INTERATRIAL SEPTAL DEFECT WITH MITRAL INSUFFICIENCY OF CONGENITAL ORIGIN

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MORTALITY due to uncomplicated congenital defects of the heart is comparatively infrequent. Cabot's analysis of 1,906 cardiac autopsies shows only seven cases of congenital defects, of which two were clinically recognized and in only one was the death solely due to the cardiac anomaly. Among the congenital cardiac disorders Muir and Brown (1934) consider that interventricular septal defects are the commonest. Varying grades of persistent foramen ovale appear also to be not infrequent. Seib (1934) observed patency of the foramen ovale in 17 per cent of all autopsies of his series. Roesler (1934) however was able to collect only sixty-two cases of interatrial septal defects, measuring one centimetre or more in diameter, from the literature of the last hundred years. Thus large interatrial septal defects appear to be sufficiently rare to warrant the reporting of the following case, which, besides the septal defect, showed other congenital valvular abnormalities :—

V. K., male, aged 20 years, was admitted into the King George Hospital on 2nd March, 1934, for extreme dyspnœa. Three months before admission, he first noticed breathlessness on slightest exertion. For one month he has been confined to bed, unable to lie on either side. On admission he showed normal development, moderate nourishment, ascitic distension of the abdomen, œdema of the lower extremities, distended veins in the left side of the neck, but no appreciable cyanosis, anæmia or clubbing of the fingers. The left side of the chest showed well-marked bulging and a diffuse pulsation in the 5th interspace, palpable as far out as the anterior axillary line. It was dull on percussion in the front below the level of the second rib, but resonant over the back. The left cardiac boundary extended to the posterior axillary line in the 6th intercostal space. Thrills were absent. The resonance on the right side was impaired about the level of the 6th interspace. Auscultation revealed a systolic murmur heard in all areas and conducted to the axilla in the mitral area. An inconstant presystolic murmur was also sometimes recognizable. The pulse (80 per minute) was of low tension and irregularly irregular. The breathing was bronchial and hurried (respiration—48 per minute). The breath sounds were suppressed on the right side about the level of the 6th intercostal space. A few rhonchi and crepitations were heard over the left base. Spleen and liver could not be palpated on account of the ascites. Death supervened on the succeeding day before radiological and electrocardiographic investigations could be undertaken. A provisional diagnosis of a decompensated double mitral lesion of the heart was entered.

Autopsy disclosed the following findings:—

Cardiac findings.—The heart was globular in shape, massive in size and weighed 26 ounces. *In situ,* the organ lay more on the left side of the middle line than on the right, though the right side of the heart showed remarkable hypertrophy and dilatation, the right ventricle forming nearly its entire front and apex. A few patches of epicardial fibrosis were observed on the anterior surface of the right atrium. All chambers showed well-marked dilatation and hypertrophy—the right chambers more than those of the left. Though the right ventricular cavity had a maximum transverse circumference equal to that of the left ventricle (15 cm.), the former had a much longer axis, since it curved round the apex of the latter. Besides, the pulmonary conus was enormously dilated, the circumference of its cavity being 10.5 cm. The walls of both ventricles measured 1 cm. in thickness. The maximum circumference of the right atrial cavity was 17.2 cm. while that of the left chamber was only 11.0 cm. The right atrial wall showed hypertrophy and fasciculation more marked than that of the left, the maximum thickness being about 0.5 cm. The interatrial septum showed a large oval defect, 4 by 3 cm., with a sharp fibrous margin in its anterior and lower part. A fibrous ledge, about 1 cm. wide, separated the a.-v. ring from the inferior margin of this defect. There was no evidence of a foramen ovale in the dorsal part of the septum. The atrioventricular orifices were of normal size. The valves of these orifices showed a varying degree of fibrosis. The posterior cusp of the mitral valve showed more marked sclerosis than the others, was abnormally short (maximum width 1.2 cm.), curled downwards and had a somewhat rounded verrucose margin with short yet moderately thin chordae tendineae (plate XXVI, figure 1). The anterior cusp, though somewhat opaque white and fibrous, was normal in size (maximum width 3.5 cm.) and appearance. No adhesions were present between the margin of the two cusps or between the chordae tendineae. The tricuspid valves had each a maximum width of 2 cm. The aorta was hypoplastic, lumen measuring only 5.7 cm. in circumference one inch above the ring. The valves were normal. The pulmonary orifice was much dilated, measuring 8.6 cm. in

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satisfactory improvement (7 of them have become fit within 10 to 23 days), but others are not responding as satisfactorily. To compare the efficacy of different drugs, I treated different sores with different things—phenol, copper sulphate, normal saline, etc.,—but my general impression is that the action of cod-liver oil is quicker than that of the other remedies.

