditis and myocarditis. Since there was only minimal inflammatory change in the epicardium, it did not seem likely that the pericarditis led to myocarditis. Although the epicardium in other hearts frequently showed inflammatory changes, in no instance were these changes sufficiently severe to indicate that pericarditis was primary.

Histologic Changes in Hearts Not Showing Myocarditis nor Endocarditis

There were 21 hearts in which the histologic findings were not considered significant. All of these showed slight swelling of muscle fibers, and in most there was minimal vacuolation of cytoplasm with some congestion and separation of muscle fibers as if by edema. The latter findings are probably explanatory of the slight to moderate increase in heart weights shown in Table I.

Report of Cases

The following case reports are presented to illustrate certain unusual findings.

Case 1

A white boy, 7 years of age, living in a community in which there was poliomyelitis, was well until August 26, 1946, when he became febrile and vomited a few times. On August 29, headache and pains in his neck developed. He was admitted to the hospital on August 31 because of dizziness and difficulty in walking. On physical examination there was cervical rigidity but no definite evidence of paralysis. The blood pressure was 130/90 mm. of Hg. The cerebrospinal fluid contained 20 lymphocytes and 7 neutrophils per cmm. and the total concentration of protein was 65 mg. per 100 cc. Hot packs were applied to the neck and back, and penicillin was given. About 12 hours after admission, dysphagia, paralysis of the soft palate, and cyanosis developed. The patient was placed in a respirator, after which it was noted that the pulse was thready. Attacks of cyanosis continued but were partially relieved by the aspiration of secretions from the pharynx. On September 1, at about 12:45 a.m., the patient suddenly became cyanotic. The pulse rate rose from 100 to 180 per minute and the axillary temperature to 104.6° F. The patient died at 1:45 a.m. on September 1, 1946, 6 days after the onset of illness.

The anatomic findings in both the medulla and the spinal cord were characteristic of acute poliomyelitis.

The pericardial sac was found to be distended and grayish blue. When

it was opened, free blood was encountered, the estimated amount being about 100 cc. Hemopericardium was due to a perforation of the right atrium, located in its posterior wall to the right of the base of the valve of the coronary sinus (Fig. 1). The defect measured about 3 by 4 mm., was oval and had slightly roughened edges. There was recent hemorrhage into the surrounding epicardium.

The heart weighed 120 gm. Except for marked dilatation of the right atrium and moderate dilatation of the right ventricle, no significant gross cardiac abnormalities were noted. Histologic study showed mainly degenerative myocardial changes. Foci of swollen muscle fibers with loss of striations and fragmentation of individual muscle fibers were present in all sections examined. Near the perforation of the right atrium such areas were larger and the changes slightly more severe than at other sites (Fig. 4). Scattered neutrophils were present in the foci of more severe degenerative change.

There was bronchopneumonia confined to the lower lobe of the left lung. No significant changes were found in the other viscera.

Case 12

A single white man, 34 years of age, had a familial history of diabetes but had been in good health. Following a poliomyelitis outbreak in his home state, on December 6, 1946, sore throat, anorexia, chills, and fever developed. On December 7 he noted difficulty in swallowing and speaking, and shortness of breath. He was admitted to the hospital on December 9. On physical examination cyanosis was evident and there was diminution of the deep reflexes of the upper extremities. Respirations were of a grunting character, preventing adequate cardiac examination. The blood pressure was 180/80 mm. of Hg; temperature, 102.6° F.; pulse, 120; respirations, 25. Leukocytes numbered 20,000 per cmm. of blood. The cerebrospinal fluid contained 45 lymphocytes and 5 neutrophils per cmm. and the total concentration of protein was 30 mg. per 100 cc. There was severe albuminuria, and a few hyaline and granular casts were found in the urine. The urine also showed a trace of reducing substance and the blood sugar was found to be 238 mg. per 100 cc. of blood. Fifteen thousand units of penicillin were given intramuscularly every 4 hours. Ten thousand units of diphtheria antitoxin were administered also. The patient was placed temporarily in a respirator but fought its use. On December 11, after the intravenous administration of a 10 per cent solution of glucose, cyanosis suddenly became more severe and the patient had a generalized convulsion. Use of the respirator was again instituted, but cyanosis continued and the patient died at 7:00 p.m. on December 11, 1946, 5 days after the onset of the illness.

The anatomic findings in both the medulla and the spinal cord were characteristic of acute poliomyelitis.

The heart weighed 340 gm. The right ventricle was slightly dilated. There were multiple, firm, translucent, grayish red vegetations, each measuring 1 to 2 mm. in diameter, near the free edge of the atrial surface of the mitral leaflets (Fig. 2). No gross evidence of old rheumatic

involvement was found. On histologic study, the vegetations were found to consist of fibrin with beginning invasion by fibroblasts (Fig. 17). No bacteria were seen in either the vegetations or the valvular stroma. The mitral leaflets showed marked separation of stromal elements as if by edema and there was extensive infiltration with cells, mainly neutrophils and, to a lesser degree, lymphocytes (Fig. 16). The valvular stroma contained thin-walled vessels the size of arterioles. There were several small masses of degenerating collagen in the tricuspid valve but the other valves did not present significant changes. The myocardium presented marked inflammatory changes, involving mainly the interventricular septum and the posterior papillary muscle. In these regions there were many foci of necrosis of muscle fibers. Fairly numerous cells, mainly neutrophils and large mononuclear cells, were found in the perivascular and interstitial connective tissue, and dense collections of neutrophils were present in the foci of severe muscle degeneration.

