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VALVULAR DISEASES OF THE HEART
WITH SPECIAL REFERENCE TO THE PATHOGENESIS OF OLD VALVULAR DEFECTS *

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The primary object of this investigation is to trace the development of old valvular defects. This involves a detailed study of all forms of acute endocarditis, especially with reference to the manner of healing. We have available for study 280 cases of valvular heart disease, not including those of syphilitic origin.

We have classified the valvular diseases as follows:

I. Rheumatic endocarditis
  1. acute
  2. recurrent or chronic

II. Bacterial endocarditis
  1. acute { *a.* primary / *b.* secondary
  2. subacute

III. Old valvular defects
  1. inflammatory { Group 1 / Group 2
  2. calcified nodular — Group 3
  3. congenital

IV. Syphilis of the aortic valve

I. RHEUMATIC ENDOCARDITIS

1. ACUTE RHEUMATIC ENDOCARDITIS. A summary of eighteen cases of this condition is given in Table 1. The diagnosis is based upon the gross appearance of the lesions on the valves. Although there are no fundamental differences, it is convenient to distinguish

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rheumatic and bacterial vegetations. The former are small, firm, discrete or fused to form a narrow ridge, and translucent to pale red in color. Their consistence is such that they do not become detached to form emboli. Bacterial vegetations are relatively large and vary in color from red to white. They are of soft consistence and portions readily break off to form emboli. The microscopic differences will be discussed later. Transition forms are occasionally seen, and frequently both types of vegetations are found in the same heart or even on the same leaflet. The cases classed as rheumatic are those in which no typical vegetations of bacterial type are found.

Seven of the eighteen patients were suffering with multiple acute arthritis at the time of death and were therefore typical clinical cases of acute rheumatic fever. Five others had clinical signs of systemic infection but had no arthritis. In the light of the postmortem findings these may also be considered acute rheumatic fever, since it is well known that rheumatic endocarditis may exist without arthritis. The case of chorea belongs definitely to the rheumatic group.

But there are five cases in which the endocarditis was an accidental postmortem finding. In Nos. 24–364 and 25–411 there are no clinical data. In the case of acute poliomyelitis, the rheumatic lesion may be interpreted as an independent terminal infection; but in the two cases of acute endometritis there is a strong suggestion that the endocarditis was produced by the organisms responsible for the uterine infection. Rheumatic endocarditis does occur secondary to infectious processes though much less frequently than the bacterial type.

Acute pericarditis was present in every case that died primarily of rheumatic fever, and this complication seems to be largely responsible for death in the acute stage.

Coincident with the formation of the vegetations there is a diffuse inflammation of the marginal part and often of the entire leaflet. The leaflet shown in Fig. 1 is opaque throughout; its capillaries are greatly dilated, and there are several small hemorrhages. Microscopically this leaflet shows an extensive lymphocytic exudate throughout. This diffuse distribution of the inflammation in the acute stage is important in the interpretation of the old valve defects to be discussed later on.

TABLE I

Acute rheumatic endocarditis

Number	Age in years	Sex	Duration	Acute arthritis	Sepsis without arthritis	Acute pericarditis	Valves involved	Aschoff bodies	Cause of death	Glomerulonephritis
10-92	14	F	2 wks.	–	..	–	mitral	+	chorea	–
15-83	28	F	several months	+	..	+	mitral	–	rheumatic fever	?
16-272	23	M	1/12	–	+	+	mitral	+	rheumatic fever	–
16-326	18	M	?	–	..	–	mitral	–	acute poliomyelitis	?
17-106	4	F	3 wks.	+	..	+	mitral	–	rheumatic fever	–
20-319	3½	M	3 wks. +	+	..	+	mitral, aortic	–	rheumatic fever	?
22-185	6	F	2 mos.	+	..	+	mitral, tricuspid	+	rheumatic fever	?
22-209	28	F	3 days	–	..	–	aortic	–	acute endometritis	–
22-595	9	F	3 wks.	–	+	+	mitral, aortic, tricuspid	+	rheumatic fever	?
23-354	12	M	2 mos. +	–	+	+	mitral	+	rheumatic fever	?
24-1a	15	F	3 mos.	+	..	+	mitral, aortic	+	rheumatic fever	?
24-275	34	M	3 wks.	+	..	+	mitral	+	rheumatic fever	–
24-364	40	M	?	–	..	–	mitral	+	undetermined	–
25-163a	16	M	3 mos.	–	+	+	mitral, aortic	+	rheumatic fever	?
25-171	19	M	2 mos.	+	..	+	mitral, aortic, tricuspid	+	rheumatic fever	?
25-207	31	F	8 days	–	..	–	mitral	–	acute endometritis	–
25-319	3 mo.	M	3 days	–	+	–	mitral	–	rheumatic fever, meningocele	–
25-411	23	F	?	–	..	–	mitral	+	acute lysol poisoning	–

2. RECURRENT OR CHRONIC RHEUMATIC ENDOCARDITIS (Table 2). In this group all hearts are included that show acute lesions of rheumatic type along with thickened scarred leaflets. It is not possible to make an anatomic distinction between chronic and recurrent forms but this may sometimes be done clinically.

Clinical Features. In this group of eighteen patients, thirteen gave a definite history of one or more attacks of acute arthritis, and of these, two had arthritis at the time of death. The history was incomplete in four cases.

Sixteen patients were suffering from chronic cardiac disease, and of these, five died apparently of cardiac failure without any clinical signs of a terminal infection, two of lobar pneumonia, one from a bleeding gastric ulcer and one from an anesthetic. Of the remaining seven, five had clinical findings suggesting an active infection, but did not have arthritis, and two had typical rheumatic fever at the time of death.

The two patients that had no signs of chronic cardiac disease died suddenly, one from a gunshot wound, the other from an undetermined cause.

A case of this group may be recognized clinically when the symptoms and signs of an active rheumatic infection are present in association with the evidences of an old valvular defect. These conditions were fulfilled in only six cases, and even these were difficult to distinguish clinically from subacute bacterial endocarditis.

Gross Pathology. The vegetations are identical grossly with those of the acute rheumatic type described above. In nine hearts, only the previously thickened valves showed acute vegetations; but in three hearts the vegetations were found on the normal valves and not on the defective ones. In six hearts both kinds of valves showed vegetations, and in nine hearts, therefore, acute lesions were found on valves not previously diseased. In a recurrent infection there seems to be a definite tendency for more valves to become involved.

The appearance of the affected thin leaflets corresponds entirely to the acute rheumatic type; but on the thickened leaflets the vegetations are usually not prominent and are easily overlooked (Fig. 2). The situation of the vegetations is the same as in the acute type.

Considering both acute and chronic changes, the mitral valve was affected in 17 instances, the aortic in 14, the tricuspid in 6 and the pulmonary in 1. The mitral alone was involved in 3 cases, but no

other valve was affected singly. There is evidently a greater tendency for the original infection to attack the mitral value. (Table 2, mitral valve defect 17, aortic valve defect 8) (*cf.* also Table 1, mitral 19, aortic 7).

Structure of Rheumatic Lesions.[1] The stages preliminary to the appearance of the vegetations are not known with certainty since the disease is recognized only when they are present. In association with the smallest vegetations there is already a widespread inflammation throughout the marginal part of the leaflet. In 25–319 (Table 1) the clinical duration was only three days and the vegetations were few and very small. Portions of the leaflets between vegetations show many fibroblasts and polymorphonuclear leucocytes, as well as edema. In well developed cases, the margins of the leaflets apart from the vegetations may show a structure such as is shown in Fig. 3, *viz.*, many large fibroblasts, a few lymphocytes and polymorphonuclears, and an intact surface endothelium.

The smallest vegetations vary somewhat in structure, depending upon the relative proportion of fibroblasts, hyalin, and serous and cellular exudate. The most common type is shown in Fig. 4 (right-hand side). There is a dense collection of fibroblasts near the surface with a little hyalin at the surface. A few polymorphonuclears and lymphocytes are present. On the left-hand side of Fig. 4, the vegetation contains a large amount of hyalin. The endothelium is detached over the central part of the vegetations.

In some vegetations hyalin is a very prominent constituent (Fig. 6). It forms in masses within the leaflet and breaks through the endothelium.

A typical well formed vegetation is elevated from the surface and sometimes pedunculated (Fig. 7). The core is formed chiefly of fibroblasts, but there is a varying amount of serous exudate (edema) and cellular exudate (lymphocytes). Small capillaries are always present. There is a surface layer of hyalin under which the fibroblasts are somewhat more closely packed than elsewhere (Fig. 8). The surface endothelium is largely detached over the hyalin. In some places small platelet thrombi form on the rough surface (Fig. 5). Underneath the vegetation there is a marked inflammatory reaction, characterized by extensive perivascular lymphocytic infiltration and numerous small fibroblasts.

The vegetations seem to be merely localized swellings on the leaflet

TABLE 2

Recurrent rheumatic endocarditis

Number	Age in years	Sex	Duration of cardiac symptoms	Previous attacks of acute arthritis *	Arthritis at time of death	Sepsis at time of death	Valves previously involved	Valves with acute lesions	Weight of heart in grams	Aschoff bodies	Cause of death	Acute pericarditis	Old pericardial adhesions	Glomerulonephritis
13–74	16	F	8 mos.	5 yrs., 4 yrs., 3 yrs., 2 yrs., 8 mos.	–	–	mitral, I_3	aortic	enlarged	+	lobar pneumonia, C. F.	–	–	–
13–142	14	F	5 yrs.	5 yrs., 3 mos.	+	..	mitral, I. S.	mitral, aortic, tricuspid	400	+	C. F., rheumatic fever	–	+	–
15–377	47	M	2 yrs.	2½ yrs.	–	–	aortic, I_1 mitral, I_1	mitral	1061	–	C. F.	–	+	?
17–227	56	M	5 yrs.	many attacks	–	–	mitral, I_1 aortic, I_1	mitral	475	–	C. F., lobar pneumonia	–	–	–
18–123	35	M	3 wks.	?	–	–	aortic, I_3, mitral, S. I.	mitral	800	+	C. F.	–	–	–
18–204	21	M	0	?	–	–	mitral	mitral	350	–	gunshot, immediate death	–	–	–
20–153	37	F	6 mos.	6 mos.	+	..	mitral, I. S.	mitral, aortic tricuspid	410	+	rheumatic fever, C. F.	–	–	–
20–163	15	M	3 yrs.	–	–	+	mitral, S_3	tricuspid	250	–	C. F., acute tonsillitis	–	–	–
21–194	35	F	1 yr.	4 yrs.	–	+	mitral, S. I., aortic, I_1	mitral	440	–	C. F., sepsis	–	–	–

21–253	23	M	7 mos.	7 mos.	–	–	aortic, I_3, mitral, S. I.	mitral, tricuspid	575	+	C. F.	–	–	–
22–28	14	F	1 mo.+	2 yrs., several later	–	+	mitral, I. S.	mitral, aortic	400	+	acute pericarditis, C. F.	+	–	–
23–153	40	M	8 yrs.	8 yrs.	–	–	mitral, S_3, aortic, I. S., tricuspid, S_3, pulmonary, I. S.	mitral, aortic, tricuspid, pulmonary	600	–	C. F.	–	–	–
23–161	48	F	1 mo.	1 mo.	–	+	mitral, S. I.	mitral, aortic	550	+	C. F., acute pericarditis	+	–	?
23–480	35	M	?	2 mos.	–	–	aortic, I_3, mitral, I_1	aortic, mitral	800	+	C. F.	+	–	–
24–519	23	F	?	?	?	?	mitral, S. I.	mitral	325	–	?	–	–	–
24–28	15	F	1 yr.	4 yrs.	–	+	mitral, I_3	mitral, aortic	300	+	C. F., rheumatic fever	+	–	?
25–112	36	M	several yrs.	?	–	–	aortic, I_3	tricuspid	800	+	C. F., gastric ulcer hemorrhage	–	–	?
25–621	41	M	10 yrs.	1 mo.	–	–	mitral, S_3	mitral	500	–	anesthetic, C. F.	–	–	?

Legend: C. F. = cardiac failure. S = stenosis. I = insufficiency. S. I. = chiefly stenosis. I. S. = chiefly insufficiency.
The degree of stenosis or insufficiency is indicated by the subnumbers 1, 2, 3.

* Months or years preceding death.

due to an uneven intensity of the inflammatory reaction. What appears grossly to be a single vegetation is usually found microscopically to be a series of small confluent vegetations (Fig. 5).

Different degrees of intensity of the inflammatory reaction are to be noted. In 25–163a the marginal part of the leaflet is involved throughout its cross-section and there is a hyaline layer on both surfaces (Fig. 9). The fibroblasts are large and numerous and some multinucleated forms are seen (Fig. 10). There are many mitotic figures.

The fibroblasts are the most conspicuous cells in a rheumatic lesion. They develop from the fixed connective tissue cells of the leaflet. They may appear as spindle-shaped, branched or rounded with abundant cytoplasm. The reaction is the same as in proliferative inflammation elsewhere. The cell body enlarges and becomes rounded. Cell division occurs repeatedly. Frequently multinucleated fibroblasts are seen. In one valve, 25–163a, a number of typical Aschoff nodules are found.[2] As far as one may judge from transition forms, the multinucleated cells, separate or in Aschoff nodules, are derived from fibroblasts.

Rheumatic inflammation is chiefly proliferative in character but it is not uncommon to find a few polymorphonuclears in the earlier lesions; and small lymphocytes are numerous, especially in the leaflet below the vegetation. The lymphocytes tend to collect around the capillaries. Areas of serous exudate (edema) are often seen in the vegetations and elsewhere, and this is one cause of the swelling.

Dense hyaline material is found constantly on the surface of fresh vegetations. Some small vegetations consist chiefly of hyalin (Figs. 4 to 6). It may also be found deep within the substance of the leaflet apart from vegetations (Fig. 11). It seems to be chiefly a coagulated exudate and not a product of tissue disintegration. When the hyalin breaks through the endothelium, platelets may accumulate upon it (Fig. 5). A platelet thrombus cannot be distinguished from this hyaline material except by its position. Fibroblasts may be found scattered through the hyalin but they are usually not so numerous as elsewhere.