(8) Four cases of otorrhœa (one complicated with mastoid abscess, which had to be operated on) were all cured within a very short time.

Another case of otorrhœa of both the ears, as a complication of typhoid fever, was satisfactorily cured by cod-liver oil drops.

(9) One case of badly lacerated wound of the hand, caused by a crushing machine, was treated with cod-liver oil, and it healed up without suppuration.

The remainder of my cases were ulcers and septic wounds on various parts of the body.

The peculiarities I have noticed about cod-liver oil treatment of wounds were—

(*i*) Checking of formation of pus in fresh wounds, and quickly clearing away of pus in already septic wounds.

(*ii*) Rapid formation of granulations, which often became exuberant.

[*Note.*—This is essentially an account of clinical results without controls; unfortunately the exigencies of practice and the necessity of curing cases as rapidly as possible rarely allow of controlled observations under such conditions.—EDITOR, *I. M. G.*]

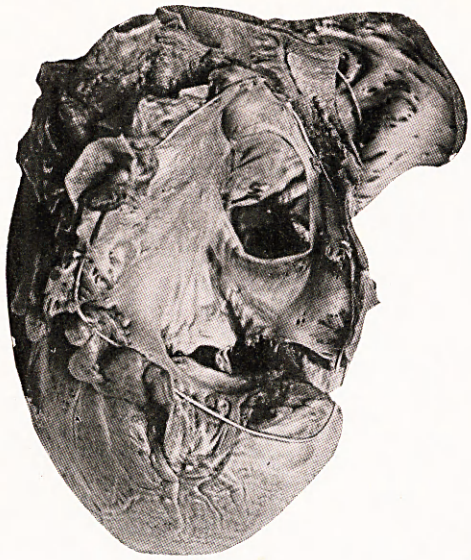

Fig. 1.

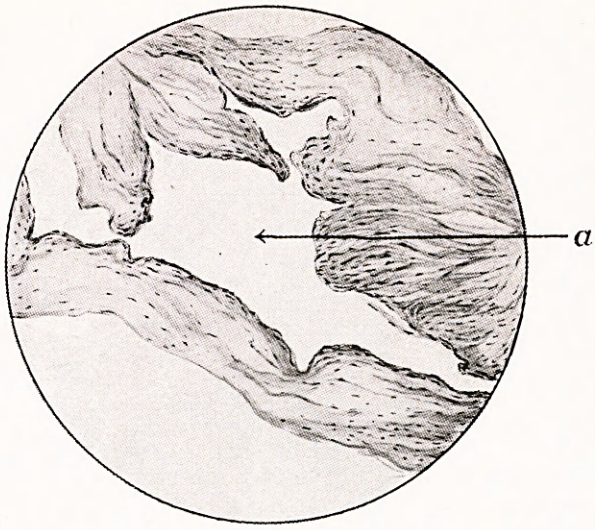

Fig. 4.

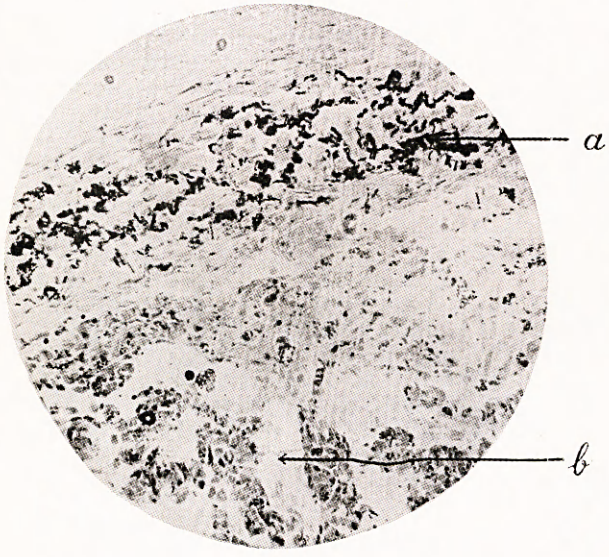

Fig. 2.

