# RHEUMATIC ACTIVITY IN AURICULAR APPENDAGES REMOVED AT MITRAL VALVOPLASTY *

R. M. Clark, M.D., and W. Anderson, M.D.
*From the Department of Pathology, University of Toronto and Toronto General Hospital, Toronto, Ont.*

Seventy-eight auricular appendages from patients with progressive cardiac failure presumably of rheumatic origin were available from valvoplasty procedures performed by Dr. W. Bigelow, of the Department of Surgery, Toronto General Hospital. Since the most recent operation in this particular group was carried out at least 18 months ago, sufficient time has elapsed to report on the incidence of recrudescence, and on any relationship which might exist between the reappearance of clinical rheumatic fever and the extent and nature of the auricular lesions encountered. Although a voluminous literature is rapidly accumulating on the subject of rheumatic activity in auricular appendages, the relatively high incidence of myocardial granulomas and a peculiar basophilic alteration of the connective tissues of both myocardium and endocardium have not hitherto been emphasized.

## Material

Included in the material were routine surgical sections from 78 left auricular appendages, together with the appendages from 25 necropsies on non-rheumatic subjects of the same age group. The patient age varied from 17 to 53 years, the average being 35.8 years. The control appendages showed no changes other than varying degrees of thickening of the endocardium.

Incidental to the study of the heart material were 29 specimens of lung taken for biopsy. They were examined for parenchymal and vascular changes which might indicate chronic pulmonary hypertension. Fourteen showed slight to moderate degrees of fibrous thickening of alveolar walls, while in another 4 cases the changes were fairly marked. Medial hypertrophy and/or fibrosis was present in small arteries and arterioles in approximately one half of the specimens of lung. Some showed evidence of intimal fibrosis as well. In only 2 cases were vascular changes present without evidence of fibrotic changes in the parenchyma. Larrabee, Parker, and Edwards[1] reported a series of 20 cases in which vascular changes were present in 75 per cent. Heart lesion cells were present in 21 cases, sometimes in considerable numbers.

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## Lesions of Auricular Appendages

The auricular lesions included endocardial and myocardial granulomas, basophilia of connective tissues, fibrosis, and cellular infiltration. Recent and old intra-auricular thrombi were present frequently.

Granulomatous lesions were encountered in both endocardium and

Table I

*Incidence and Severity of Lesions in 78 Auricular Appendages*

| | Granulomas | | | | Basophilic degeneration | | | | Cellular infiltration | | | | Fibrosis | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Endocardial | | Myocardial | | Endocardial | | Myocardial | | Endocardial | | Myocardial | | Endocardial | | Myocardial | |
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| Mild | 31 | 39.7 | 6 | 7.7 | 29 | 37.2 | 19 | 24.4 | 34 | 43.6 | 14 | 17.9 | 25 | 32.1 | 7 | 8.9 |
| Moderate | 5 | 6.4 | 1 | 1.3 | 6 | 7.7 | 4 | 5.1 | 1 | 1.3 | 1 | 1.3 | 3 | 3.9 | 0 | .0 |
| Severe | 3 | 3.9 | 0 | .0 | 6 | 7.7 | 3 | 3.9 | 0 | .0 | 0 | .0 | 0 | .0 | 0 | .0 |
| Total | 39 | 50 | 7 | 9 | 41 | 52.6 | 26 | 33.4 | 35 | 44.9 | 15 | 19.2 | 28 | 36.0 | 7 | 8.9 |

myocardium (Table I). They varied in shape from round to elliptic, and their site of predilection was between myocardium and endocardium, or in the deeper layers of the latter. They were occasionally so numerous as to form an almost continuous band (Fig. 1). The relatively small number found in myocardium (Fig. 2) had usually a perivascular distribution. The lesions were largely characteristic Aschoff nodules (Figs. 3 and 4), with a central nidus of fragmented, swollen, collagen fibers. Within the loose connective tissue were numerous large, darkly staining, mononuclear and multinucleated Aschoff cells, often of bizarre shape and with pale or dark nuclei. Small numbers of round cells and very occasional polymorphonuclear leukocytes and plasma cells were present in the lesions. Other lesions were devoid of multinucleated Aschoff cells, and contained numerous, fairly large, elongated, mononuclear cells with dark cytoplasm and nucleus. Some of the older lesions did not show fibrinoid or basophilic change, and contained only a few compressed fibers throughout their length. In a few cases, areas of rather dense acellular connective tissue, having a somewhat concentric appearance, may have represented healed lesions. The collagen fibers in and around the granulomatous foci frequently showed a basophilic tinctorial change, and the latter was found also throughout the connective tissues uninvolved by granulomas. Fibrinoid change was most marked in relation to the Aschoff lesions, although occasional collagen fibers in the deep layers of endocardium showed similar alteration.