There was early bronchopneumonia. No embolic phenomena were observed. No significant changes were found in the other viscera.

Case 13

A white girl, 7 years old, was well until August 2, 1946, when she complained of pains in her legs. Poliomyelitis was known to exist in her community. On August 3 difficulty in swallowing developed and she was admitted to the hospital. Physical examination showed palatal weakness but no other evidence of paralysis. The temperature was 100° F.; pulse, 80; respirations, 20. The cerebrospinal fluid contained 25 lymphocytes and 20 neutrophils per cmm. and the total concentration of protein was 50 mg. per 100 cc. The patient's condition remained apparently unchanged except for the development of tachycardia (140 per minute). At 6:00 p.m. on August 6, the patient rather suddenly went into a state of vascular collapse and, despite the intravenous administration of plasma, died at 1:06 a.m. on August 7, 1946, 5 days after the onset of the illness.

The anatomic findings in the spinal cord and medulla were characteristic of acute poliomyelitis.

The heart weighed 140 gm. The right ventricle was moderately dilated. No other significant gross cardiac abnormalities were noted. There was a small, irregular, brownish red, friable thrombus, about 3 mm. in diameter, projecting from the pulmonary ostium of a patent ductus arteriosus, the lumen of which measured about 2 mm. in diameter at the pulmonary end (Fig. 3).

Histologic examination of the myocardium showed foci of severe degeneration of muscle fibers in the right ventricle (Fig. 20). In these regions there were small groups of infiltrating cells, mainly neutrophils and large mononuclear cells. Other sections of the myocardium showed only minimal inflammatory changes.

The vegetative thrombus in the ductus arteriosus was apparently of very recent origin, consisting mainly of leukocytes held together loosely by fibrin. Beginning invasion by fibroblasts was noted along the area of attachment to the vessel wall (Figs. 18 and 19). No bacteria were seen in either the vegetation or the wall of the ductus. There was moderately severe superficial arteritis, indicated by subintimal edema, many neutrophils, and slight endothelial proliferation. The left pulmonary artery was uninvolved.

No embolic phenomena were demonstrated. Except for beginning bronchopneumonia, no significant changes were found in the other viscera.

Correlation of Clinical and Anatomic Findings

Age

The youngest patient found to have myocarditis was 7 years of age; the oldest was 44 years. The average age of the patients who had myocarditis was 23.0 years in contrast to the average of 15.3 years of the patients who did not have myocarditis. The average age of the patients who had severe or moderately severe myocarditis, acute or subacute, was 26.5 years, whereas the average age of the patients who had minimal myocarditis was 10.3 years. It appeared that older patients were more often subject to myocarditis than young patients and that the severity of myocarditis tended to be greater in proportion to age.

Sex

The over-all incidence of myocarditis was greater in male patients, with a ratio of about 2.5:1. Since there were, however, only 8 females in this series of 35 patients, the relative incidence of myocarditis was actually somewhat greater among females. It is of interest that both of the 2 pregnant women in this study (cases 7 and 10) were found to have myocarditis.

Duration of Illness

The patient with myocarditis who had the longest survival after onset of symptoms lived 57 days (case 14). The myocardial lesions in this case were classified as healed. The remaining 13 patients who had myocarditis lived less than 11 days after onset of symptoms, averaging 5.2 days of illness. This is only slightly more than half of the average length of illness (9.5 days) of the patients who did not have myocarditis, but since 2 of the patients without myocarditis had relatively long survivals (30 and 60 days, respectively) the importance of this comparison is questionable.

Neurologic Findings

Bulbar symptoms were present in 8 of the 14 patients who had myocarditis and in 14 of the 21 patients who did not have myocarditis. Five patients had severe, generalized paralysis, including symptoms of bulbar involvement. Three of these had myocarditis and 2 did not have myocarditis. Thus there seemed to be no correlation of either bulbar or severe generalized paralysis with the presence of myocarditis in this group of cases.

Cardiac Findings

Since respiratory distress in cases of poliomyelitis may result from involvement of either the spinal cord or the medulla, it was not surprising that dyspnea and cyanosis *per se* were found to be of little apparent value in the diagnosis of myocarditis. Among the 14 patients who had myocarditis, dyspnea had been recorded as a symptom in 12 and cyanosis in 11 patients. Among the 21 patients who were not found to have myocarditis, dyspnea had been noted in 18 and cyanosis in 13 patients. These findings do not, of course, exclude the possibility that a thorough clinical evaluation of the cardiac function of patients who have acute poliomyelitis, correlated with evidence of neurologic causes of respiratory distress, might disclose some diagnostic value for these symptoms.

Although the presence of pulmonary râles was frequently recorded, they could not be attributed definitely to cardiac failure, since it was impossible to exclude inflammatory congestion and the edema which frequently accompanies encephalitis. No peripheral edema was observed.

Precordial pain was present in only one patient. This patient was found not to have myocarditis.