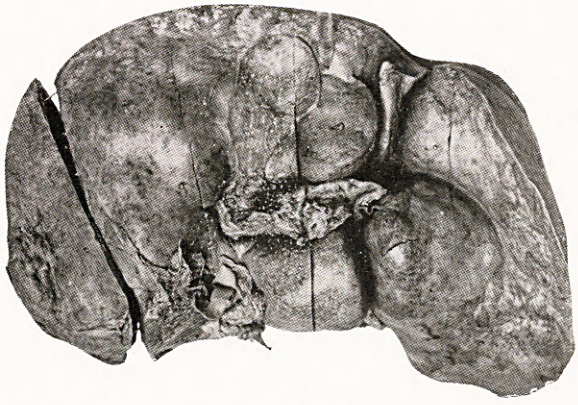

Fig. 5.

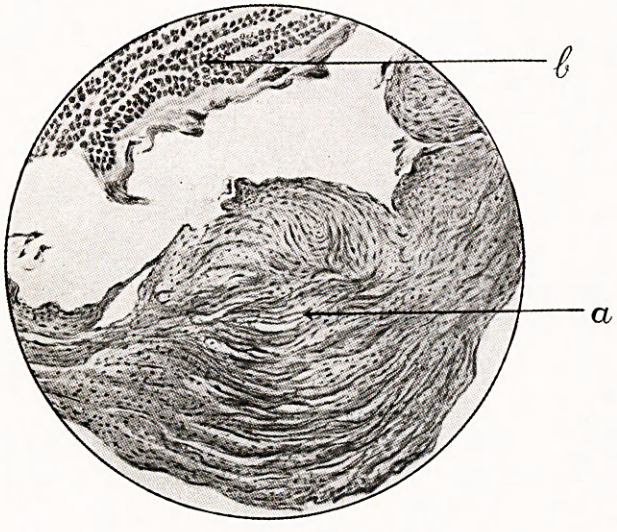

Fig. 3.

Fig. 1.—Photograph of the heart showing the large interatrial septal defect.

Fig. 2.—Photomicrograph of the right atrial wall showing—
(*a*) the cluster of calcifying fibroblasts in the thickened subendocardial connective tissue.
(*b*) œdematous distension of the interstitial lymph spaces in the myocardium.
(E. Leitz apochromat. objective 8 mm. periplanat. Eye-piece 4 mm.)

Fig. 3.—Drawn from a low-power photomicrograph of a section of the septal cusp of the mitral valve—
(*a*) nodular fibrous swelling a little above the margin of the valve.
(*b*) myocardium.
(E. Leitz achromat. objective 22 mm. periplanat. Eye-piece 4 mm.)

Fig. 4.—Drawn from a photomicrograph of the central portion of one of the thickened tricuspid valves—
(*a*) a dilated tortuous lymphatic.
(E. Leitz apochromat. objective 8 mm. periplanat. Eye-piece 4 mm.)

Fig. 5.—Photograph of the liver showing the cardiac type of cirrhosis.

circumference. The pulmonary artery and its main branches were also markedly dilated. The lumen of the artery measured 7 cm. and that of its left branch 6.3 cm. in circumference and the intima was free from atheromatous change. The cusps of the pulmonary orifice were unequal in size, the posterior cusp being larger in size than either of the two anterior cusps. The right branch appeared to arise at a slightly higher level from the main artery than the left branch. The opening of the coronary sinus was also much dilated and measured about 1 cm. in diameter. The myocardium was firm, friable and like bacon in appearance.