Basophilic degeneration of connective tissue was the most common finding. The myocardial interstitial connective tissue and endocardium

were involved, sometimes extensively. This altered tissue stained metachromatically with toluidine blue. The fibers occasionally were swollen, or thin and frayed. The muscle fibers often were more widely separated than usual, due to abundant loose basophilic connective tissue (Fig. 6). The basophilic alteration frequently occurred independently of either Aschoff granulomas or fibrinoid degeneration. Fibrous endocardial thickening was common and tended to be irregular in distribution. The control material showed a fairly wide variation in this respect and it was difficult to assess minor degrees of endocardial thickening. Lymphocytic infiltration often was observed in endocardium and myocardium, and occasionally was accompanied by small numbers of polymorphonuclear leukocytes and plasma cells. The cellular infiltration usually was associated with granulomas, intra-auricular thrombi, or endocardial thickening.

Only 10 of the 78 appendages did not show one or more of the lesions, although this is not indicated in Table I. The changes were graded as mild, moderate, or severe. Sections containing only one or two granulomas were listed as showing mild changes, those with eight or ten or more, as severe, the intermediate grade being grouped as moderate.

Evidence of old intra-auricular thrombosis (Figs. 5 and 7) was present in 25.6 per cent of cases and of recent thrombosis in 20.5 per cent. Of these, 3 cases, or 3.9 per cent, showed both recent and old thrombi.

Myocardial granulomas never were present without endocardial granulomas, and in only one case was myocardial basophilic change present without similar degeneration in the endocardium. The incidence of endocardial Aschoff lesions (50 per cent) approximated fairly closely the figure of 45.3 per cent reported by Decker *et al.*[2] and by McNeely *et al.*[3] in a series of 183 cases. These authors reported no truly myocardial lesions, although these were present in a perivascular distribution in 9 per cent of the series here reported. Enticknap[4] reported granulomas in 41 per cent of a series of 71 cases and McKeown[5] found them in 45 per cent of 53 biopsies. However, Janton *et al.*[6] found an incidence of only 13 per cent in 88 cases.

## Interrelationship of Lesions

The most common change was basophilic degeneration of connective tissue. This was present without accompanying granulomas in 19 cases (24.4 per cent). Conversely, in 16 cases (20.5 per cent), Aschoff lesions were present without basophilic change outside the granulomas. The two were associated in 23 cases (29.5 per cent). The Aschoff

lesions were found with endocardial or myocardial fibrosis in 16 cases, although in only 2 of these was fibrosis found alone with granulomas. In 12 cases, the latter were associated with thrombi.

Basophilic degeneration accompanied fibrosis in 15 cases, and the latter change was associated with thrombi in 16 cases. The degeneration was present with recent or old thrombi in 16 cases, and in some instances the connective tissue in organized thrombi showed the same basophilic change as that in the appendage.

## Clinical Correlation

In none of the cases was there clinical evidence of rheumatic activity preoperatively, using such criteria as increased white blood cell count, increased blood sedimentation rate, and temperature elevation.

Sixty-nine per cent of the cases in the series were female, and Aschoff lesions were found in 50 per cent of these, and in 42 per cent of the males. The likelihood of finding granulomatous lesions, that is, a positive biopsy, was found to vary inversely with the patient age. Twenty-one patients aged 30 years and under were included, and, of these, 76.2 per cent had positive biopsies, whereas only 40.4 per cent of those over 30 had such lesions. The presence of auricular fibrillation preoperatively bore no relationship to the incidence of Aschoff lesions. Only 3 (14.3 per cent) of the patients less than 30 years of age were fibrillating, and, of these, one had a positive biopsy, while 29 (50.9 per cent) of those over 30 years were fibrillating, and only 4 of these had positive biopsies.

Thrombi, recent and/or old, were found in 33 cases (42.3 per cent) and 28 of these patients were fibrillating either preoperatively (22 cases) or postoperatively (6 cases). As noted, 32 had auricular fibrillation.

Table II

*Postoperative Clinical Results Compared with Incidence of Positive Auricular Findings*

| Results | No. of cases | Per cent with positive biopsy |
|---|---|---|
| Excellent | 37 | 46.0 |
| Good | 16 | 44.0 |
| Fair | 11 | 36.5 |
| Unchanged | 8 | 50.0 |
| Died | 6 | 66.0 |

Patients with granulomatous lesions appeared to do as well postoperatively as the remainder (Table II).