The presence of cardiac murmurs was indicated in the clinical records of 3 patients, each of whom was found to have myocarditis (cases 3, 4, and 10). In each instance the murmur was at the base of the heart. In one patient it was transmitted to the cardiac apex. In another patient (case 7) the heart tones were muffled and the apex of the heart was displaced to the left. Since this patient was pregnant, the latter finding was of questionable significance. This patient was the only one in the series in whom severe bradycardia (44 per minute) was noted. Her case is one of those in the group with moderately severe myocarditis.

Tachycardia was commonly observed, but the incidence and severity of this finding were about the same in the group of patients without myocarditis as in the group with myocarditis. Irregularity of pulse was noted in 2 patients, only one of whom (case 4) had myocarditis.

Cardiac lesions were suspected clinically in 2 patients, one of whom

had a congenital fusion and fenestration of the cusps of the aortic valves but no myocarditis. The other patient (case 3) had myocarditis.

In none of the cases in this study was there a past history or other clinical evidence of rheumatic fever.

Suddenness of Death

Six patients died rather suddenly, 3 of whom (cases 1, 10, and 14) were found to have myocarditis. Except in case 1, in which a perforation of the right atrium was found at necropsy, it was impossible to determine whether or not myocarditis had actually caused sudden death, since bulbar involvement with poliomyelitis was present in each case.

A general correlation of clinical and anatomic findings is presented in Table II.

Etiology and Pathogenesis

Before one ascribes the production of myocarditis to the virus of poliomyelitis it is necessary to consider, as has been indicated by Saphir, other possible etiologic factors, such as bronchopneumonia, serum reactions, and sulfonamide sensitivity, each of which has been reported to have caused myocarditis.

Bronchopneumonia was present in only 4 of the cases in which myocarditis was found, and in none of these patients was the pneumonia severe. It seemed unlikely that bronchopneumonia was of much significance in the pathogenesis of myocarditis.

Although myocarditis has been produced experimentally by the injection of horse serum and has even been reported in a few cases in which human beings have been treated with horse serum, this factor did not seem important as a cause of myocarditis in this group of cases. Only 3 patients who had myocarditis (cases 4, 9, and 12) had received horse serum, and in each the injections were begun 2 days or less before death. None showed clinical evidence of sensitivity to serum.

As has been shown both experimentally and clinically by French and Weller, sulfonamide compounds may cause myocarditis. In the present study 4 patients who had myocarditis (cases 7, 8, 10, and 14) had received a sulfonamide compound, in each instance sulfadiazine. Three of these were given the drug for 2 days or less. There was no associated clinical nor other histologic evidence of toxicity. Administration of sulfonamide compounds seemed of minimal importance as a cause of myocarditis in this series of cases.

The effects of anoxia and general toxemia were impossible to assess adequately. It is probable that these factors may have caused at least some of the minimal cardiac changes observed in the cases in this study.

The reported occurrence of myocarditis in other virus diseases, in-

TABLE II

Correlation of Clinical and Anatomic Findings in 14 Patients Who Had Significant Cardiac Lesions

Case	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Age, years	7	9	15	21	22	26	36	21	31	32	44	34	7	17
Sex	M	M	M	M	M	M	F	F	M	F	M	M	F	M
Approximate duration of illness, days	6	6	7	3	4	10	4	3	6	5	4	5	5	57
Type of paralysis	Bulbar	Bulbo-spinal	Spinal	Spinal	Spinal	Bulbar	Bulbar	Spinal	Spinal	Bulbo-spinal	Bulbar	Bulbo-spinal	Bulbar	Spinal
Dyspnea*	3	2	3	2	3	3		3	2	3		3		3
Cyanosis*	3	3	3		3	3	2	2	3	3		3		3
Oral temperature, °F.†	103	101	102	100.5	102.5	101	102	103	102.5	101	102	101	100	100
Pulse rate, beats per min.†	130	90	120	120	110	80	125	110	80	95	100	110	120	120
Respiratory rate, per min.†	35	33	20	36		20	30	22	30	30		20	30	20
Cardiac murmurs			Basal and apical system	Pul-monary system					Basal system					
Leukocyte count, per cmm. of blood		20,600	9,900			10,600	9,800	11,400	22,700				20,500	14,600
Myocarditis*	1‡	1	1	2	2	2	2	3	3	3	3	3	3	3
Valvulitis*												3		
Endarteritis of a patent ductus arteriosus*													2	
Pneumonia*	2								1			1	1	

* Severity on a basis of 1 to 4.
† Approximate average during period of hospitalization.
‡ Even though myocarditis was minimal in case 1, there was a perforation of the right atrium.

cluding mumps, virus influenza, and epidemic encephalitis, suggests that it is not illogical to consider the virus of poliomyelitis to be capable of causing myocarditis.

Recently Helwig and Schmidt have succeeded in isolating a virus with both neurotropic and cardiotropic features. When injected into mice this virus was shown to cause paralysis of the extremities and myocarditis. These authors did not state the immunologic relationships, if any, of this virus to the virus of poliomyelitis, but this report of a virus disease with features grossly resembling poliomyelitis and with associated myocardial lesions again suggests that it is not unreasonable to suspect the poliomyelitic virus of causing myocarditis.