Microscopically there was no evidence of active inflammation in any part of the heart except the left atrial epicardium where a few scattered round cells were seen. The myocardium showed general cloudy swelling, patchy fatty degeneration of the muscle fibres (particularly under the endocardium), passive congestion of the vessels and œdematous distension of the interstitial spaces. Hypertrophic stretching of myocardial fibres with flattening of their nuclei was best seen in the right atrial myocardium, where also the interstitial œdema was most pronounced. The mural endocardium of both atria showed subendocardial loose œdematous sclerosis, particularly marked near the valvular rings. A few clusters of shrunken calcifying fibroblasts with hyaline swelling of the interstitial collagen fibres were present in the subendocardial fibrous tissue of the right atrium (plate XXVI, figure 2). The a.-v. valves and their rings showed a considerable degree of non-deforming loose sclerosis. Both the auricular and ventricular layers of the valves showed swelling, which appeared to be more the result of a non-inflammatory œdematous infiltration of the collagenous and elastic fibres than a proliferative fibrosis of inflammatory origin. The tip of the posterior cusp of the mitral valve showed a well-marked nodular swelling of its auricular layer (plate XXVI, figure 3). Dilated lymphatic vessels were observed in the region of the valvular rings and in the centre of the thickened valves (plate XXVI, figure 4). Both the valves and their rings were completely free from any inflammatory infiltration.

Other findings.—Generalized œdema, flat chest with precordial bulging, clear fluid in all serous cavities, congestion and ulceration of left faucial tonsil, congestion and hyperplasia of the lingual tonsil, congestion and enlargement of the tracheo-bronchial lymph glands, passive congestion of all viscera, a tuberculous scar with a caseous centre in the upper lobe of the left lung. Slight enlargement of the spleen (12 oz.) and well-marked nodular chronic congestive cirrhosis of the liver (plate XXVI, figure 5) were also present.

[*Note.*—The measurements given above were taken from the formalin-fixed specimen.]

DISCUSSION

Nature of the lesion.—In the case under report, the large defect in the anterior and inferior part of the interatrial septum, which did not reach down to the radix of the inter-ventricular septum, in the absence of any evidence of the development of a foramen ovale in the upper and dorsal part of the septum is evidently a result of incomplete union between the septum superius and septum intermedium, as in the third class of defects noted in Costa's classification. Clinically the case comes under the 'cyanose tardive' group of congenital cardiac defects mentioned by Abbot.

Pathogenesis.—The genesis of septal defects has been often traced to an increased tension in the left auricle owing to either a congenital mitral stenosis or hypoplastic aorta. In this instance the aortic hypoplasia was inconsequential and, instead of a mitral stenosis, the imperfect development and degenerative sclerosis of the septal cusp had actually led to a certain degree of incompetency of the mitral orifice. In a similar case reported by Roesler (1934), the septal defect has been considered by him as probably the result of a primary agenesis independent of valvular lesion. In this case the defective development of the septal cusp of the mitral valve and the inequality in the size of the semilunar cusp of the pulmonary valve are to be regarded only as additional independent congenital deformities. Markham and also Abbot have pointed out the invariable or frequent presence of such deformities in other parts of the heart along with interatrial septal defects.

Age.—Though the majority of Cabot's series of congenital cardiac defectives died young (7 to 30 years), instances of comparatively large interatrial communications when combined with mitral stenosis, permitting active and useful life to a fairly advanced age, are not rare. Firket's case lived 74 years. Lutembacher's case lived 61 years and Abbot and Kaufmann's case 64 years. But the few cases on record, of atrial septal defects combined with mitral incompetence, appear to have terminated early, as in our case. Roesler's case survived only 14 years.

Effects of the defect.—The occurrence in these cases of a left to right shunt of the blood through the defect has been thoroughly discussed by Roesler (1934) in his exhaustive review of the subject. This shunt occurs irrespective of the presence or absence of the mitral lesions (Gibson and Roos, 1935). The anatomical changes in the heart resulting from this shunt were well illustrated in the case reported above. The globular outline, the hypertrophy and dilatation of the right atrium and ventricle—the heart apex being formed by the latter—the dilatation of the pulmonary conus and artery and the comparative hypoplasia of the aorta, all reflect the equalization of the pressure in the two sides of the heart, and the increase in the output of the right side with a corresponding diminution in that of the left side brought on by the shunt. Peacock has pointed out the excess of dilatation over the hypertrophy in the right side, in instances of large patency of the foramen ovale. Measurements in our case showed an enquality in the myocardial thickness in the walls of the two ventricles. Enlargement of the left atrium had also been noted in Reosler's case of septal defects associated with mitral insufficiency and, as in our case, was evidently the result of a systolic regurgitation into it through the incompetent mitral orifice. To the latter may also be attributed, the systolic murmur conducted to the axilla seen in our case.