The reaction in the leaflet apart from the vegetations is very important in determining the subsequent effects upon the valve. The marginal part of the leaflets, especially of the mitral and tricuspid

TABLE 3

Acute primary bacterial endocarditis

Number	Age, in years	Sex	Duration	Arthritis, time before death	Valves involved	Acute pericarditis	Aschoff bodies	Glomerulonephritis
11–128	42	M	2 days	?	mitral	–	–	–
14–209	21	F	1 wk.	?	mitral	–	–	mild acute exudative
14–232	55	F	5 wks.	–	mitral	–	–	–
15–159	54	M	10 days	?	mitral	+	–	–
15–391	43	M	3 wks.	?	aortic	–	–	–
16–54	35	M	2 wks.	–	mitral	–	–	–
16–128	19	F	5 days	?	mitral	–	–	–
17–31	19	M	3 wks.	–	aortic	–	–	glomerular abscess
19–197	34	F	6 days	?	mitral, aortic	–	–	–
20–2	18	M	5 wks.	?	aortic	–	–	–
21–124	78	M	4 wks.	1 mo., still present	mitral, aortic	–	–	–
22–148	19	F	4 wks.	1 mo.	aortic	–	–	embolic
17–213	43	F	2 wks.	2 wks., still present	all four	+	–	embolic

TABLE 4

Acute secondary bacterial endocarditis

Number	Age, in years	Sex	Duration	Arthritis, time before death	Valves involved	Acute pericarditis	Aschoff nodules	Primary disease	Glomerulonephritis
10–59	7	F	5 days	–	mitral	+	–	otitis media	–
12–18	33	F	10 days	–	mitral	–	?	acute endometritis	–
13–16	31	F	?	?	mitral	–	–	tuberculosis with cavities	(amyloid)
14–255	39	M	4 wks.	6 yrs.	aortic	–	–	lobar pneumonia	acute diffuse
16–89	30	M	2 wks.	4 yrs.	aortic, mitral	–	–	erysipelas	subacute diffuse
16–308	23	F	1 wk.	?	mitral	–	–	acute endometritis	–
16–358	62	M	?	?	mitral	–	–	postoperative peritonitis	–
16–381	23	F	a few days	?	mitral	–	–	acute endometritis	–
17–233	38	F	?	has chronic arthritis	mitral	+	–	abdominal tumor	–
17–248	38	F	a few days	?	mitral	–	–	acute endometritis	–
18–39	39	M	?	?	mitral	–	–	pernicious anemia	–
18–53	47	M	?	?	aortic	–	–	carcinoma of stomach	–
19–94	46	F	9 days	?	mitral	+	–	postoperative peritonitis	–
20–209	56	M	?	?	mitral, aortic	–	–	peritonitis (carcinoma of stomach)	–

20-267	25	F	?	?	mitral, tricuspid	–	–	acute endometritis	acute diffuse
20-388	38	F	?	many in past 2 yrs.	mitral	–	–	leukemia	–
20-428	65	M	1 wk.	?	mitral	–	–	influenzal pneumonia	–
21-150	21	F	4 wks.	?	mitral	–	–	acute endometritis	–
21-237	36	F	3 wks.	?	aortic	–	–	acute endometritis	–
21-307	54	M	10 days	2 mos.	mitral	–	–	primary hypertension	–
22-134	46	F	9 days	?	mitral	–	–	influenzal pneumonia	–
22-149	68	M	?	?	mitral	–	–	carcinoma of prostate	–
22-229	23	F	?	?	mitral	+	–	peritonitis	–
23-252	31	F	1 wk.	?	mitral, aortic	–	?	scarlet fever	?
24-212	26	M	?	–	mitral	+	–	multiple sclerosis	embolic
24-566	26	M	?	?	mitral, aortic, tricuspid	–	–	thrombosis of cavernous sinus	–
24-745	12	M	?	?	mitral	–	–	acute osteomyelitis	–
25-103	68	M	?	?	mitral	+	–	infected wound	–

valves, nearly always shows a diffuse inflammation. Rarely this is of an acute proliferative character (Figs. 9 and 10); but more frequently it is of a more chronic type with large numbers of small fibroblasts, prominent blood vessels and some lymphocytes (Fig. 12). The inflammation may extend through the distal half of the valve (Fig. 1) or even to its attached margin. A section through the center of the opaque part of the leaflet shown in Fig. 1 shows a lymphocytic infiltration with many small fibroblasts. It is easy to understand how this lesion may give rise to a thickened scarred valve in the course of healing.

The structure of the vegetations in the recurrent cases is identical with that of the acute rheumatic lesions except that in general the lesions on defective valves are less active. There are usually fewer lymphocytes, smaller fibroblasts and more collagenous fibers. Healing processes are more in evidence and healed or partially healed vegetations are found along with the active ones. The valve underlying the vegetation is composed largely of scar tissue (Fig. 13).

Healing of Rheumatic Lesions. Relatively few persons die during the acute stage of rheumatic endocarditis. Death is usually due either to deformities of the valves that occur in the course of healing or to the subsequent development of a bacterial endocarditis on the diseased leaflets. Evidences of healing were found in all the recurrent and in two of the acute cases (24–364 and 24–1a) of rheumatic endocarditis. In the vegetations the first change noted is the formation of many new collagenous fibers along with a decrease in the size of the fibroblasts. These cells soon recede to the size of fixed tissue cells, and in the denser parts of the scar they usually disappear entirely. The central part of the vegetation becomes a scar-like structure. The lymphocytes emigrate or disintegrate. The peripheral hyaline layer becomes more homogeneous and glassy (Figs. 14 and 15) and remains in this condition indefinitely. It is not absorbed and does not become organized. Hyalin in the deeper parts of the vegetation or in the body of the leaflet may likewise persist indefinitely or it may become calcified. Within the hyaline masses there are very few fibroblasts and these disintegrate without forming collagenous fibers (Fig. 15). The end result of healing of a rheumatic vegetation is scar tissue sometimes with a thin hyaline layer on its surface. In the body of the leaflet healing results in an

increased amount of fibrous tissue which commonly assumes the appearance of a scar. This topic will be discussed further in connection with old valvular defects.

II. Bacterial Endocarditis [3]

This group includes all cases of active endocarditis except the rheumatic and the syphilitic. The vegetations are larger and softer than the rheumatic type. Their consistence is such that portions may become detached to form emboli. Bacteria are commonly present in the vegetations and in the circulating blood, but they cannot be demonstrated in all cases. There are no fundamental distinctions from rheumatic endocarditis, and lesions of the rheumatic type are present in a large percentage of the hearts of this group; but all hearts in which some of the vegetations are large and soft have arbitrarily been classified as bacterial.

1. Acute Bacterial Endocarditis. On clinical grounds it is convenient to classify all cases of less than six weeks' duration as acute and those of longer continuance as subacute. The acute cases may be further subdivided into those in which endocarditis is the only prominent clinical finding (*primary*) and those in which endocarditis is definitely overshadowed by some major illness which causes death (*secondary*).

a. In the *primary* group (Table 3) there are thirteen cases. The clinical picture is that of severe septicemia with or without physical signs of endocarditis. One death was due to cerebral embolism. Associated infections, presumably secondary to the septicemia, were found in four cases, *viz.*, bronchopneumonia, meningitis and pericarditis.

The vegetations are usually large and soft, but some small firm lesions of rheumatic type were occasionally seen. Ulceration of the leaflets was present in only one instance. In ten of the thirteen hearts only one of the valves was involved.

Only four hearts were available for microscopic study of the valves. Two of these showed necrosis of the marginal part of the leaflet with large platelet thrombi, and an exudate of polymorphonuclears and lymphocytes within the valve. In both of these, areas of inflammation of rheumatic type were found on the inner surface of the leaflet midway between the free and attached margins.

TABLE 5

Subacute bacterial endocarditis

Number	Age, in years	Sex	Duration acute symptoms	Valves involved	Old valvular defect	Arthritis, time before death	Weight of heart, in grams	Aschoff bodies	Pericarditis	Duration chronic valvular disease	Rheumatic lesions	Glomerulonephritis
10–73	42	F	3 mos.	mitral	–	several attacks	393	–	–	..	–	?
10–76	25	M	3 mos.	mitral	–	?	normal	–	–	..	..	–
10–164	36	M	?	aortic	aortic, I_3	–	530	–	–	?	..	–
12–76	46	M	10 wks.	mitral	–	continuous during attack	310	–	–	..	..	–
12–131	33	M	3 mos.	mitral, aortic	mitral, S. I. aortic, S. I.	–	460	–	–	?	+	subacute diffuse
13–100	39	M	?	aortic	aortic, I_3	?	675	–	–	?	..	embolic and mild acute diffuse
13–165	33	M	4 mos.	mitral, aortic	aortic, I_3	a few years	640	–	–	0	+	acute diffuse
13–180	63	M	?	mitral	mitral, S_3	?	normal	–	acute	2 yrs.	–	mild acute diffuse
13–189	48	M	3 mos.	mitral	mitral, I_3	–	675	–	–	0	..	embolic
13–190	35	F	6 mos.	mitral	–	20 yrs., 13 yrs., many other attacks	525	–	old	..	+	acute diffuse
14–49	25	M	3 mos.	aortic, mitral	aortic, I_3, mitral, S. I.	several attacks	575	–	–	0	–	acute diffuse

14–207	43	M	6 mos.	aortic	aortic, I_3	one	620	–	–	o	+	–
15–30	55	M	3 mos.	aortic, mitral	aortic, I_3, mitral, S. I.	?	475	–	–	o	+	–
15–81	35	M	6 mos.	mitral	mitral	–	575	–	–	o	..	–
15–97	29	F	9 wks.	mitral	–	?	normal	–	–	..	+	acute diffuse
15–176	42	M	6 mos.	aortic, mitral	aortic, S_3, mitral, I_1	–	480	–	–	o	..	–
15–209	35	F	?	mitral, aortic	mitral, I. S., aortic, S. I.	?	425	–	–	?	..	mild acute diffuse
15–312	24	M	9 mos.	aortic, mitral	aortic, S. I., mitral, I_1	9 mos.	723	–	–	o	+	embolic
15–393	59	M	6 mos.+	mitral, aortic	–	?	normal	–	–	..	+	–
16–124	45	M	5 mos.	mitral	–	?	400	–	acute	..	+	embolic
16–152	6	F	3 mos.	mitral	–	–	243	–	acute and old	..	–	acute diffuse
16–203	61	M	2 mos.	aortic	aortic, S. I.	?	680	–	–	?	–	?
16–251	33	M	10 wks.+	mitral, tricuspid	mitral, S_3	21 mos.	574	–	–	15 mos.	..	embolic
16–295	11	F	2 mos.+	mitral, tricuspid	mitral, I_1	2 yrs. (chorea)	250	+	–	2 yrs.	+	embolic

TABLE 5 — *continued*

Number	Age, in years	Sex	Duration acute symptoms	Valves involved	Old valvular defect	Arthritis, time before death	Weight of heart, in grams	Aschoff bodies	Pericarditis	Duration chronic valvular disease	Rheumatic lesions	Glomerulonephritis
16–413	38	M	3 mos.	aortic, mitral	aortic, I. S., mitral, I_1	5 yrs.	860	–	–	?	+	embolic
17–28	29	M	11 mos.	aortic, mitral, tricuspid	aortic, I_2, mitral, I_2	11 yrs., 6 yrs.	690	+	acute	0	+	embolic
17–36	29	F	6 mos.	mitral	mitral, I_1	9 yrs., many since	250	–	–	14 yrs.	..	embolic, mild acute diffuse
17–174	28	M	7 mos.	mitral	mitral, I. S.	10 yrs.	565	+	–	4 yrs.	..	–
17–202	25	M	8 mos.	mitral	mitral, I_2	10 yrs., 9 yrs.	640	–	old	6 yrs.	..	acute diffuse
17–260	25	M	7 mos.	aortic, mitral	aortic, I_2 mitral, S_2	11 yrs., 7 mos.	570	–	–	11 yrs.	–	embolic, severe
18–102	23	M	4 mos.	aortic, mitral	aortic, I_2	?	690	–	–	0	+	–
18–105	13	F	11 mos.	mitral	–	–	350	–	–	..	–	–
18–122	30	M	3½ mos.	mitral, aortic	–	–	565	–	–	..	..	acute diffuse
18–175	34	M	8 mos.	aortic, mitral	–	?	480	–	–	..	..	embolic, severe
18–178	24	F	?	mitral, aortic	mitral, S_2	?	410	–	–	?	..	?
19–23	31	F	7 wks.	aortic	–	–	300	–	–	..	–	glomerular hemorrhages

19–141	55	M	6 wks.	aortic	–	–	325	–	–	..	+	–
19–161	23	F	8 mos.	mitral, tricuspid	–	–	365	–	acute	..	+	embolic, severe
19–264	29	M	?	mitral	–	2 yrs., 1 yr.	435	–	–	..	+	chronic diffuse
19–273	66	M	2 mos.	aortic	–	–	480	–	–	..	+	–
19–276	16	M	?	aortic, tricuspid	aortic, I_3	?	620	–	–	2 yrs.	–	acute diffuse
20–88	51	M	6 wks.	aortic, tricuspid	–	?	314	–	–	..	..	–
20–122	63	M	?	aortic	–	?	450	–	acute	..	–	–
20–165	43	M	6 mos.	aortic, mitral	–	–	625	–	–	..	+	–
20–296	16	M	7 wks.	mitral	–	–	330	+	–	..	..	–
20–326	28	M	2 mos.	mitral, aortic	mitral, I_1, aortic, I_3	12 yrs., 8 yrs., 5 yrs., 2 yrs.	920	–	old	several yrs.	+	?
20–344	12	F	5½ mos.	mitral, aortic	–	5½ mos.	280	–	–	..	+	embolic, severe
20–368	18	M	6½ mos.	mitral	–	?	340	–	acute	..	+	embolic and acute diffuse
21–45	55	M	4 mos.	mitral, aortic	–	–	420	+	–	..	+	embolic, severe
21–65	52	M	?	mitral	–	?	400	–	–	..	+	embolic
21–283	24	M	7 mos.	mitral	–	–	400	–	–	..	..	embolic
21–414	50	M	2 mos.+	mitral	–	35 yrs.	enlarged	–	old	..	–	–