Since myocarditis was present in 40 per cent of the cases in this series and since other investigators have found an even greater incidence of myocarditis in acute poliomyelitis, it is evident that myocarditis occurs frequently in poliomyelitis. Inasmuch as it has not been possible to explain satisfactorily the etiology of myocarditis in the cases in this series without ascribing it to the virus of poliomyelitis, we are led to the assumption that the virus may invade and destroy cardiac muscle.

The occurrence of endocarditis and ductal endarteritis, such as was observed in cases 12 and 13, is more difficult to relate to the virus of poliomyelitis. Certain proof of the exact etiology of lesions of this type occurring in poliomyelitis, as well as proof of the cause of myocarditis, will depend on the isolation of the virus from such lesions and the experimental production of similar changes.

If it is assumed that the virus of poliomyelitis causes cardiovascular lesions, we are confronted with the problem of the mode of invasion of cardiovascular structures by the virus. It may be of some significance that the virus has been demonstrated in the blood stream of monkeys with poliomyelitis. On the other hand, most investigators believe that the virus migrates along nerves. Evidence of injury to nerves was observed in many of our cases and Saphir and Wile pointed out that nerve fibers of the myocardium were found to be separated by an "edema-like material." Further study will be necessary to evaluate such changes.

It is of interest that cases in which myocarditis was found tended to occur in chronologic sequence. This fact suggests that the poliomyelitis virus manifests marked cardiotropic features in only certain epidemics. This may explain why competent observers frequently have not found evidence of myocarditis.

Comment

Since acute myocarditis is seldom characterized by histologic features which will permit an etiologic diagnosis, it was not surprising that myo-

carditis in this series of cases presented a nonspecific picture. The lesions observed were similar to those which have been described in other infectious diseases and in Fiedler's myocarditis. No Aschoff bodies were found, although there was some degeneration of collagen such as has been described in rheumatic myocarditis. This finding seemed of minimal importance since degeneration of the collagen is rather frequent in the presence of inflammation, regardless of its cause.

It is unfortunate that blood cultures were not made in the 2 cases in which vegetative lesions were found, but the absence of demonstrable bacteria in these lesions is negative evidence in favor of infection by poliomyelitis virus. It is of interest that the lesions in both of these cases involved regions in which there was probably diminished resistance to infection—in one case a patent ductus arteriosus, in the other case a valve which was vascularized, indicating possible previous valvular injury. The absence of such *loci minoris resistentiae* in most patients who have poliomyelitis may partially explain why so few lesions of this character are observed.

The failure of physicians to establish the clinical diagnosis of myocarditis in cases of acute poliomyelitis is not difficult to understand. Myocarditis other than that occurring in rheumatic fever is almost always extremely difficult to diagnose. Moreover, serious neurologic symptoms in acute poliomyelitis have diverted clinical attention from the cardiovascular system. Perhaps a general awareness of the frequency of myocarditis in acute poliomyelitis will facilitate the clinical diagnosis of myocarditis.

Conclusions

Myocarditis occurs frequently in acute poliomyelitis, having been observed in 14 (40.0 per cent) of 35 cases of fatal poliomyelitis.

Acute vegetative endocarditis and endarteritis of a patent ductus arteriosus may occasionally be found in acute poliomyelitis. One example of each of these lesions was present among the cases in this study.

Since the cardiovascular lesions occurring in the cases included in this study were otherwise unsatisfactorily explained, poliomyelitis virus must be considered as a possible cause of such lesions.

Proof that cardiovascular lesions in acute poliomyelitis are caused by the poliomyelitis virus will depend on demonstration of the virus in the lesions and the experimental production of such lesions.

The diagnosis of myocarditis in acute poliomyelitis is seldom made during life. Myocarditis should be suspected in every patient who is seriously ill with acute poliomyelitis.

Myocarditis, as observed in this series of cases, was usually more

severe and proportionately more common in adults than in young children.

The ratio of males to females in the group of patients with myocarditis was 2.5:1, but since the ratio of males to females in the study was more than 3:1, actually a slightly greater proportion of females had myocarditis.

There was no specific correlation of type of paralysis—bulbar or spinal—with the presence or absence of myocarditis.

The actual rôle of myocarditis as a cause of sudden death in acute poliomyelitis could not be determined in this study, except in one patient, who had a perforation of the right atrium. Three of the 6 patients who died suddenly were found to have myocarditis, but all of these patients had bulbar involvement, which might have explained their sudden deaths.

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[*Illustrations follow*]

DESCRIPTION OF PLATES

PLATE 48

FIG. 1. Case 1. Perforation of the posterior wall of the right atrium. The defect is located just to the right of the ostium of the coronary sinus.

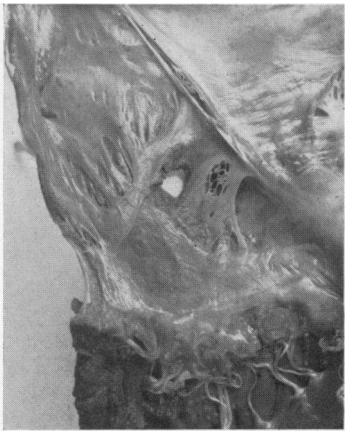
FIG. 2. Case 12. Left atrium and ventricle showing vegetations along the line of closure of the mitral valve. The absence of gross evidence of old rheumatic involvement is apparent.