Specific murmurs.—Systolic murmurs best heard over the 3rd interspace (Abbot), inconstant presystolic, early systolic or late diastolic murmurs of varying rhythm, localized at

the 4th left interspace have been described in instances of patent foramen ovale or septal defects. These with a weak aortic or strong pulmonary sound are also said to be characteristic. But the first-mentioned finding has been noted also in interventricular septal defects by Muir and Brown and the belief that interatrial septal defects can exist without giving rise to murmurs has many adherents. Potain contended that murmurs when present in cases of septal defects are always of extraneous origin. Roesler suggested that systolic murmurs extending into diastole or early diastolic murmurs are more likely to arise only in instances of smaller interatrial openings. Even this has been denied by Miller (1936). As the case under report came under observation only in the terminal stages of decompensation, the findings in this case offer no answer to the question of existence or otherwise of murmurs specific to septal defects.

Cyanosis.—In large interatrial septal defects cyanosis fails to appear until almost the end. On the other hand, cyanosis has been stressed (Miller 1936) as diagnostic of patency of the foramen ovale. This is easily understood when it is remembered that in the latter the valve-like action of the imperfectly-developed septum secundum, which permits only a one-way right-to-left flow whenever the right atrial pressure rises above that of the left atrium, is absent in the former. In large interatrial septal defects cyanosis sets in only as a terminal manifestation of a failing compensation and increasing right atrial pressure. The failure of even this terminal cyanosis in Cramer and Prommel's case of septal defect with mitral stenosis was attributed to an earlier onset of right atrial asystole. In our case, besides the onset of fibrillation of the right atrium, the systolic regurgitation into the left atrium might have tended to prevent the terminal reversal of the shunt, by keeping up the pressure inside the left atrium. The systolic venous pulse of mitral regurgitation is however abolished in cases of interatrial communication when the over-full right atrium begins to fibrillate. The pulsatory phenomena, such as systolic lower central precordial propulsion, systolic epigastric and aortic pulsation and thrill, usually mentioned as present in interatrial septal defects, apparently disappear as in this case in the final stage of decompensation.

Endocardial sclerosis.—The degenerative non-deforming sub-endocardial sclerosis in the atria and auriculo-ventricular valves and even the nodular thickening of the margins of the septal cusp of the mitral valve appear to have resulted from the increased stress and strain in the atria, aggravated by the subendocardial œdema due to coronary venous congestion. It is interesting to note that the loose fibrous swelling of the subendocardial connective tissue was maximum near the auriculo-ventricular rings and progressively diminished further away from this area. Shoval and Gross have recently explained the non-deforming sclerosis of the valves and endocardium as the result of an individual predisposition to collagen involution, lipoid and calcareous deposition, aggravated by increased stress and strain. The incidence of varying degrees of a non-deforming sclerosis of the auriculo-ventricular valves and atrial endocardium is not at all rare in our autopsy material. The absence of Aschoff's nodes, vegetations, adhesions between margins of the cusps or chordae tendineae in this instance, discounts the changes of an inflammatory origin of the subendocardial fibrosis. Abbott has emphasized this rarity of subacute endocardial lesions, either at the defect or in the valves in cases of interatrial defects, unlike interventricular septal defects. Roesler as well as Gibson and Roos, however, come to the conclusion that the prognosis in interatrial septal defects is not materially altered by the presence or absence of an endocarditis. The terminal auricular fibrillation in these instances must be presumed to be of non-rheumatic origin.

Cause of the decompensation.—In interatrial septal defects the lesion is stationary, but the demand on the output of the heart due to growth and increased activity is progressive. Eventually a stage is reached, of an 'acquired progressive hydraulic disturbance', when the already overloaded right side of the heart fails with the usual signs of a right heart failure.