Postoperatively, 8 cases developed clinical evidence of rheumatic activity. In the majority of these patients the recrudescence occurred within 2 months of operation. Of these, 5 had positive biopsy findings. In one of the 3 re-

maining cases, no changes of any kind were noted in the auricular appendage. In a ninth case, questionable clinical signs of activity appeared, but, here too, the biopsy specimen was negative.

## Discussion

The most frequent finding was the basophilic alteration in connective tissues. This change could be demonstrated well with toluidine blue, the altered tissue staining pink or violet.

The tissue basophilia is not specific, and may be seen in myxedema, in degenerating fibrocartilage, and in the vessels in hypertension. The metachromasia is considered to be due to the presence of certain sulfated mucopolysaccharides. Taylor[7] reported the accumulation of this metachromatic substance in areas of medial degeneration associated with aortic atherosclerosis, and stated that it was intimately and constantly associated with fragmentation of the elastic fibers. In about half the cases of rheumatic infection, basophilia of the media of arterioles is said to occur. In the present study, the basophilia was found associated with granulomas in 23 cases (29.5 per cent), but the change was seen in the absence of granulomas in 19 cases (24.4 per cent), and the question arises as to whether the basophilia may be related to the increased tension and stress on the auricular wall consequent to mitral stenosis, or to continued rheumatic activity.

The possibility that the basophilia of connective tissues in the surgical material might be attributable to the manipulations necessary for its removal has been entertained. That this is probably not so is suggested by the finding of similar changes in auricular appendages from known cases of rheumatic fever at necropsy.

Two possibilities are suggested by the fact that granulomas were encountered more frequently in the younger age group. First, the rheumatic process, although sub-clinical, may be continuously active. Alternatively, the presence of lesions could be explained by recrudescences becoming less frequent with advancing age. According to the clinical histories, rheumatic fever was present in some of these cases from 6 to 41 years before operation. Of the 8 cases developing clinical activity postoperatively, 5 had granulomatous lesions at biopsy. This is not significantly greater than the incidence of these lesions in the entire series.

The frequency with which pathologic changes were present in the lungs appears to be of some practical importance. Vascular changes and fibrotic changes in the alveolar walls, although variable in degree,

doubtless are permanent. It is difficult to conceive of their resolution even after marked alteration in pulmonary hemodynamics following valvoplasty.

## SUMMARY

Portions of 78 auricular appendages, obtained in the course of mitral valvoplasty, were examined microscopically. In only 10 of them were lesions completely absent. Histologic evidence of rheumatic activity in the form of Aschoff nodules was found in 50 per cent of the cases, sometimes many years after the initial attack and in the absence of signs of clinical activity. These lesions were almost twice as frequent in patients under 31 years of age than in the remainder of the series. The change observed most frequently was basophilic connective tissue degeneration, which was present in 54 per cent of cases. The other lesions encountered included cellular infiltration in endocardium and myocardium in 51 per cent, fibrosis in 40 per cent, and intra-auricular thrombi in 42 per cent. Thrombi were most frequently found in association with auricular fibrillation, but no correlation could be found between Aschoff lesions and arrhythmias. The presence of Aschoff lesions and postoperative course could not be correlated.

In an incidental study, about one half of 29 specimens of lung taken for biopsy were found to show changes indicative of chronic pulmonary hypertension.

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[ *Illustrations follow* ]

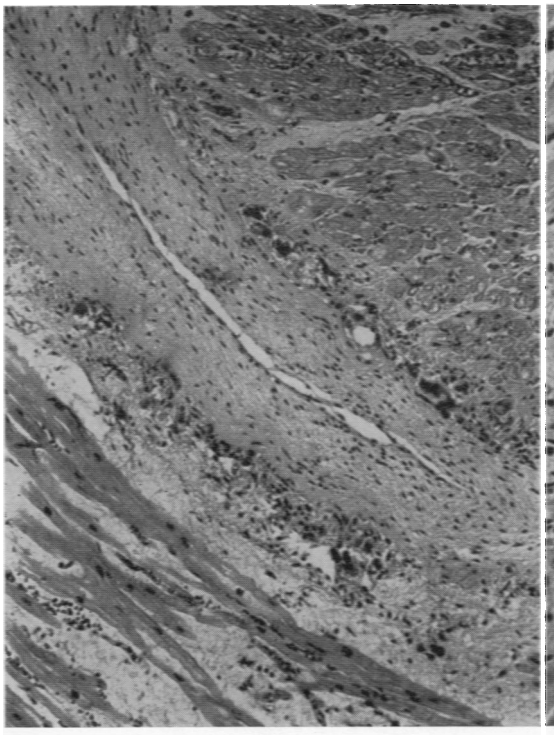
## LEGENDS FOR FIGURES

FIG. 1. Subendocardial granulomas in a continuous band. Hematoxylin and eosin stain. × 81.