FIG. 3. Case 13. Portion of left pulmonary artery with aortic arch and descending aorta in background. Small vegetative thrombus may be seen at pulmonary ostium of a patent ductus arteriosus.

FIG. 4. Case 1. Right atrium near site of perforation shown in Figure 1. Myocardial fibers have become granular and coalescent. A few neutrophils have infiltrated the area. Hematoxylin and eosin stain. × 580.

FIG. 5. Case 5. Myocardium showing abundant interstitial collections of neutrophils and large mononuclear cells with degenerative alterations of myocardial fibers. Hematoxylin and eosin stain. × 160.

FIG. 6. Case 10. Myocardium with focus of severe degeneration and infiltration of neutrophils. Hematoxylin and eosin stain. × 190.



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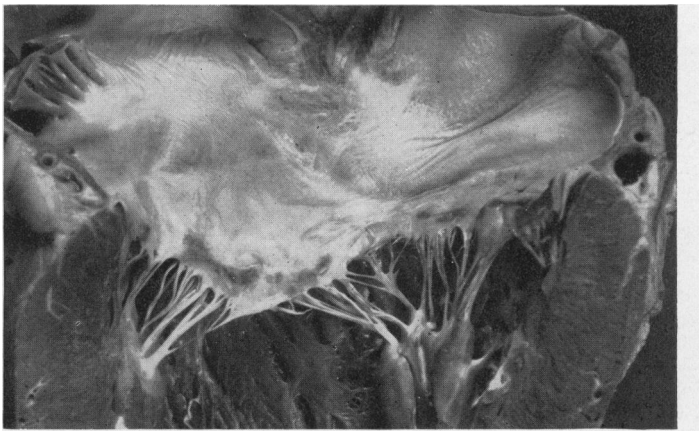

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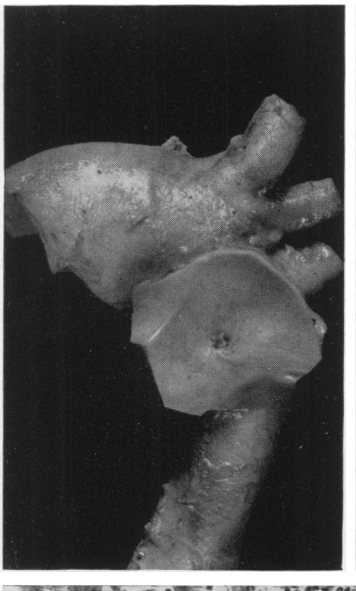

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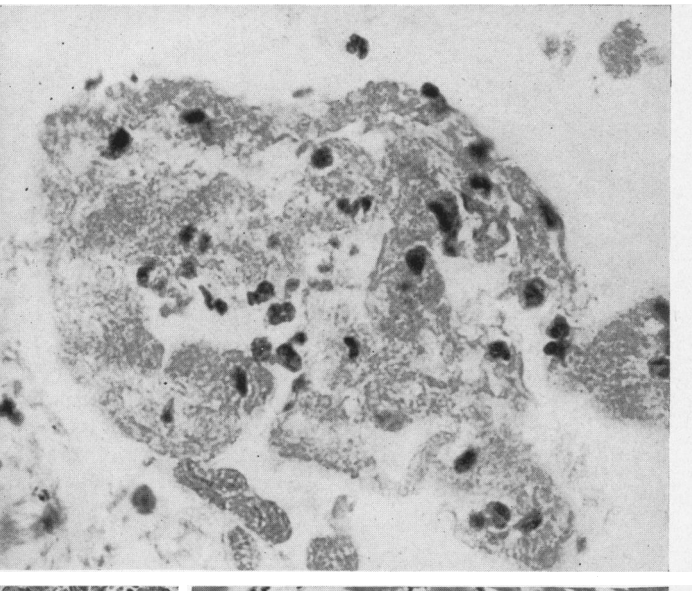

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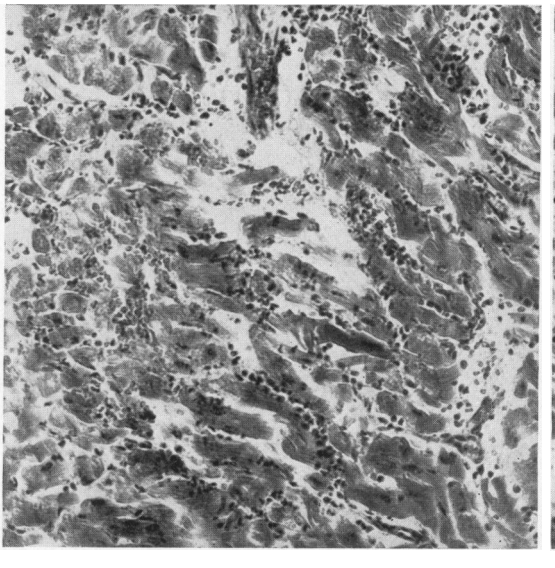