Summary

A case of large interatrial septal defect, with mitral insufficiency due to a disgenetic hypoplasia of the septal cusp, with the following characteristic findings is reported :—

(1) Evidence of a long-standing left to right shunt in the circulation—even in the absence of a stenosis of the mitral valve—such as the remarkable hypertrophy and dilatation of the right side of the heart including the pulmonary conus and artery;

(2) concomitant developmental inequality in the size of the cusps of the pulmonary and mitral valves and consequent mitral incompetency, systolic murmur, hypertrophy and dilatation of the left ventricle;

(3) hypoplasia of the aorta;

(4) terminal fibrillation of the right auricle which also showed the maximum histological evidence of strain and exhaustion, such as myocardial hypertrophy and œdema;

(5) chronic congestive cirrhosis of the liver apparently due to the increase in the pressure in the right atrium as a result of the shunt;

(6) comparative soundness of the pulmonary circulation till the end, as shown by the total absence of a delayed cyanosis usually seen in such cases, a quiescent healing tuberculous focus in the left lung, and by the absence of any atheromatous change in the pulmonary vessels;

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A COLOUR CHART FOR THE DETERMINATION OF HYDROGEN-ION CONCENTRATION

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THE study and the control of hydrogen-ion concentration is of fundamental importance in many branches of research work and is of great value in industrial processes, where minute changes in the reaction may have considerable effect on the quality of certain products. With the introduction of modern colorimetric methods the determination of pH value has become a routine procedure in many laboratories and because of the comparative ease with which the estimations can be made the actual determination is frequently carried out by laboratory assistants or technicians. It is only when exact determinations are required that electrometric methods must be employed and the advice of an experienced physical chemist sought. The colorimetric methods are invaluable when a large number of estimations has to be made and only approximations are needed, for example, in the preparation of media for bacteriological or other work.

In the colorimetric methods discs are commonly used, which show the change of colour of indicators between certain pH values. Individual investigators are familiar with the range of colour at given pH values of the reagents they use in their particular work, but in every laboratory there are circumstances when it becomes necessary to determine the pH values at a range different from the one at which the worker is familiar, and this necessitates the selection of other indicators. Although there are many textbooks in which long lists of indicators are tabulated, the selection of a suitable indicator is somewhat difficult except for experienced chemists. The colour chart in that excellent textbook by Clark (1928) shows the shades of colour of certain sulphonphthalein indicators at differences of 0.2 pH values. The range is from a pH of 1.2 to 9.6 with a gap from 2.8 to 3.1.

In order to overcome difficulties in the ready selection of indicators for general purposes we have chosen thirteen indicators for which standard coloured discs (as, for example, the Hellige Comparator) are available. These indicators cover a range from 0.2 to 12.8 and are so arranged in the chart that a ready selection of an indicator for a particular pH range can be made. The colours at given pH values of a 'universal' or mixed indicator have also been shown in the chart but no attempt has been made to indicate the variations in the shades of the colours. It must be stressed that in no reproduction can the intensity or the quality of the colour be exactly depicted. This colour chart is not designed to take the place of the standard solutions or even the standard discs but has been prepared to serve as a guide for the selection of indicators and to show the gradations of colour that occur at different pH values. Further, it may be necessary to select other indicators for special work, but for all ordinary types of work the indicators given in this chart will be found useful.

TABLE

List of indicators used in the chart

Indicator	pH range	Colour
1. Methyl violet I	0.2 to 1.8	Yellow to blue.
2. Thymol blue (acid)	1.2 to 2.8	Red to yellow.
3. Methyl violet II	1.8 to 3.2	Blue to violet.
4. Methyl orange ..	2.8 to 4.4	Red to yellow.
5. Bromo cresol green	4.0 to 5.6	Yellow to blue.
6. Bromo cresol purple	5.2 to 6.8	Yellow to purple.
7. Bromo thymol blue	6.0 to 7.6	Yellow to blue.
8. Phenol red ..	6.8 to 8.4	Yellow to red.
9. Cresol red ..	7.2 to 8.8	Yellow to red.
10. Thymol blue (alkaline).	8.0 to 9.6	Yellow to blue.
11. Thymolphthalein	9.4 to 10.6	Light blue to blue.
12. Alizarin yellow R	10.4 to 12.0	Brown to dark brown.
13. Tropaeolin O ..	11.2 to 12.8	Yellow to brown.

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(7) non-inflammatory degenerative sclerotic thickening of imperfectly devascularized auriculo-ventricular valves and of the subendocardial connective tissue of the atria in which a tendency to metaplastic transformation of the connective tissue cells into osteoblasts were observable; and lastly

(8) total absence clinically of signs such as thrills, rough bruits, cyanosis, clubbing of fingers, arrested growth, suggestive of congenital abnormalities of the heart and histologically of any of the evidences of inflammation either rheumatic or otherwise in any part of the heart.

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