TABLE 5 — *continued*

Number	Age, in years	Sex	Duration acute symptoms	Valves involved	Old valvular defect	Arthritis, time before death	Weight of heart, in grams	Aschoff bodies	Pericarditis	Duration chronic valvular disease	Rheumatic lesions	Glomerulonephritis
21-468	36	M	14 wks.	mitral	–	3½ mos.	450	–	–	..	..	?
21-513	42	M	10 wks.	aortic, mitral	–	8 yrs.	545	–	–	..	+	?
21-559	28	M	14 wks.	mitral, aortic	mitral, I_2	–	490	–	–	0	..	–
22-217	55	M	6 wks.	tricuspid	–	–	245	–	–	..	–	–
22-287	50	M	?	aortic, mitral	aortic, I. S., mitral, I_1	4 yrs., 8 mos.	660	–	–	4 yrs.	+	–
22-418	41	M	?	aortic	–	?	675	–	–	..	–	–
22-465	21	M	?	aortic	aortic, I_2	?	450	–	–	3 yrs.+	..	?
22-554	43	M	5 mos.	aortic, mitral	–	?	610	–	acute	..	+	chronic diffuse
23-390	45	M	?	aortic	–	–	575	–	–	..	+	acute diffuse
23-484	46	M	3½ mos.	aortic, mitral	aortic, S. I.	9 yrs.	725	–	acute	9 yrs.	+	–
23-508	76	M	7 wks.+	aortic, mitral	aortic, S. I.	several attacks past few yrs., 12 wks.	550	–	–	?	–	embolic
24-4	30	M	5 mos.	tricuspid	–	–	300	–	–	..	..	embolic
24-91	39	M	11 mos.	aortic	aortic, I. S.	20 yrs., 11 mos.	580	–	–	10 yrs.	+	embolic

24-121	59	M	7 mos.	aortic, mitral	–	–	560	–	old	..	+	–
24-241	23	F	11 wks.	aortic, mitral	–	7 yrs., 11 wks. to present	330	–	old	..	+	embolic
24-605	35	M	3½ mos.	aortic	–	–	550	–	–	..	+	embolic
24-769	14	F	5 mos.+	mitral	mitral, I_1	chorea, 3 yrs., 7 mos., 5 mos.	255	+	–	3 yrs.	+	embolic, severe
24-770	10	F	4 mos.	aortic	–	4 mos.	380	–	acute	..	+	?
24-807	20	F	6½ mos.	mitral, tricuspid	–	–	400	–	–	..	–	acute diffuse
25-142	4	F	6 wks.	mitral	–	has chorea	125	–	–	..	..	–
25-362	42	M	6 wks.	pulmonary	–	–	420	–	acute	..	..	–
25-589	30	F	3 mos.	mitral, aortic	mitral, I. S., aortic, I_2	8 attacks past 12 yrs., present now	350	–	old	?	+	acute diffuse
11-122	51	M	6 wks.	mitral, aortic	mitral, S_3	16 yrs., 1 yr., several between	575	–	–	16 yrs.	+	–

Legend: S = stenosis. I = insufficiency. S. I. = chiefly stenosis. I. S. = chiefly insufficiency. The degree of stenosis or insufficiency is indicated by the subnumbers 1, 2, 3.

In the two others there were large fresh soft thrombi with an extensive exudative reaction within the leaflet. The leucocytes were chiefly polymorphonuclears. There was some proliferation. Numerous bacteria were found in the thrombotic material of one of these.

b. Twenty-seven cases of *secondary acute bacterial endocarditis* (Table 4) were studied. The clinical symptoms were always those of the major illness. The endocarditis was not recognized clinically in any case, but perhaps it might have been diagnosed in some had more attention been given to the heart. The heart lesion was not considered by the pathologist as the main cause of death in any instance. In this group are seven cases of puerperal sepsis following induced abortion. The inclusion of this disease presumably explains the preponderance of females.

In twenty cases there was clinical evidence of septicemia which was attributable to the major illness, but in the remaining seven the usual signs of infection were absent.

The mitral valve was affected twenty-five times, the aortic five times and the tricuspid once. More than one valve was involved in only four cases. In only one heart was the acute lesion found on a previously thickened valve. The vegetations cannot be distinguished grossly from those of subacute bacterial endocarditis. In general, however, they are fewer in number. Ulceration of a leaflet was found only once.

Six hearts of this group were available for microscopic study of the valves. Four showed a large soft thrombus with necrosis of the leaflet and a purulent exudate within the valve. In one of these the single vegetation was 1 cm. in diameter. Bacteria were very prominent in another.

In the fifth and sixth cases there was very little exudate, the lesions being of proliferative type with prominent evidences of healing.

The lesions of acute bacterial endocarditis do not differ in any essential respects grossly or microscopically from those of the subacute bacterial type. Any distinction that is made must therefore be based chiefly on clinical data.

2. SUBACUTE BACTERIAL ENDOCARDITIS. Seventy-four cases of this group have been studied (Table 5). The literature on this form of endocarditis has previously been reviewed by one of us.[4] These cases correspond clinically with subacute bacterial endocarditis as defined by Libman.[5]

The duration of symptoms in our series was as follows: 6 weeks to 3 months, 27; 3 to 4 months, 9; 4 to 5 months, 2; 5 to 6 months, 9; 6 to 7 months, 7; 7 to 8 months, 3; 8 to 9 months, 1; 10 to 11 months, 3; indefinite duration, 13. All the patients died within one year of the first appearance of symptoms.

Thirty-one of the seventy-four patients gave a history of one or more attacks of *acute arthritis*, and in eleven of these the fatal illness began with such an attack. A valvular lesion associated with acute arthritis may therefore be of the subacute bacterial type. The number of attacks varied from one to eight, and some occurred as long as twenty years before death. Twenty-four patients had never had arthritis, and in the nineteen others the history was indefinite on this point.

Relation to Previous Valvular Disease. Twenty-three patients gave a definite history of chronic valvular disease. In fifteen the duration was from one to sixteen years, and in eight the exact duration was unknown. Fifteen of these twenty-three patients gave a history of acute rheumatic fever which apparently caused the valvular defect.

In thirty-four instances the leaflets were grossly thickened and scarred, indicating a previous inflammation; but, since a considerable amount of scar tissue may form during the course of a subacute case, only extreme thickening can be considered positive anatomic evidence of a previous old valve defect. In forty cases there was no clinical evidence of old valve defect and the valves were not notably thickened. Apparently over half the subacute cases begin on previously normal valves. It is to be noted that when old defective valves are present in these hearts they always show an active inflammation. Apparently they are more susceptible to infection than normal leaflets.

In several instances the endocarditis appeared to develop secondarily to some other infectious process, *viz.*, otitis media (2 cases), lupus erythematosus (1), empyema (1), tonsillitis (1).

In the 74 hearts the mitral was diseased in 56, the aortic in 44, the tricuspid in 9 and the pulmonary in 1. A single valve was affected in 38 instances; mitral 22, aortic 13, tricuspid 2, pulmonary 1. The most frequent combination was mitral and aortic, 29 hearts.

Gross Appearance of Valves. The diagnostic feature is the large soft vegetation, but the appearance of the valves varies widely with the

number and size of the vegetations, and the extent of ulceration, thickening and calcification. Ulceration with loss of substance of the leaflet was present in thirty-two hearts. The term "ulcerative" endocarditis can properly be applied only to this number. The ulcers vary from a diameter of a few millimeters to complete destruction of a leaflet. They are more frequently found on the aortic valve. In three cases there was perforation of a leaflet, and in two there were ulcers penetrating to the right auricle from the aortic area.

Varying degrees of calcification of the valves were noted in twenty-five hearts. Calcium is deposited in the thrombotic material and in the old hyaline scar tissue. In the former position it is commonly present in moderate amounts, such as to give a gritty feel when cut; in the latter position, however, it is often of bony density. Calcium is readily deposited in the larger thrombi independently of the stage of healing. Frequently it is found in definitely active vegetations and even in association with bacteria.

In addition to the larger vegetations, small firm vegetations of the rheumatic type can be seen grossly in about three-fourths of the hearts, if a careful search is made for them. Sometimes one valve shows only rheumatic vegetations, but usually both types are found on the same leaflet.

Situation of the Lesions in Active Endocarditis. (*a*) *Aortic valve.* In acute rheumatic endocarditis the vegetations were always found on the ventricular surface of the leaflet in a line about one-third the distance from the free to the attached margin. This corresponds to the line of contact of the leaflets when the valve is closed. In recurrent rheumatic endocarditis the situation of the vegetations was the same except in one case in which they were found only on the free margin of one leaflet. In twenty-one cases of the subacute bacterial type, the vegetations occupied the same position as in the rheumatic form, but in twelve other cases they extended from this line around the free edge onto the aortic surface. In one case they were found only on the free margin of the leaflet.

(*b*) *Mitral valve.* In the acute rheumatic type the line of vegetations was always on the auricular surface, 1 to 2 mm. from the free margin, with one exception in which the vegetations were larger and extended over the free margin onto the chordae. In the recurrent type the vegetations occupied the same position as in the

acute type with two exceptions, in one of which they were on the free margin only and in the other on the ventricular surface only, near the free margin. In eighteen cases of the subacute bacterial type the vegetations extended from a line 1 to 2 mm. back of the free margin for varying distances upon the auricular surface. In thirteen other cases they extended from the auricular surface around the free margin onto the ventricular surface. In five hearts the vegetations were found only on the ventricular surface of the aortic leaflet of the mitral, extending from the central part of its surface toward the free margin. In all five of these the adjacent aortic leaflet also showed similar vegetations. A vegetation on this aortic leaflet may strike against the central part of the ventricular surface of the aortic leaflet of the mitral.

(*c*) *Tricuspid valve.* Acute lesions of both types were always found on the auricular surfaces of the leaflets near the free margin.

(*d*) In the single instance in which the *pulmonary valve* was involved, the lesion was of bacterial type and affected the margins as well as both surfaces of the leaflets.

Microscopic Structure. In forty-six hearts the valves were studied microscopically, one or two areas from each valve. Both exudative and proliferative forms of inflammation are usually found in the sections examined from each heart; but frequently one type of reaction predominates. Both types may be found in the same leaflet. The proliferative reaction is most common.

The exudative lesions are similar to acute exudative inflammation in other tissues. Rarely they are definitely purulent in character. The leucocytes are either polymorphonuclears or mononuclears. In one valve a number of embolic abscesses were found (Fig. 16). The thrombus overlying an exudative lesion is fresh and soft.

Proliferative inflammation is seen more frequently than the exudative. In the valve underneath the thrombus are large numbers of fibroblasts with relatively few leucocytes. The fibroblasts may be small and separated by a considerable number of collagenous fibers (Fig. 17); or they may be large with only a minimum of intercellular fibers (Fig. 18). In slowly progressive or healing lesions the fibroblasts tend to be smaller and the intercellular collagenous fibers more prominent. In sixteen hearts the proliferative lesions were prominent and the exudative inconspicuous. In five hearts large

multinucleated fibroblasts, such as occur in Aschoff bodies, were found (*cf.* Fig. 18). The histologic structure of the lesions in the valves seems to have no direct relation to the clinical course of the disease.

Necrosis of part of a leaflet is frequently seen. Ulceration is a direct result of necrosis.

In addition to the bacterial lesions just described, which predominate in these hearts, lesions of the rheumatic type were found in thirty-five of the forty-six that were examined microscopically. These vegetations have the same structure as those found in typical rheumatic endocarditis. In four hearts the tricuspid valve showed typical gross rheumatic vegetations but none of the bacterial type. Usually both types are found on the same valve. The rheumatic lesions may be continuous with the bacterial. The rheumatic vegetations were active in 22 hearts, healing in 9, and both active and healing in 4. In the 35 cases with rheumatic lesions 18 gave a positive history of rheumatic fever, 9 a negative history, and in 7 the history was incomplete. In the 31 cases with positive history of rheumatic fever, rheumatic lesions were present in 18 and absent in 5 (8 not examined). In 11 cases that began with acute arthritis, rheumatic lesions were present in 7 and absent in 2 (2 not examined). It cannot be said that the rheumatic vegetation is pathognomonic of rheumatic fever since it is found in three-fourths of subacute bacterial cases.

Evidences of healing are found in a great majority of these valves, and often the signs of active inflammation have largely disappeared. There may be active inflammation in one part of a leaflet and advanced healing in another part. In the leaflet itself the fibroblasts decrease in size while many new collagenous fibers are being formed. The leucocytes emigrate or disappear. The final result is dense scar tissue underlying a hyaline thrombus (Fig. 19).

The thrombus may soften and disintegrate, especially when it contains a large proportion of leucocytes. Portions may become detached to form emboli. Those portions that remain permanently attached to the leaflet soon become homogeneous in structure. They may persist indefinitely in this condition, or they may become calcified. Calcification may give rise to hard nodular masses or to diffuse hardening. Organization is rarely seen, and seems never of sufficient extent to convert a thrombus into scar tissue.

The most serious valvular defects result from necrosis and sloughing, but some deformities are due to the contraction of scar tissue. The importance of bacterial endocarditis in the production of old valvular defects will be discussed in a subsequent paragraph.