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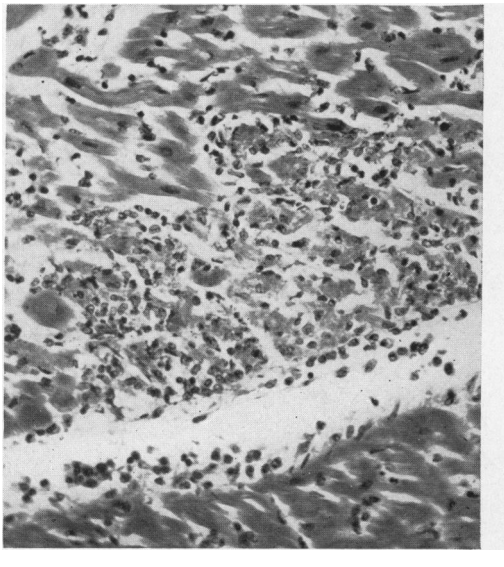


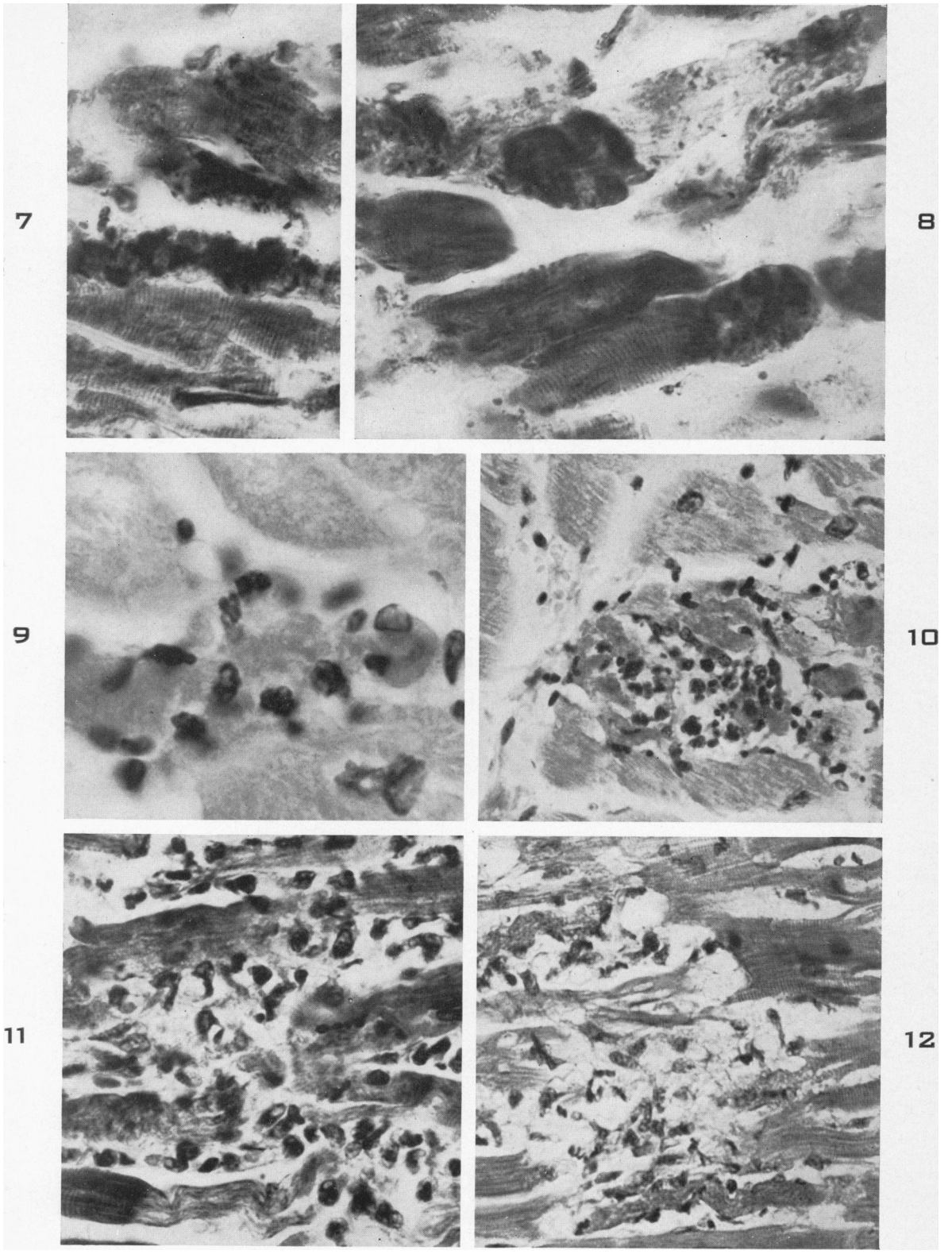
6

Ludden and Edwards

Carditis in Poliomyelitis

PLATE 49

FIGS. 7 to 12. The apparent manner of progression of myocardial lesions is illustrated in this series of photomicrographs. Characteristic coagulation necrosis of myocardial fibers is well shown in *Figures 7 and 8* (case 8), stained with Mallory's phosphotungstic acid stain. In *Figures 9 and 10* (case 9) and in *Figure 11* (case 11) infiltration of neutrophils into areas of myocardial necrosis appears. In *Figure 12* (case 12) there is a small area of absence of myocardial fibers. Such a sequence of events probably explains the lesion seen in Figure 13. (Figures 7 and 8 were stained with Mallory's phosphotungstic acid stain; Figures 9 to 12 with hematoxylin and eosin. Figure 7, × 880; Figure 8, × 800; Figure 9, × 1275; Figure 10, × 435; Figure 11, × 600; and Figure 12, × 450.)