FIG. 2. Myocardial lesion consisting of a group of Aschoff nodules. Hematoxylin and eosin stain. × 154.

FIG. 3. Details of granulomatous lesions. Hematoxylin and eosin stain. × 308.

FIG. 4. Details of granulomatous lesions. Hematoxylin and eosin stain. × 308.



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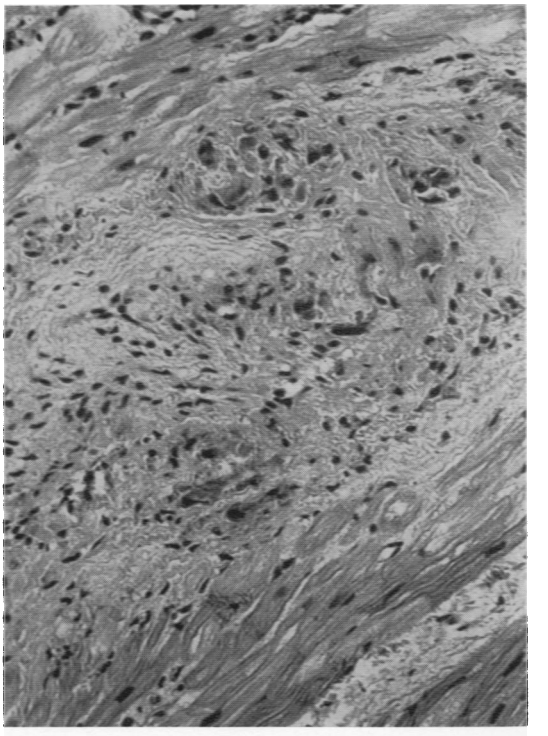

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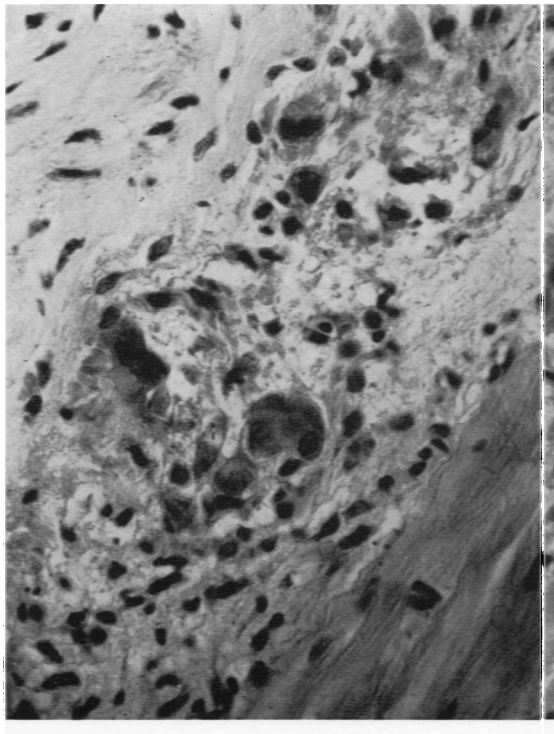

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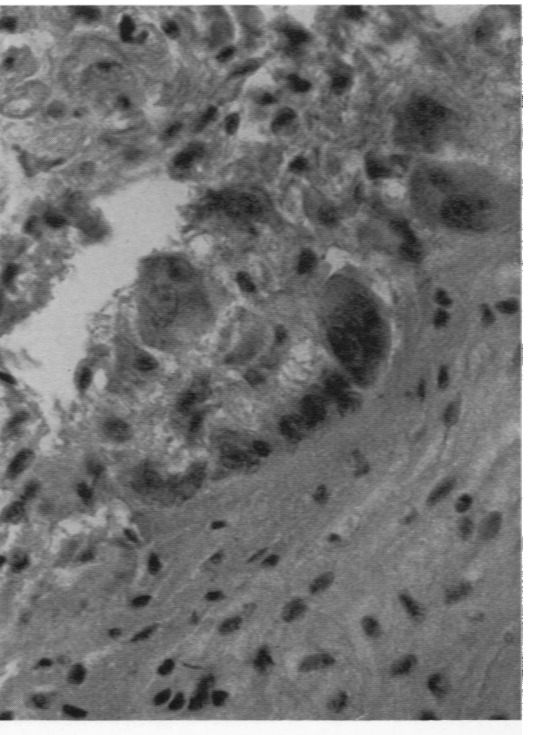