III. Old Valvular Defects[6]

This group includes cases of chronic valvular disease in which there were no clinical indications of active endocarditis, and in which the valves showed gross thickening and scarring. In 114 of the 130 cases of this group death was due to cardiac failure. In the 16 remaining cases the immediate cause of death was as follows: coronary sclerosis, 2; primary hypertension, 2; intestinal obstruction, 1; pyemia, 1; tuberculosis, 1; Addison's disease, 1; peritonitis, 1; suicide, 1; hemorrhage from gastric ulcer, 1; luetic aortitis, 1; cirrhosis of liver, 1; embolism of the stenosed mitral orifice, 1; and undetermined, 2.

The mitral valve was diseased in 95, the aortic in 82, the tricuspid in 13, the pulmonary in 3. The mitral alone was involved in 44, the aortic alone in 32, the tricuspid alone in none, the pulmonary alone in 3. The aortic and mitral were both diseased in 50 cases. The aortic, mitral and tricuspid valves were all three involved in 12 cases.

There were thirty-seven cases of pure mitral stenosis (*i.e.*, extreme stenosis with negligible insufficiency), and twelve cases with varying degrees of mitral insufficiency in which stenosis was negligible. In forty-three other hearts the mitral was both stenosed and insufficient, the stenosis dominating in thirty-five, the insufficiency in eight. In three hearts in which the mitral only was diseased, the lesion was not severe enough to cause any functional disturbance. In nineteen hearts an adherent pericardium was found, and in some of these it was the chief cause of the cardiac failure.

There were twenty cases of pure aortic stenosis, and seventeen with varying degrees of insufficiency without stenosis. In forty-one hearts the aortic valve was both stenosed and insufficient, the stenosis dominating in twenty-eight, the insufficiency in thirteen. In four hearts the lesion caused no functional disturbance. Aortic stenosis is not a rare type of chronic valvular disease.

The tricuspid lesions were usually of mild degree. The three pulmonary lesions were pure stenosis of congenital type.

Patients with mitral stenosis died at an earlier average age than those with aortic stenosis. In forty-three cases in which the mitral lesion was chiefly or entirely stenosis with a normal aortic valve, the average age at death was 41.7 years. In twenty-nine cases in which the aortic lesion was chiefly or entirely stenosis, with a normal mitral valve, the average age at death was 55.8 years.

The duration of symptoms of chronic valvular disease of all types was as follows: less than 1 day, 5 cases; 1 day to 3 months, 18; 3 to 6 months, 8; 6 to 12 months, 12; 1 to 2 years, 15; 2 to 3 years, 9; 3 to 4 years, 11; 4 to 5 years, 4; 5 to 10 years, 13; 10 to 20 years, 9; 20 to 34 years, 3; indefinite number of years, 4; and unknown duration, 14. With respect to the duration of symptoms there are no important differences between mitral and aortic stenosis.

There was a positive history of one or more attacks of rheumatic fever in fifty of the 130 patients, and a negative history in thirty. In fifty cases there was no mention of rheumatic fever. In one negative case the symptoms began after an attack of tonsillitis.

In sixteen cases of pure mitral stenosis without pericardial adhesions and without involvement of other valves, the average weight of the heart was 441 gm.; minimum weight 270 gm.; maximum 680 gm. The enlargement is chiefly right ventricular hypertrophy.

In thirteen cases of pure aortic stenosis without pericardial adhesions and without involvement of other valves, the average weight of the heart was 705 gm.; minimum 475 gm.; maximum 1130 gm.

The average weight of the heart in all the cases of chronic valvular disease was 580 gm.

Adherent pericardium (old adhesions) was found in nineteen cases, and acute pericarditis in six.

The most frequent gross change in the valves is thickening and stiffening with resulting loss of elasticity and narrowing of the orifice; but often there is retraction and curling with insufficiency which may be more pronounced than stenosis. The leaflets of the aortic valve are often fused together at the aortic attachment where they come into contact.

Calcification is a very common change in old defective valves, being present in varying degree in eighty-five of the 130 cases. The calcium is either distributed diffusely or in the form of large nodular

masses. Diffuse calcification was found in the mitral in forty-one instances and in the aortic in thirty. The calcium is deposited in the hyaline scar tissue within the leaflet.

Seventy-three of the 130 hearts of this group had been preserved and were available for careful gross and microscopic study. The remaining fifty-seven were described in the necropsy protocols, but no material except pieces of ventricular muscle was kept. Tables 6, 7 and 8 were made from the seventy-three preserved specimens. These hearts have been arranged in three groups for convenience of description: Group 1, in which the thickened valves are incompletely healed; Group 2, in which the valves are thickened and stiffened from newly formed fibrous tissue but show no unhealed areas; Group 3, in which the thickening of the leaflets is due chiefly to large calcareous nodules.

Group 1. Incompletely Healed Valves
30 Cases (Table 6)

The unhealed areas can usually be seen with the unaided eye, but often they are more readily recognized with a small hand lens. In eleven hearts they appeared as small firm pale vegetations, usually in the form of a slightly elevated ridge but sometimes very conspicuous (Fig. 20). Some of these valves are not distinguishable grossly from the recurrent rheumatic group, but usually the lesions are less prominent. In three hearts there were large ulcerated areas covered by a thin layer of thrombus (Fig. 22). In the remaining sixteen hearts the lesions appeared as small roughened denuded areas (Fig. 24).

Microscopic Structure. The thickened valves of this group are composed largely of dense fibrous tissue, often hyaline in structure, such as results from the healing of inflammatory processes in any tissue. But sections cut through the unhealed areas show a recognizable rheumatic or bacterial lesion in some stage of healing. It may be a well defined elevated vegetation, easily recognized as rheumatic. The one shown in Fig. 25 has a core composed of dense fibrous tissue in which capillaries are still present, and the surface hyaline layer is conspicuous. The one shown in Fig. 26 is of dense hyaline structure, but the surface hyaline layer may still be recognized on one side. A microscopic section of the vegetations seen in

TABLE 6

Old defective valves. Group 1. Incomplete healing

Number	Age, in years	Sex	Duration	Acute arthritis, time before death	Valves				Weight of heart in grams	Old pericardial adhesions	Calcareous nodules	Incomplete healing	Aschoff bodies
					mitral	aortic	tricuspid	pulmonary					
10–9	45	M	6 yrs.	20 yrs.	S. I.	S_3	I_1	–	540	–	–	mitral, raw area	–
10–142	47	M	?	?	S. I.	–	–	–	250	–	–	raw area	–
11–121	34	M	1 yr.	6 yrs., 3 yrs.	I_3	–	–	–	350	–	–	vegetations	–
12–117	54	M	16 mos.	?	I. S.	–	–	–	400	–	–	thrombus on large ulcer	–
12–168	27	M	4 yrs.	12 yrs., 8 yrs., 2 yrs.	S_3	S. I.	–	–	400	+	–	mitral, raw area	–
14–20	20	M	2 yrs.	?	S_3	I_1	0	–	370	–	–	tricuspid, vegetations; aortic, raw area	–
15–323	49	M	?	several attacks	S_3	–	–	–	325	–	–	thrombus on large ulcer	–
15–324	53	M	3 yrs.	28 yrs.	S. I.	I. S.	–	–	795	–	–	mitral, aortic, vegetations	–
16–16	29	M	27 mos.	10 yrs.	S_3	–	–	–	350	–	–	raw area	–
16–185	46	M	?	?	S. I.	–	–	–	320	–	–	thrombus on large ulcer	–
19–26	45	M	3 yrs.	?	S_3	–	–	–	510	–	–	raw area	?
19–286	51	M	1 yr.	?	S_3	–	–	–	550	–	–	raw area	–
20–157	61	M	3½ yrs.	?	S_3	S. I.	S_1	–	550	–	–	mitral, raw area	+
20–250	65	M	4 yrs.	?	0	S_3	–	–	715	–	aortic, mitral	aortic, raw area	–

20–358	21	F	12 hrs.	?	S_3	0	–	–	270	–	–	aortic, vegetations	–
20–433	57	M	5 mos.	40 yrs.	0	S_3	–	–	720	–	aortic, mitral	raw area, one leaflet	–
20–463	37	M	3 yrs.	19 yrs., 13 yrs., 4 yrs., 3 yrs.	I. S.	I. S.	–	–	825	–	aortic	mitral, aortic, raw area	–
21–259	52	F	2 wks.	–	S. I.	–	0	–	325	–	–	tricuspid, vegetations	–
21–285	53	M	10 yrs.	20 yrs.	–	I_3	–	–	475	–	aortic	raw area	–
21–416	46	M	6 wks.	20 yrs.	I. S.	I. S.	–	–	900	+	–	mitral, vegetations	–
21–473	58	F	7 mos.	?	S. I.	–	–	–	550	–	–	raw area	–
21–485	60	F	?	?	S_3	–	–	–	410	–	–	raw area	–
22–197	41	F	9 mos.	?	S_3	–	–	–	350	–	–	vegetations	–
23–142	35	M	5 yrs.	5 yrs.	–	S_3	–	–	850	–	–	raw area	–
23–324	42	M	3½ mos.	–	I. S.	S. I.	–	–	550	–	–	raw area	+
24–307	43	F	?	?	0	–	–	–	430	–	–	vegetations	–
24–482	40	M	?	?	S. I.	–	–	–	365	–	–	vegetations	–
24–613	38	F	?	?	0	–	–	–	375	–	–	vegetations	–
25–322	33	M	5 yrs.	?	S. I.	I.S.	–	–	690	–	–	aortic, mitral, raw areas	–
25–328	70	M	?	?	0	–	–	–	300	–	–	vegetations	–

Legend: S = stenosis. I = insufficiency. S. I. = chiefly stenosis. I. S. = chiefly insufficiency. The degree of stenosis or insufficiency is indicated by the subnumbers 1, 2, 3.

Fig. 20 is shown in Fig. 21. It consists of a rather thick layer of old hyaline thrombus resting on dense scar tissue. It suggests a healed bacterial type of lesion because of the thickness of the thrombus.

The raw areas show a variety of microscopic appearances. Occasionally fibroblasts are to be seen and there are other signs of low grade activity. Usually there are no signs of active inflammation. A layer of hyaline thrombus rests upon dense fibrous tissue (Fig. 27) or upon hyaline scar tissue (Fig. 28).

In one instance (25–322) the leaflet underlying the raw area showed areas of necrosis and numerous polymorphonuclear leucocytes as well as dense fibrous tissue. The ulcer shown in Fig. 22 likewise shows an active exudative inflammation within the substance of the valve (Fig. 23). Neither of these patients had any clinical signs of active endocarditis. They died apparently from the valvular defect and not from toxemia. The two hearts shown in Figs. 20, 21, 22 and 23 as well as one other are interpreted by us as old valvular defects resulting from subacute bacterial endocarditis. The other hearts of this group are considered to have developed from the rheumatic type of endocarditis.

There was a history of rheumatic fever in eleven of this group of thirty patients. The mitral valve was involved alone in 18; the aortic alone in 4; mitral and aortic, 6; mitral, aortic and tricuspid, 3. In four hearts there were calcareous aortic nodules characteristic of Group 3. In seventeen hearts one or more valves were partly calcified.

Group 2. Thickened Valves Composed of Dense Fibrous Tissue; No Unhealed Areas

28 Cases (Table 7)

In this group the valves have the same gross appearance and microscopic structure as those of Group 1 except that there are no areas of incomplete healing. All signs of active inflammation are absent except occasionally a little perivascular lymphocytic infiltration in the central part of the leaflets. The leaflets are composed of dense fibrous tissue which is often hyaline in appearance. At the surface one frequently sees a thin hyaline layer that suggests the surface hyaline layer of a rheumatic vegetation (Fig. 29). The valves of this group usually show areas that correspond in structure

to the undoubted healed rheumatic lesions found in recurrent rheumatic endocarditis (Fig. 15). The histologic structure, therefore, offers strong support for the interpretation of these valves as healed rheumatic endocarditis. The clinical and gross pathologic features parallel the cases of Group 1 in which this interpretation seems amply justified.

There was a history of acute arthritis in thirteen of the twenty-nine cases of this group. The mitral valve was involved alone in 12; the aortic alone in 2; mitral and aortic in 10; mitral, aortic and tricuspid in 5. The calcareous aortic nodules characteristic of Group 3 were found in two hearts.

Group 3. Cases of Aortic Stenosis Due to Calcareous Nodules; No Satisfactory Evidence of Inflammatory Origin

15 Hearts (Table 8)

In the fifteen hearts of this group, ten were pure stenosis and in the other five stenosis predominated but there was some insufficiency. There is a very marked thickening and stiffening of the leaflets due to large calcareous nodules within them (Fig. 30). The portions of the leaflets between the nodules are of normal thickness. There is usually fusion of the adjacent edges of the leaflets where they are attached to the aorta. The nodules are found on the aortic surfaces of the leaflets but when very large they cause projections on the ventricular surfaces also. The most frequent site is near the aortic attachment but they usually extend well out into the leaflet, frequently to its free margin. In one instance a row of nodules extended about 2 cm. up the root of the aorta. In twelve of the fifteen hearts there were similar nodules in the central part of the ventricular surface of the aortic leaflet of the mitral and frequently there was a continuous row of nodules from the aortic leaflet to those on the mitral.

The root of the aorta is almost invariably free of arteriosclerotic lesions. The nodules are of whitish color, never yellowish. There seems to be no relation between these nodules and the atheromatous lesions so frequently seen on the valves.