Ludden and Edwards Carditis in Poliomyelitis

PLATE 50

FIG. 13. Case 14. Posterior wall of left ventricle. Healed myocarditis, apparently representing the end-result of resolution of an acute process, as shown in Figures 7 to 12. Myocardial fibers have disappeared, leaving only stroma. Hematoxylin and eosin stain. × 85.

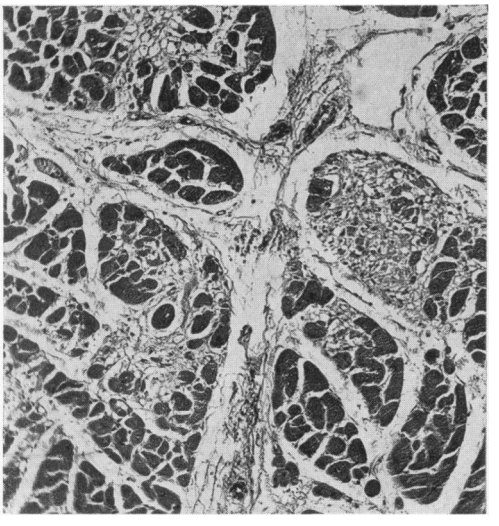
FIG. 14. Case 14. Higher magnification of a lesion shown in Figure 13. Lace-like pattern of remaining myocardial stroma is evident. Hematoxylin and eosin stain. × 295.

FIG. 15. Case 8. Mitral valve. Edema of valvular stroma and thickening of collagen fibers, such as were commonly observed with and without associated myocarditis. Hematoxylin and eosin stain. × 260.

FIGS. 16 and 17. Case 12. Mitral valve. In Figure 16 is seen infiltration of valvular stroma with neutrophils. Figure 17 shows an organizing fibrinous vegetation. Hematoxylin and eosin stain. Figure 16, × 800; Figure 17, × 275.

FIG. 18. Case 13. Low-power magnification of a section of the junction of the patent ductus arteriosus and the left pulmonary artery. The lumen of the left pulmonary artery occupies the upper portion of the field. The pulmonary ostium of the patent ductus arteriosus is occluded by a thrombus. Verhoeff's elastic tissue stain counterstained with van Gieson's connective tissue stain. × 11.

13



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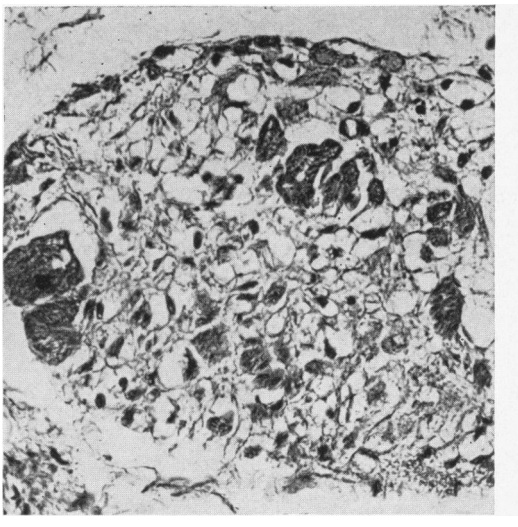

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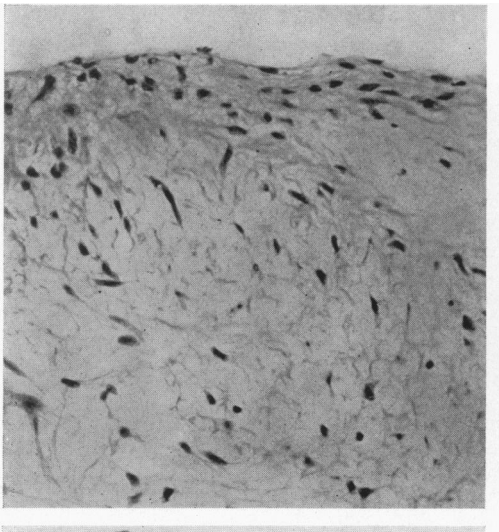

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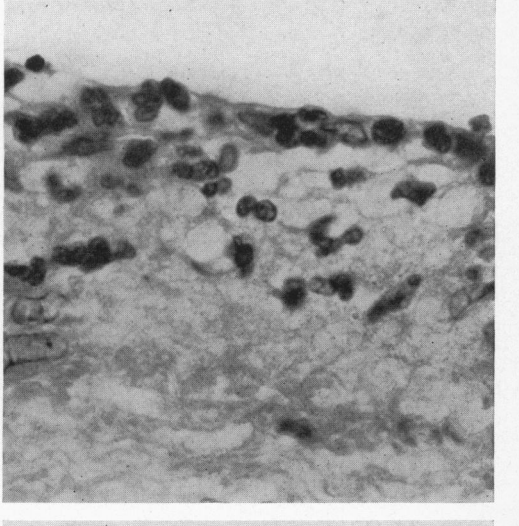