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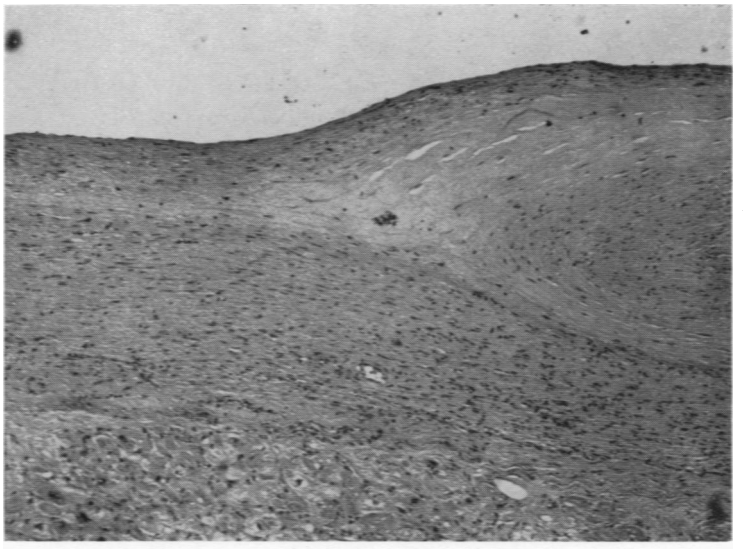
FIG. 5. Organized auricular mural thrombi. Hematoxylin and eosin stain. × 40.

FIG. 6. Separation of muscle fibers by swollen connective tissue. Hematoxylin and eosin stain. × 230.

FIG. 7. Organized auricular mural thrombi, with canalization. Hematoxylin and eosin stain. × 40.



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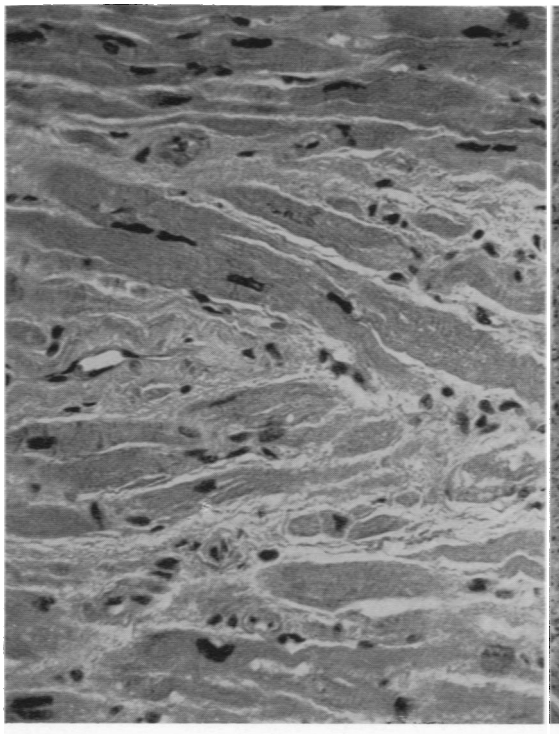

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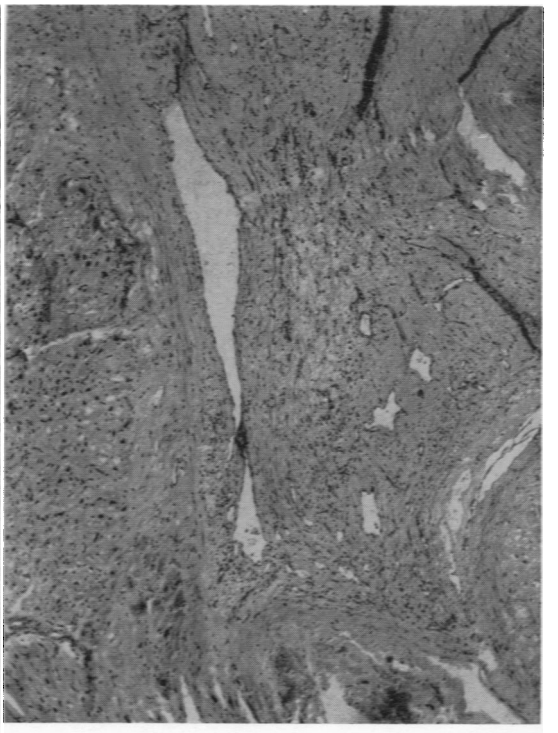

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