The surface endothelium is usually intact over the nodules but occasionally it is denuded so that the calcareous material is ex-

TABLE 7

Old defective valves. Group 2. Complete healing

Number	Age, in years	Sex	Duration	Acute arthritis, time before death	Valves				Weight of heart, in grams	Old pericardial adhesions	Calcareous nodules	Aschoff bodies
					mitral	aortic	tricuspid	pulmonary				
16–212	27	M	14 yrs.	14 yrs., several attacks since	S_3	I. S.	–	–	700	+	–	+
17–139	33	F	15 yrs.	–	S. I.	–	–	–	525	–	–	–
18–67	22	M	7 mos.	10 yrs., 5 yrs.	S_3	S. I.	–	–	750	–	–	–
18–124	32	F	18 mos.	12 yrs., 9 yrs.	I_3	–	–	–	675	+	–	?
19–58	39	M	4 yrs.	–	S. I.	I_1	–	–	585	–	–	–
19–120	43	F	6 mos.	29 yrs., 16 yrs., 3 yrs.	S_3	S. I.	S. I.	–	600	–	–	–
19–145	16	F	7 yrs.	–	S. I.	S. I.	S. I.	–	400	–	–	–
20–452	32	M	3 yrs.	5 yrs., 4 yrs.	S_3	I. S.	I_1	–	500	+	–	–
20–459	40	F	8 yrs.	–	S. I.	I_1	I_1	–	410	–	–	–
21–205	22	F	?	?	o	I_3	–	–	490	–	–	+
21–478	38	M	2 mos.	3 yrs.	S. I.	S. I.	–	–	400	–	–	–
22–147	47	M	several years	?	S_3	S.I.	–	–	600	–	aortic, mitral	–
22–300	28	M	6 yrs.	?	S. I.	–	–	–	550	–	–	–
22–309	39	M	6 yrs.	–	S_3	–	–	–	510	–	–	–

22–354	68	M	2½ yrs.	–	I_3	0	–	–	645	+	–	–
22–365	51	M	10 yrs.	many attacks 25 yrs. to 3 yrs.	S_3	S_3	–	–	640	–	–	–
22–476	48	M	many years	?	S_3	–	–	–	550	–	–	–
22–480	27	M	5 yrs.	8 yrs, 5 yrs.	S_3	I_1	S. I.	–	550	–	–	–
23–101	43	M	3½ mos.	5 yrs.	I. S.	S. I.	–	–	550	+	–	+
23–135	48	F	5 mos.	date (?)	S_3	–	–	–	350	–	–	–
23–142	35	M	5 yrs.	5 yrs.	–	S_3	–	–	850	–	–	–
23–741	22	M	10 yrs.	–	–	I_3	–	–	1150	+	aortic	–
24–14	42	M	4 yrs.	22 yrs.	I. S.	I.S.	–	–	610	+	–	–
24–29	44	F	3 yrs.	28 yrs., 10 yrs.	S_3	–	–	–	500	–	–	–
25–389	45	F	2 yrs.	?	S_3	–	–	–	360	–	–	–
25–574	39	M	3 mos.	–	S. I.	–	–	–	600	–	–	–
25–655	21	F	2 yrs.	7 yrs., 6 yrs., 2 yrs.	I. S.	–	–	–	420	–	–	–
25–666	64	F	4 yrs.	?	I_1	I. S.	–	–	595	–	–	–

Legend: S = stenosis. I = insufficiency. S. I. = chiefly stenosis. I. S. = chiefly insufficiency. The degree of stenosis or insufficiency is indicated by the subnumbers 1, 2, 3.

posed. The position of the nodules in no way corresponds to the vegetations of active endocarditis. Mönckeberg [7] finds that they originate within the fibrous layer of the leaflets which is continuous with the wall of the aorta.

Microscopic Structure. The nodules consist chiefly of masses of calcium. When decalcified a homogeneous material remains. It has not been determined what kind of tissue calcifies. Surrounding the calcium there is usually some loose connective tissue, containing fat both within the cells and in the stroma, such as is found in atheromatous areas in the aorta. There are also areas of hyaline fibrous tissue. Often the adjacent tissue is very vascular and contains many mononuclear leucocytes, a reaction which may be interpreted as a change preliminary to the replacement of the calcium by bone. In one valve true cartilage and bone were found. A similar reaction is often seen in the calcified mitral leaflets of an ordinary mitral stenosis in which no calcified nodules are present.

Our material is not sufficient to enable us to trace the development of these aortic nodules. They were found in the aortic valves in twelve out of 100 adults dead of primary hypertension. Their incidence in other diseases has not been studied by us. Mönckeberg [7] believes that they begin as small calcified areas in the fibrous layer of the valve leaflet near the aortic attachment and gradually increase in size and number until an aortic stenosis may develop. He considers them entirely unrelated to inflammations of the valves.

These calcareous aortic nodules were found in four hearts of Group 1 and two hearts of Group 2 (see Tables 7 and 8), in fifteen out of fifty-four cases of subacute bacterial endocarditis and in three cases of recurrent rheumatic endocarditis. Whether they are the result of the inflammation in these valves or merely accidentally associated with it was not determined. It is to be noted that they were present in one person only 22 years old (23–741, Table 7).

Small calcified nodules are sometimes found in thickened leaflets at the site where vegetations occur. These seem not to be related to the aortic nodules just described, although they cannot be distinguished microscopically.

Calcareous nodules similar to those on the aortic valves are found occasionally on the ventricular surface of the marginal leaflet of the mitral at its attachment to the ventricle. These may occur independently of any other lesion in any valve.

TABLE 8

Old defective valves. Group 3. Calcified nodular type

Number	Sex	Age, in years	Duration	Acute arthritis, time before death	Valves				Weight of heart, in grams	Old pericardial adhesions	Calcareous nodules	Aschoff bodies
					mitral	aortic	tricuspid	pulmonary				
15–38	M	66	9 wks.	1 yr.	o	S. I.	–	–	600	–	aortic, mitral	–
18–38	F	70	1 hr.	?	o	S. I.	–	–	425	–	aortic, mitral	–
18–143	M	51	10 yrs.	21 yrs.	–	S_3	–	–	600	–	aortic	–
18–167	M	50	1 yr.+	?	o	S_3	–	–	780	–	aortic, mitral	–
19–93	M	40	2 mos.	–	o	S_3	–	–	760	–	aortic, mitral	+
19–213	M	68	3 wks.	–	–	S_3	–	–	650	–	aortic	–
21–49	M	59	2 yrs.	?	o	S. I.	–	–	795	–	aortic, mitral	–
21–433	M	71	1 yr.	–	o	S_3	–	–	475	–	aortic, mitral	–
22–99	M	50	?	?	o	S_3	–	–	560	–	aortic, mitral	–
23–112	M	56	7 yrs.	?	o	S. I.	–	–	575	–	aortic, mitral	+
23–236	M	70	20 yrs.	?	o	S_3	–	–	500	–	aortic, mitral	–
23–320	M	44	?	?	o	S_3	–	–	1130	–	aortic, mitral	+
25–82	M	64	2 yrs.	?	–	S. I.	–	–	725	+	aortic	–
25–104	M	38	2 yrs.+	–	o	S_3	–	–	575	–	aortic, mitral	–
25–586	M	66	1 yr.+	?	o	S_3	–	–	500	+	aortic, mitral	–

Legend: S = stenosis. I = insufficiency. S. I. = chiefly stenosis. I.S. = chiefly insufficiency. The degree of stenosis or insufficiency is indicated by the subnumbers 1, 2, 3.

The average age of the twenty-one cases with aortic nodules is 54.5 years. Excluding the three youngest cases the average is 58 years. Apparently this type of valvular disease usually does not produce symptoms until late in life.

Nineteen of the seventy-three hearts with old valvular defects that are listed in Tables 6, 7 and 8 were examples of aortic stenosis (chiefly or entirely stenosis) without involvement of any other valve, and it is to be noted that in seventeen of these the aortic defect was due to calcareous nodules. Aortic stenosis in the absence of involvement of any other valve is therefore usually due to calcareous nodules.

Discussion

The initial stages of acute endocarditis are not definitely known. It has not been recognized in the absence of vegetations. There is a diffuse inflammation throughout the part of the leaflet adjacent to the free margin in the earliest stages, but it is not known whether this precedes the vegetations or *vice versa*. The study of serial sections from early cases, however, gives one a strong impression that the inflammation begins within the leaflet and extends to the surface, resulting in a vegetation. When only a few vegetations are present they are almost invariably situated on the inner surface along the line where the leaflets come into contact, but when there are many they often cover both surfaces of the leaflet, especially near its free margin. It may be inferred, therefore, that the trauma of contact has some causal relation to the first vegetations but not to those that form subsequently. It is now known that normal valves are supplied with blood vessels (Bayne-Jones,[8] L. Gross,[9] Kerr[10]) and that it is therefore anatomically possible for bacterial emboli to lodge within the valves as was maintained by Köster,[11] Rosenow[12] and others. We have no new observations as to the route of the primary infection except the finding of numerous bacterial emboli in one valve (Fig. 16).

In five hearts with aortic bacterial lesions the only mitral vegetations were situated on the central part of the outer surface of the aortic leaflet. In these instances the mitral lesion probably resulted from contact with an infected aortic leaflet.

To understand the structure of old defective valves it is very im-

portant to note that in the acute stages the vegetation is not the only lesion but that there is a diffuse inflammation of the leaflet, always in its distal part and often extending well toward its attached margin (Figs. 1 and 12). This is the reason why an old defective valve leaflet is commonly thickened throughout, with the maximum involvement near the free margin.

Rheumatic vegetations are largely proliferative in character. There are some lymphocytes and occasionally a few polymorphonuclears, but most of the cells are fibroblasts. There is practically no necrosis or ulceration and there is no organization since there is almost no material to be replaced. Lymphocytes are numerous in the valve apart from the vegetations. Healing occurs readily and always results in thickening of the leaflet, since the fibroblasts form many new collagenous fibers. As in any healing inflammation the newly formed fibrous tissue contracts, compressing the blood vessels and forming scar tissue. In time the scar tissue becomes hyaline in structure and it frequently becomes calcified. The thin layer of hyaline material on the surface of fresh rheumatic vegetations can often be recognized in old defective valves long after all signs of active inflammation have disappeared (Fig. 29).

In recurrent rheumatic endocarditis there is either an activation of a latent infection or a reinfection. Fresh vegetations form on valves already thickened by a previous inflammation and fresh leaflets become involved. Each attack leaves the valves thicker and more rigid than they were previously.

It is only a short step from the recurrent rheumatic to the old defective valve. The inflammation subsides and the clinical picture changes from infection to valvular defect. There is often a striking gross resemblance between these two stages (Fig. 20), though they may be distinguished by the clinical history and microscopic structure. Partially or completely healed vegetations may be found (Figs. 25 and 26), and in the raw areas the remnants of rheumatic inflammation are readily recognized (Fig. 28). Twenty-seven of the old defective valves of Group 1 show incompletely healed lesions recognizable as rheumatic. When the valves are completely healed (Group 2) the evidence of a rheumatic origin is not so obvious; but they are strikingly similar in structure to known healed rheumatic lesions (*e.g.*, those of recurrent rheumatic endocarditis, *cf.* Fig. 15 with Fig. 29), and they are parallel in clinical and gross pathologic

features to Group 1. Fifty-five of the seventy-three old defective valves are interpreted as of rheumatic origin.

Bacterial lesions differ from rheumatic only in the intensity of the inflammatory reaction. There are no sharp distinctions. Exudation is more abundant, the fibroblasts are more numerous, thrombi form on the injured areas and there is often necrosis and ulceration. Healing processes are found almost constantly but complete healing rarely occurs. The leaflet becomes fibrous and hyaline in certain parts. The thrombus soon becomes homogeneous. Portions may become detached. It may persist indefinitely as a hyaline thrombus or it may become calcified. We have found no evidence that organization occurs to any appreciable extent. Only three of the seventy-three old defective valves are interpreted by us as healed bacterial lesions, but even these were not clinical examples of bacterial endocarditis.

Rheumatic vegetations were found in three-fourths of the hearts of subacute bacterial endocarditis, and numerous transitions between the two types of vegetations were seen. Unless the improbable assumption is made that three-fourths of the subacute bacterial cases have a simultaneous acute rheumatic infection, it must be granted that rheumatic and subacute bacterial endocarditis are caused by the same organism.

Glomerulonephritis was found in 38 of 64 cases of subacute bacterial endocarditis. The type of glomerulonephritis was embolic in 19, acute diffuse in 13, subacute or chronic diffuse in 3, and a combination of embolic and acute diffuse in 3. Diffuse glomerulonephritis as a complication of subacute bacterial endocarditis is about as frequent as the embolic form. Baehr and Lande [13] called attention to this relationship in 1920.

Aschoff bodies were found in the different forms of endocarditis as follows: acute rheumatic, 61 per cent; recurrent rheumatic, 55 per cent; acute bacterial, 0 per cent; subacute bacterial, 8 per cent; old valvular defects, 10 per cent.

The calcified nodular type of old valvular defect may originate entirely independently of an inflammatory process, as Mönckeberg believes; but its frequent association with known inflammatory lesions has not been satisfactorily explained. It is noteworthy also that Aschoff bodies were found in the myocardium in three cases of this group.

Summary

In addition to the vegetations in acute endocarditis there is a diffuse inflammation always in the free edge and often involving the greater part of the leaflet. This circumstance explains the uniform thickening so commonly seen in old defective valves.

Rheumatic vegetations are composed chiefly of fibroblasts, and in the process of healing they readily become converted into fibrous tissue. There is no ulceration and no organization. Fifty-five of seventy-three old defective valves are considered the result of rheumatic endocarditis, and in twenty-seven of these incompletely healed rheumatic lesions were recognizable.

Bacterial endocarditis is a more intense inflammation than the rheumatic. Proliferation predominates but exudation is often prominent. Large thrombi are formed on the raw surfaces and there is often ulceration. Healing consists in the conversion of the leaflet into scar tissue. Such portions of the thrombi as do not become detached persist indefinitely without becoming organized, although they may become calcified. Complete healing rarely occurs. Three of seventy-three old defective valves were interpreted as the result of bacterial endocarditis.

Transitions between rheumatic and bacterial vegetations are frequently seen. Rheumatic vegetations were found in association with bacterial in three-fourths of the cases of subacute bacterial endocarditis.