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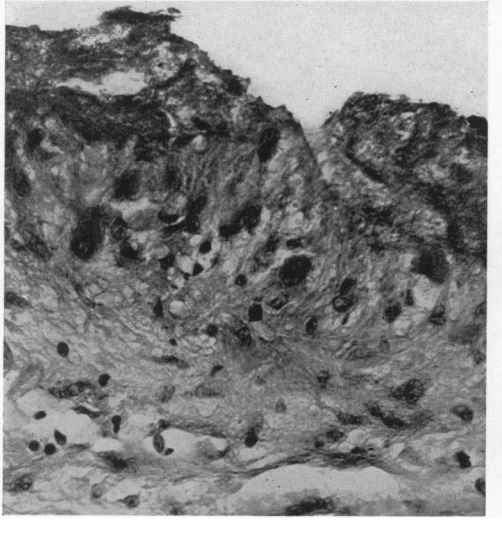

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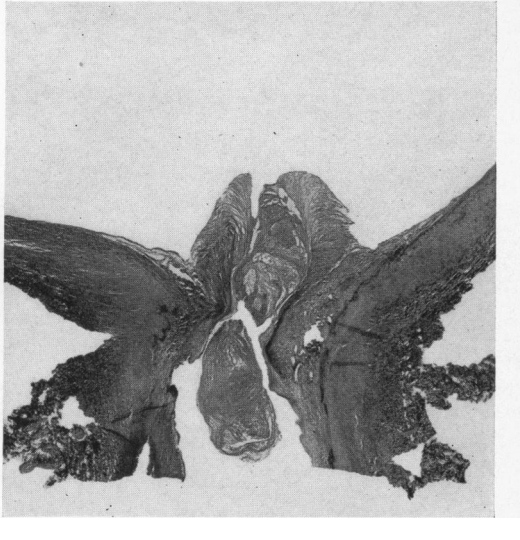

Ludden and Edwards Carditis in Poliomyelitis

PLATE 51

FIG. 19. Case 13. Recently formed thrombus and acute endarteritis of patent ductus arteriosus. Subintimal collection of neutrophils. Hematoxylin and eosin stain. × 320.

FIG. 20. Case 13. Severe acute myocarditis. Focal necrosis of myocardial fibers and infiltration of neutrophils. Hematoxylin and eosin stain. × 200.

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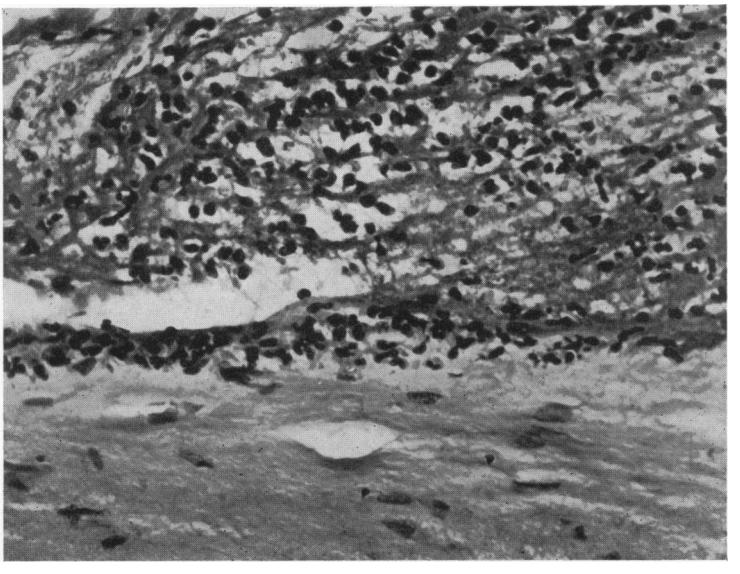

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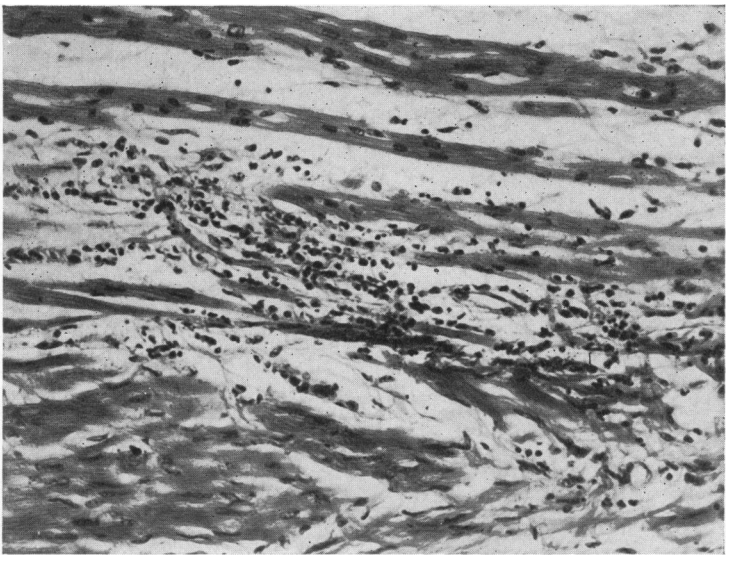

Ludden and Edwards Carditis in Poliomyelitis