Fifteen of seventy-three old defective valves belong to the aortic calcified nodular group. The etiology of this type is unknown. There is no satisfactory evidence that it is of inflammatory origin, and it seems unrelated to atheroma. Aortic stenosis in the absence of disease of any other valve is usually of this form.

Stenosis is more frequent than insufficiency in old defective valves.

The only old pulmonary valve defects seen were of the congenital type (three cases of pulmonary stenosis).

An acute rheumatic endocarditis may terminate in several different ways: (*a*) death during the acute stage from toxemia; (*b*) partial or complete healing followed after a variable interval by the reappearance of fresh rheumatic vegetations (recurrent rheumatic endocarditis); (*c*) partial or complete healing followed by the forma-

tion of bacterial vegetations on the valves — a more active inflammation (subacute bacterial endocarditis); (*d*) slow incomplete healing giving rise to deformed leaflets on which rheumatic inflammation is still recognizable; (*e*) complete healing resulting in thickened, stiffened valves with smooth surfaces.

As to pathogenesis, 76 hearts with old valvular defects are interpreted as follows: 55 from rheumatic endocarditis, 3 from bacterial endocarditis, 15 (all aortic stenosis of the calcified nodular type) of undetermined origin and 3 (pulmonary stenosis) congenital.

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DESCRIPTION OF PLATES

PLATES 33–40

PLATE 33

FIG. 1. 25–171. Acute rheumatic endocarditis. Ridge of small, firm vegetations near the edge on the auricular surfaces. Opacity of the leaflet above with prominent blood vessels and small hemorrhages.

FIG. 2. 22–28. Recurrent rheumatic endocarditis. Thickened leaflets with a ridge of very small vegetations near the edge on the auricular surfaces.

FIG. 3. 10–92. Early rheumatic lesion — area between vegetations. Endothelium intact, many large fibroblasts, a few lymphocytes and polymorphonuclears.

FIG. 4. 22–595. Early rheumatic vegetations. Closely packed fibroblasts. Abundant hyalin in one, a little in the other. A few polymorphonuclears and lymphocytes. Endothelium partly detached.

PLATE 34

FIG. 5. 22–185. Rheumatic endocarditis. The multicentric character of the lesion is shown. Platelet thrombi have formed where the hyalin has broken through the endothelium. Under the vegetations there is a diffuse inflammatory reaction — many small fibroblasts and extensive perivascular lymphocytic infiltration.

FIG. 6. 22–185. Small vegetation composed largely of hyalin.

FIG. 7. 18–204. Recurrent rheumatic endocarditis. A typical well formed fresh vegetation. Surface hyaline layer. Edema. Many fibroblasts. Central capillaries. The valve underneath shows scarring from a previous attack.

FIG. 8. 10–92. Acute rheumatic endocarditis. Detail of surface vegetation. Surface hyaline layer. Zone of large fibroblasts. Serous exudate.

PLATE 35

FIG. 9. 25–163a. Acute rheumatic endocarditis. Diffuse intense involvement of marginal part of leaflet. Hyaline layer on both surfaces. Numerous large fibroblasts.

FIG. 10. 25–163a. Higher magnification of an area of Fig. 9.

FIG. 11. 22–185. Acute rheumatic endocarditis. Cross-section of a leaflet showing hyalin in the central portion.

FIG. 12. 22–185. Acute rheumatic endocarditis. Section of valve above the level of the vegetations showing a diffuse proliferative inflammation. Large numbers of small fibroblasts. Prominent blood vessels. Some lymphocytes.

PLATE 36

FIG. 13. 25–631. Recurrent rheumatic endocarditis. Active vegetations on a thickened scarred valve. There is a little cellular exudate in the scar tissue underlying the vegetation.

FIG. 14. 24–364. Acute rheumatic endocarditis. Vegetation in stage of healing. Scar tissue with retrogressive changes in fibroblasts. Homogeneous hyaline layer at surface.

FIG. 15. 17–227. Recurrent rheumatic endocarditis. Healed vegetation. The surface hyaline layer of the vegetation blends with the hyaline fibrous tissue.

FIG. 16. 17–28. Subacute bacterial endocarditis. Bacterial emboli in capillaries surrounded by a zone of polymorphonuclears (embolic abscess).

PLATE 37

FIG. 17. 18–102. Subacute bacterial endocarditis. Proliferative inflammation within the valve. Large fresh soft thrombus with extensive deposits of calcium in its deeper part.

FIG. 18. 21–513. Subacute bacterial endocarditis. Proliferative inflammation. Large closely packed fibroblasts (some multinucleated). Very few collagenous fibers.

FIG. 19. 13–180. Subacute bacterial endocarditis; stage of healing. Hyaline thrombus; no organization. Valve largely converted into scar tissue.

PLATE 38

FIG. 20. 25–328. Old valvular defect with incomplete healing. Ridge of vegetations near the margin of the thickened leaflet. See Fig. 21 for microscopic structure.

FIG. 21. 25–328. Section through the ridge of vegetations shown in Fig. 20. Dense scar tissue underneath an old hyaline thrombus. Very little evidence of organization. This may represent a healed bacterial lesion.

FIG. 22. 16–185. Old valvular defect with incomplete healing. Large ulcers covered by thrombus. Small denuded areas near the free margin. See Fig. 23.

FIG. 23. Section of the large ulcer shown in Fig. 22. Hyaline thrombus; very little organization. Many leucocytes within the valve. Healing bacterial lesion.

PLATE 39

FIG. 24. 15–324. Old valvular defect with incomplete healing. Denuded areas on the thickened leaflets.

FIG. 25. 11–121. Old valvular defect with incomplete healing. Rheumatic vegetation with a dense connective tissue core. The surface hyaline layer is easily seen.

FIG. 26. 25–328. Section of a healed vegetation composed of scar tissue. The superficial hyalin is visible on the left side. No organization.

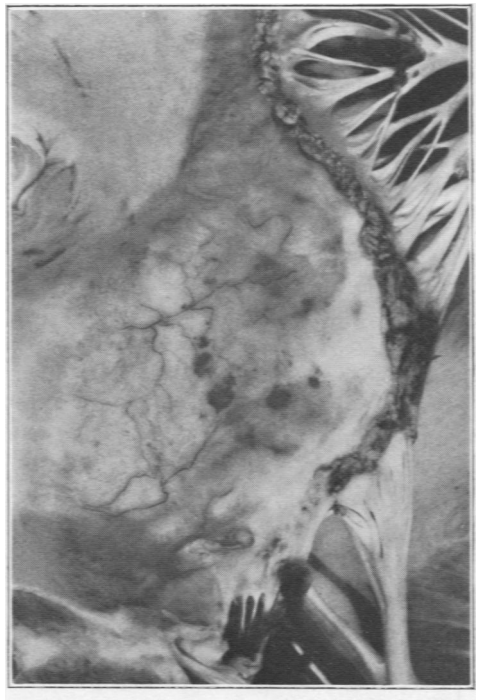
FIG. 27. 25–322. Old valvular defect with incomplete healing. Section through a raw area showing a thin layer of thrombus overlying dense fibrous tissue.

PLATE 40

FIG. 28. 20–250. Old valvular defect with incomplete healing. Old hyaline thrombus resting on hyaline scar tissue.

FIG. 29. 23–101. Old valvular defect with complete healing. Dense fibrous tissue in which a few capillaries are visible. A thin layer of hyalin at the surface suggesting the surface hyaline layer of a rheumatic vegetation.

FIG. 30. 25–82. Old valvular defect, calcified nodular type (Group 3). Aortic valve seen from above.



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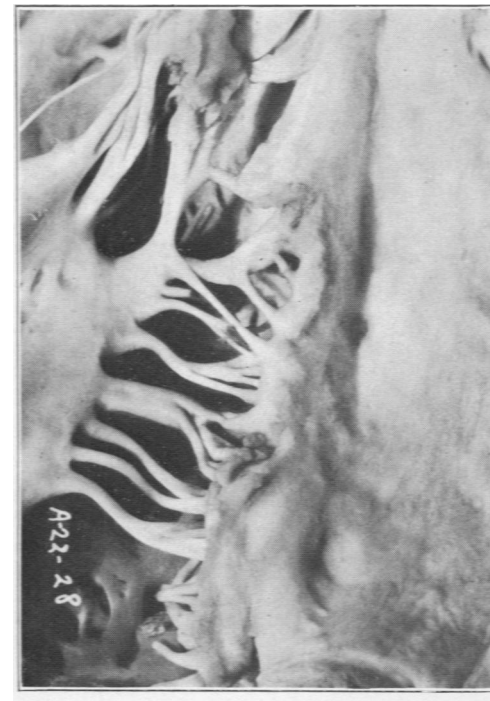

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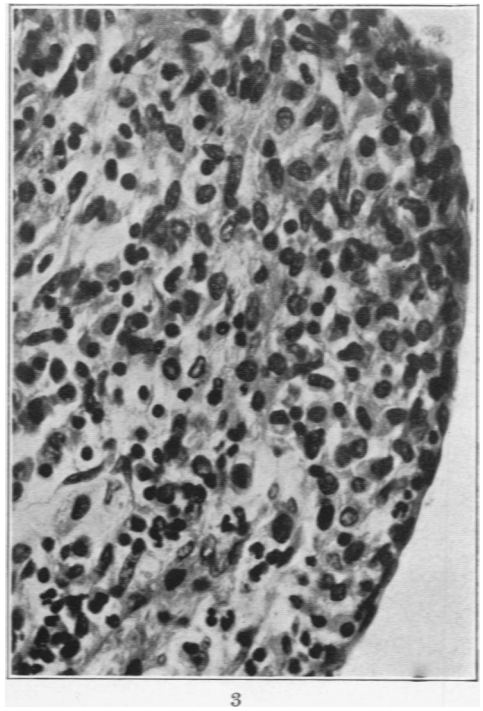

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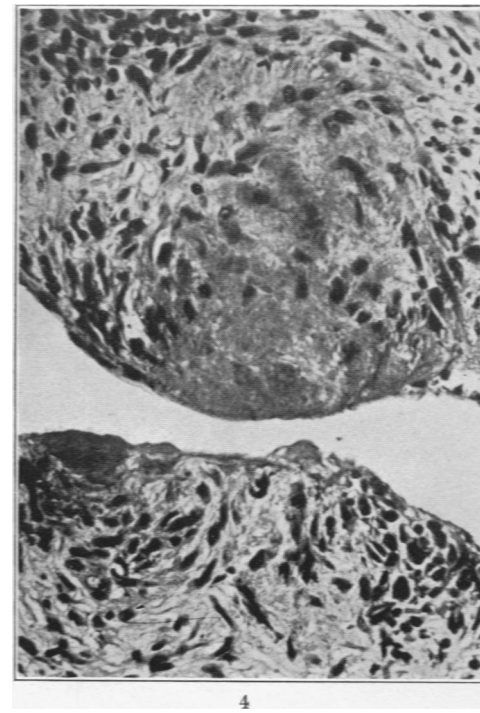

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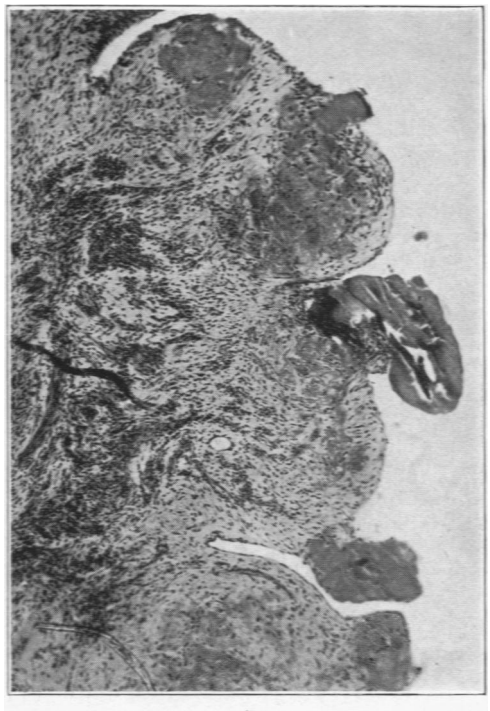
Clawson, Bell and Hartzell

Valvular Diseases of the Heart



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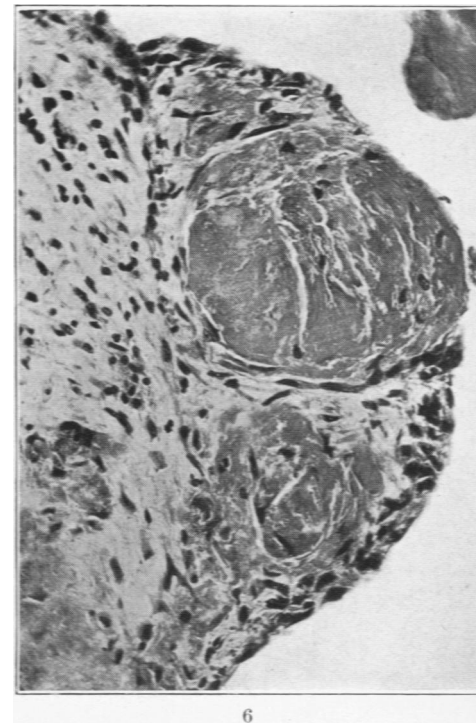

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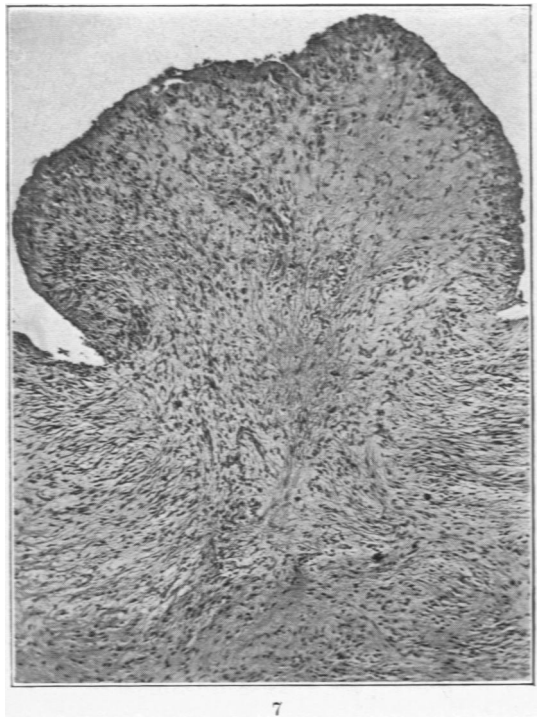

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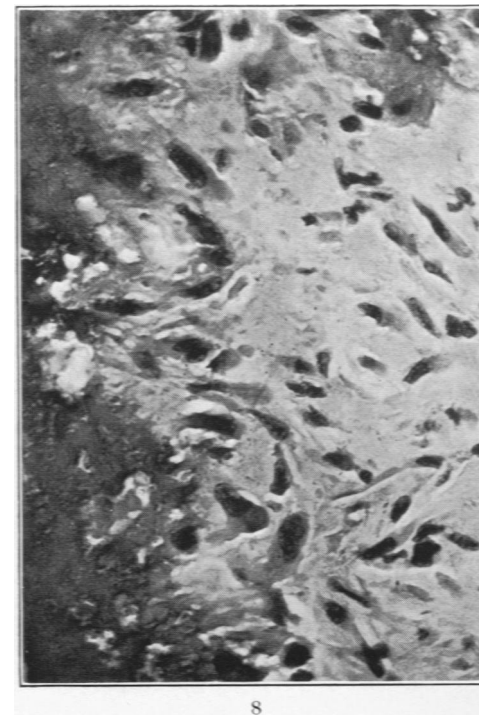

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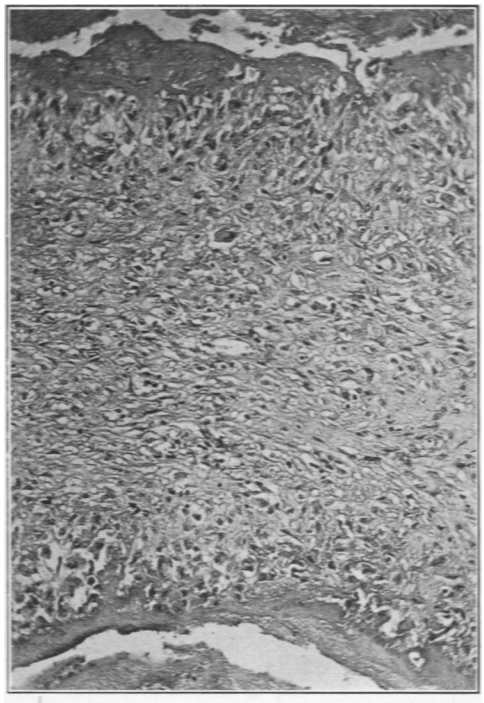
Clawson, Bell and Hartzell

Valvular Diseases of the Heart



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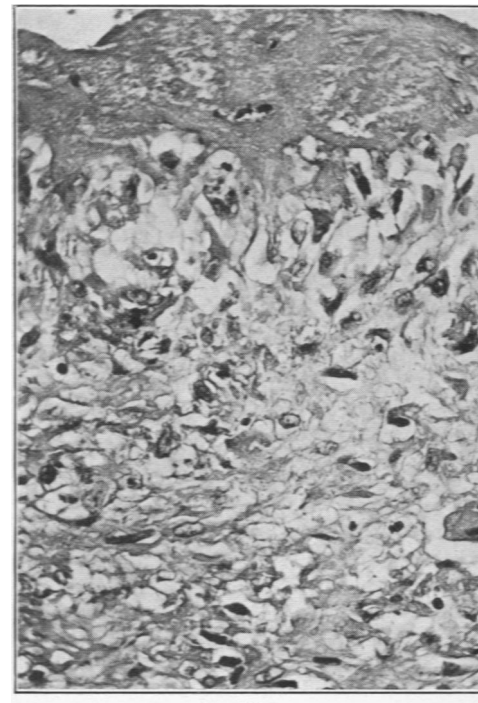

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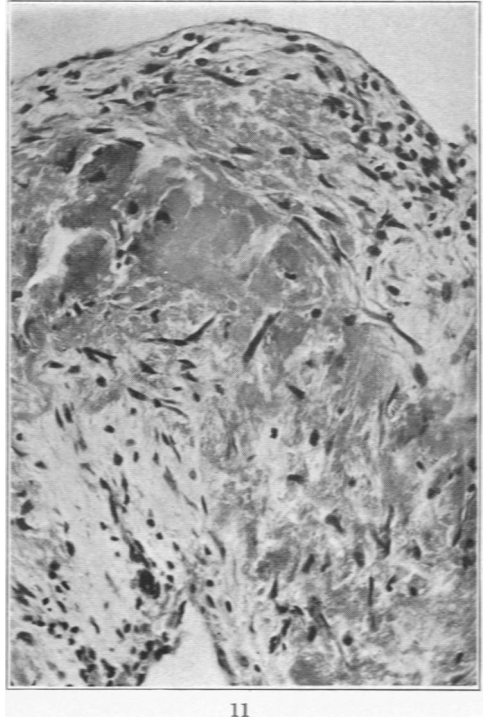

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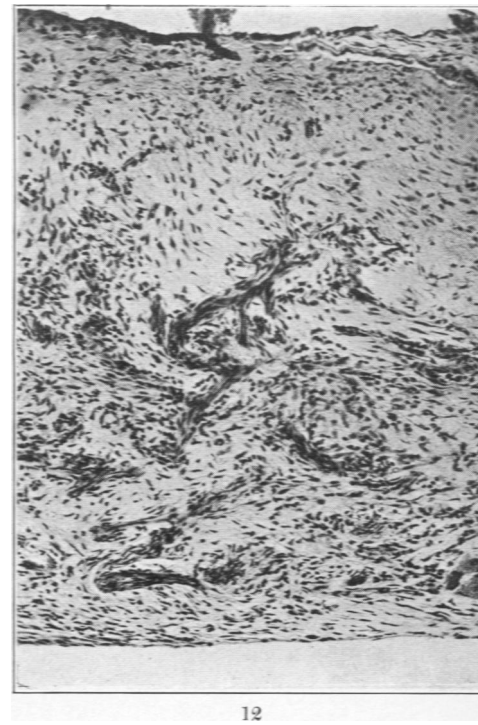

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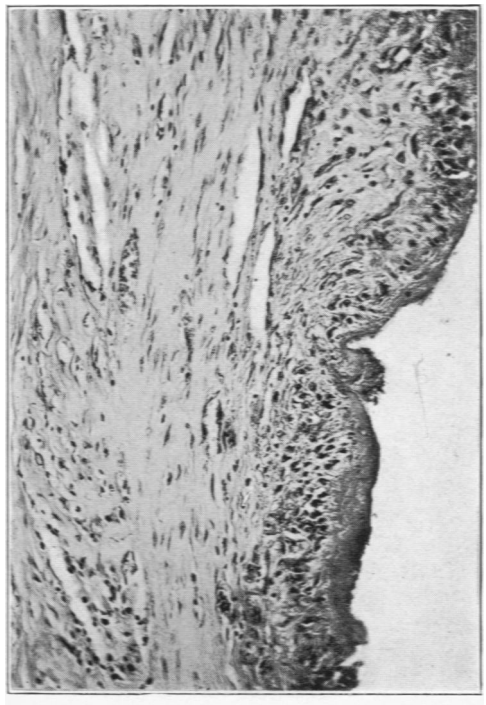
Clawson, Bell and Hartzell Valvular Diseases of the Heart



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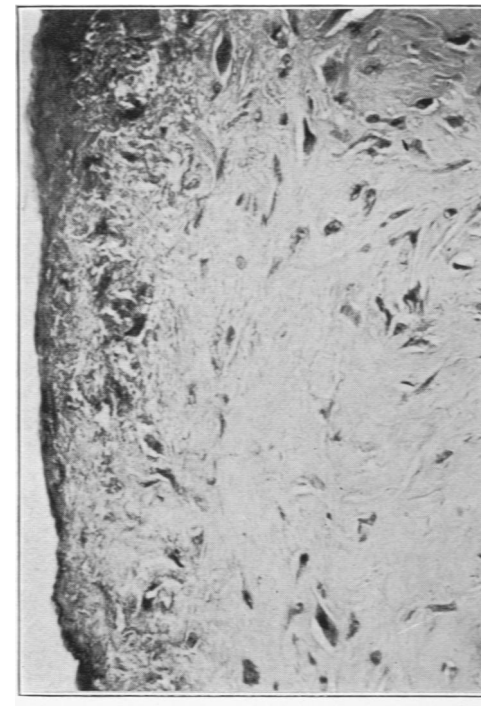

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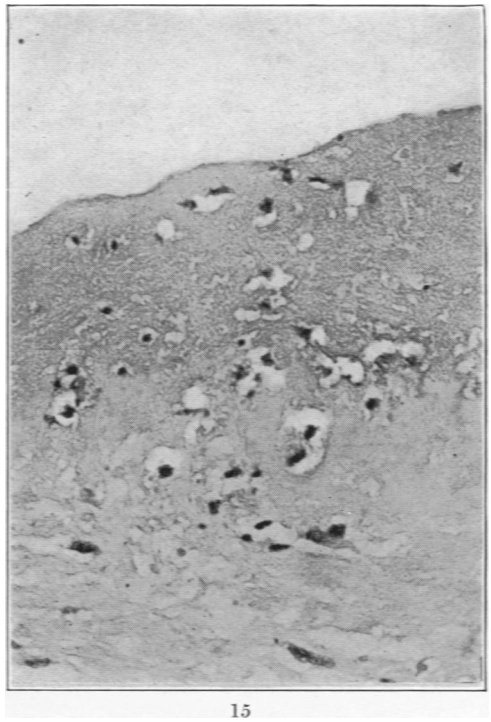

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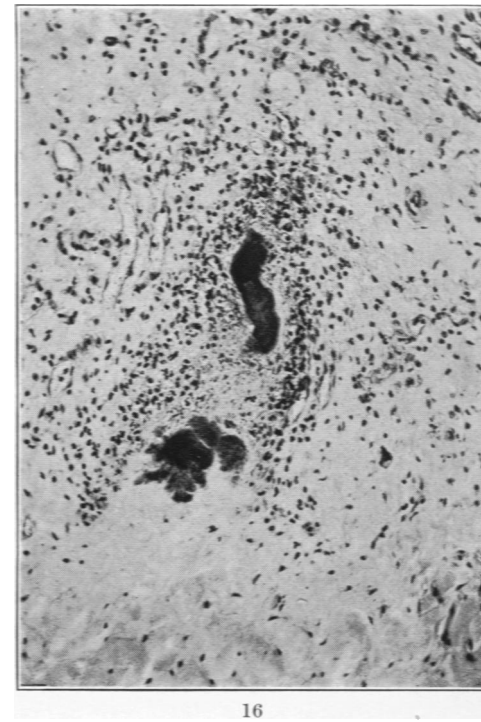

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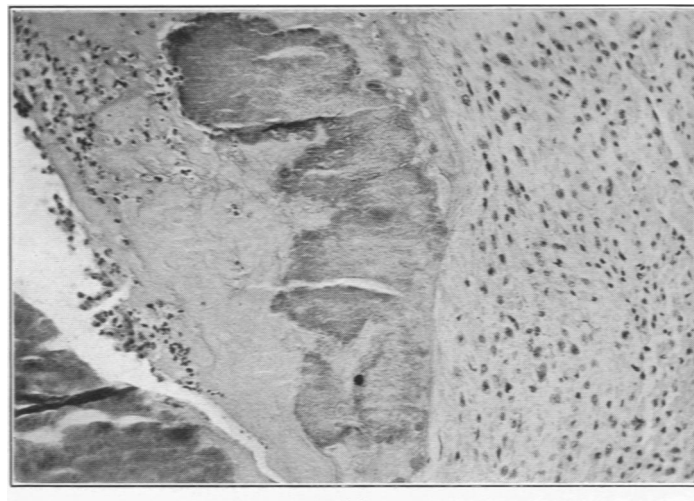

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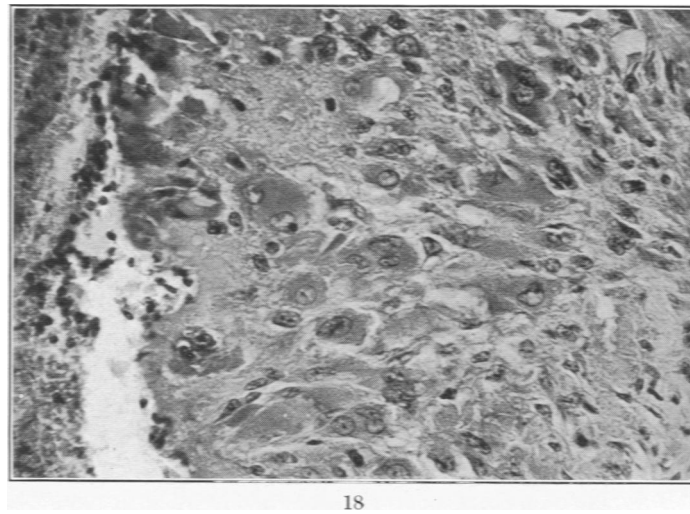

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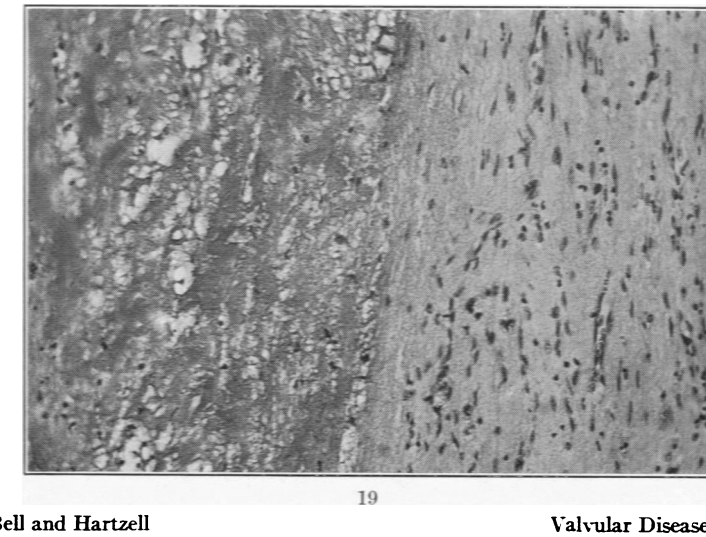

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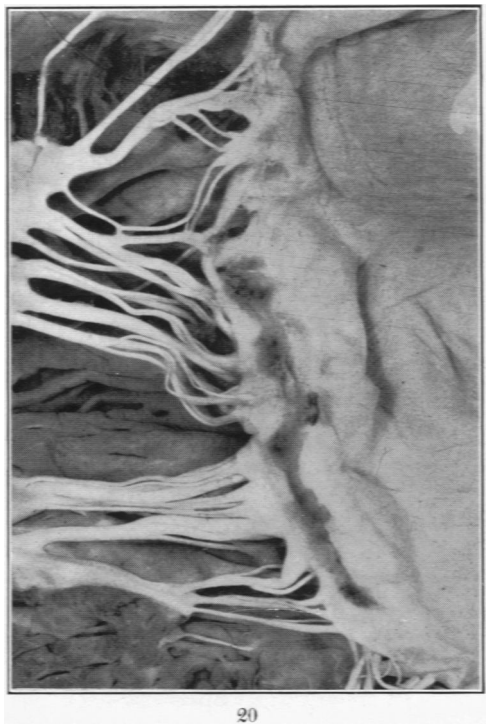

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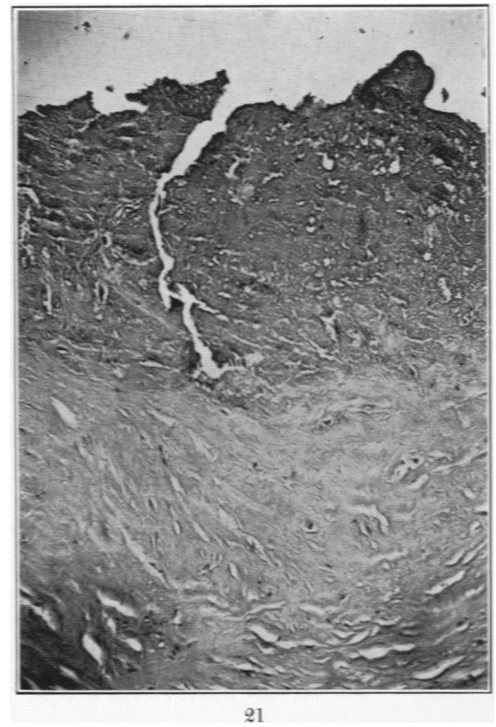

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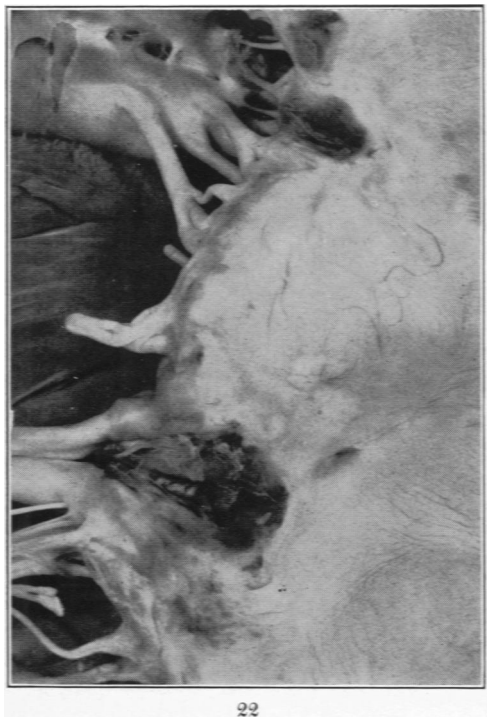

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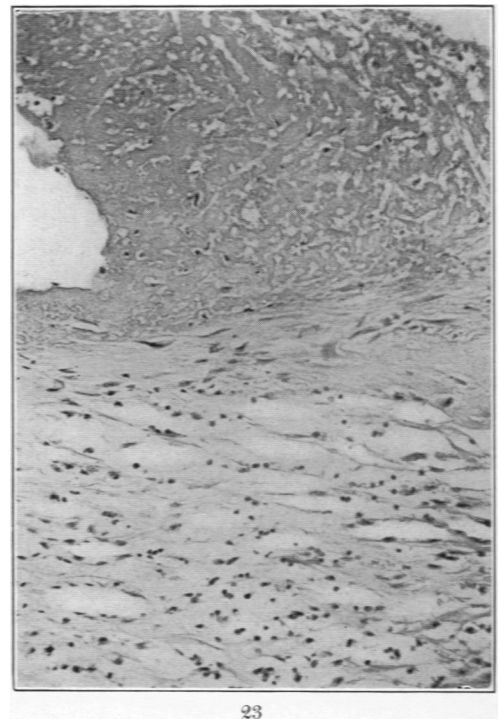

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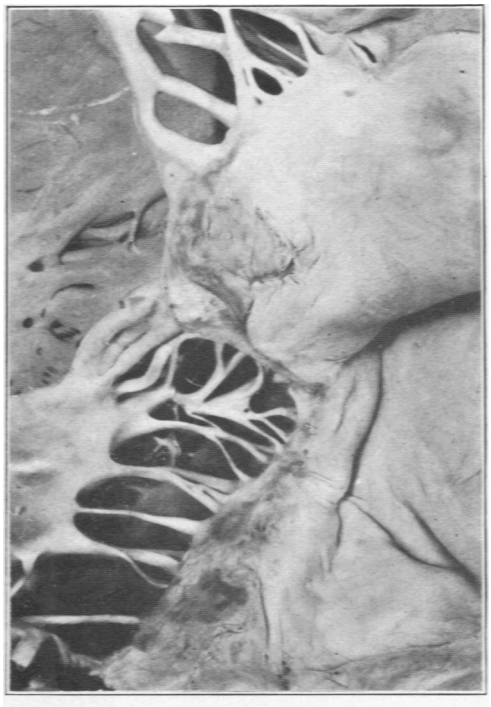
Clawson, Bell and Hartzell

Valvular Diseases of the Heart



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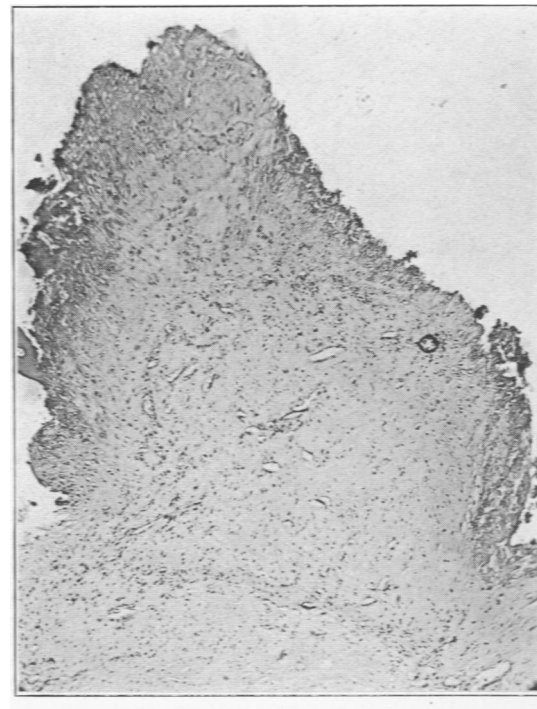

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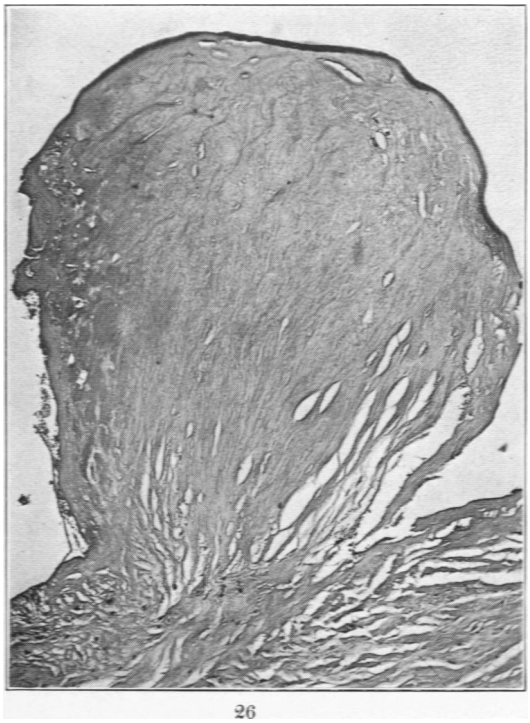

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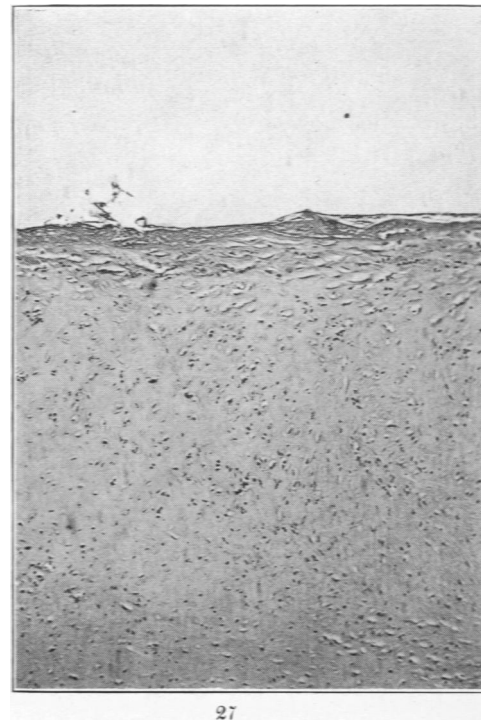

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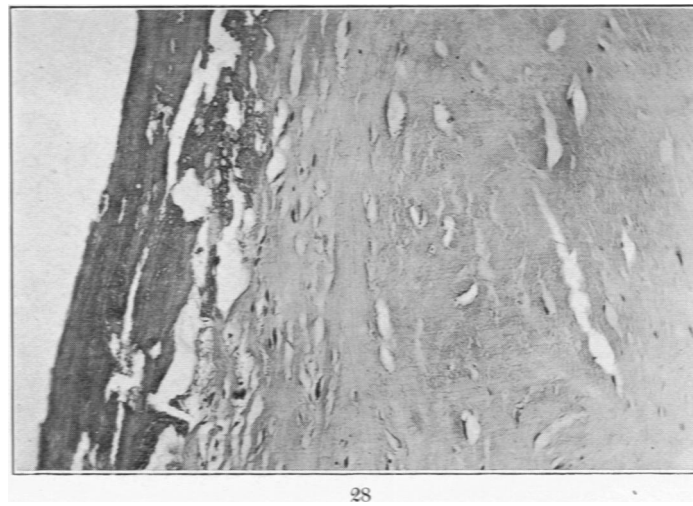
Clawson, Bell and Hartzell

Valvular Diseases of the Heart



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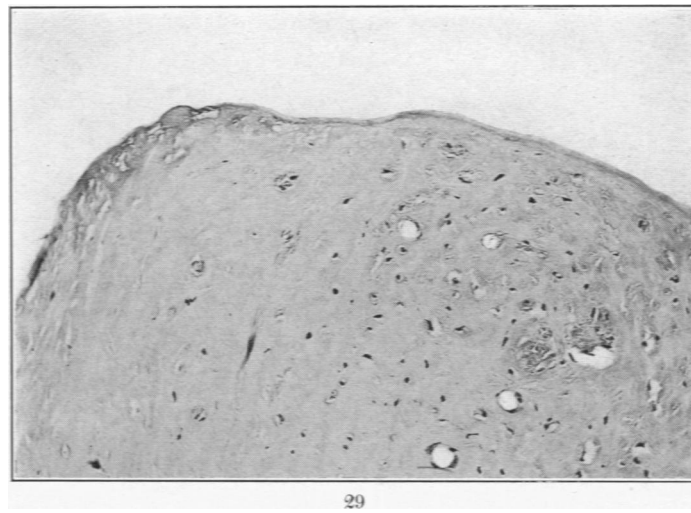

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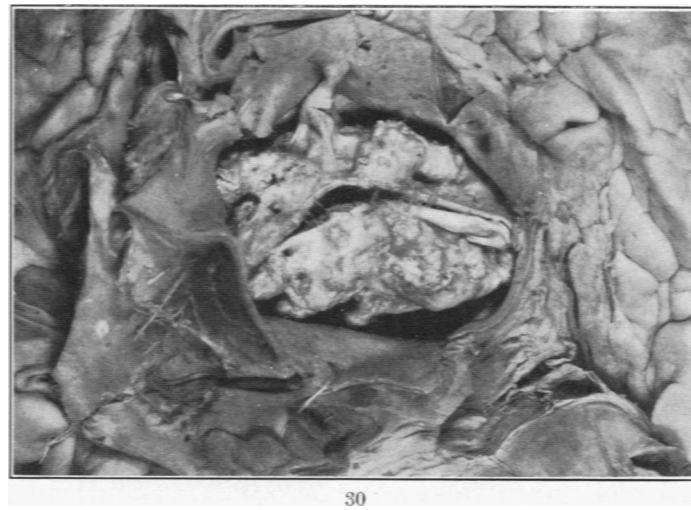

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