STUDIES IN MITRAL STENOSIS. III. OBSERVATIONS ON THE INCIDENCE AND DISTRIBUTION OF CEREBRAL EMBOLI WITH REGARD TO THE POSSIBILITIES OF THEIR PREVENTION DURING OPERATIVE PROCEDURES

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ONE OF the major dangers in the surgical treatment for mitral stenosis is cerebral embolism. Hemiparesis is obviously a great menace to patients with difficulties of respiration, causing further atelectasis and hypoxia in the postoperative state. Prevention of cerebral embolization by compression of the right carotid artery has been advised by Baker and associates[1] or of both carotid arteries by Harken and associates.[2] We have considered to be of interest the testing of the rationality of such procedures, partly by studying 10 years' material of autopsies from the Department of Pathology, University Hospital, Lund, and partly by experimental studies on the rabbit. So far, we have investigated the relative distribution of emboli in the right and the left hemisphere in mitral stenosis and in experiments; however, studies on the effect of procedures aiming at partial occlusions of one or both carotid arteries for short periods are in progress. This article deals with the first part only. The examination of the autopsy material was performed by P.H. and the experimental studies by S.J.D.*

CEREBRAL EMBOLISM IN MITRAL STENOSIS

(An analysis of 240 autopsies on subjects with valvular heart disease)

A perusal of the literature shows that, although there are several works dealing with the incidence of cerebral embolism in mitral stenosis, very little attention has been paid to the relative distribution of emboli in the right and left hemispheres. This is easily understood, as the problem has had no practical significance until the last few years. Previous studies[3,4,5] indicated that cerebral embolism predominantly affected the left cerebral arteries, a statement which is corroborated by Boyd.[6]

We have examined the autopsy reports for the period 1940 to 1949 from the Department of Pathology of the University Hospital, Lund. The total number of autopsies was 5,300. Of these, 240, or 4.5 per cent, had valvular heart disease.

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No patients with clinical or patho-anatomic evidence of syphilis were included in this figure. These 240 cases were equally distributed between both sexes (120/120).

The incidence of rheumatic valvular disease varies considerably in different parts of the world. The figure, 4.5 per cent, in our material may seem somewhat low in comparison with some statistics from the New England section of the United States,[7,8] but it is in good agreement with the figures from the 1950 material of valvular heart disease at the Malmö General Hospital, recently published by us.[9]

The distribution of the various types of valvular lesions is seen in Table I. The valvular lesions are divided into four groups, the first (I) including all "pure" affections of the mitral valve, the second (II) combined mitral and aortic valvular defects, and the third (III) all "pure" aortic defects. The fourth (IV) is a mixed group with all kinds of combinations of mitral, aortic, and tricuspid valvular diseases. The second and largest group is divided into four subgroups: (A) predominant mitral lesions, (B) minor defects of the same degree in both orifices, (C) major lesions of the same degree in both orifices, and (D) predominant aortic lesions.

TABLE I. ANATOMIC DISTRIBUTION OF VALVULAR DEFECTS IN AUTOPSY MATERIAL

I		II								III		IV	
		MITRAL AND AORTIC											
MITRAL		A. PREDOMINANT MITRAL		B. BOTH EQUALLY SLIGHTLY AFFECTED		C. BOTH EQUALLY SEVERELY AFFECTED		D. PREDOMINANT AORTIC		AORTIC		THE REST	
♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
19	59	15	20	14	11	13	12	16	2	33	10	9	7
32.5%		14.5%		10.4%		10.4%		7.5%		18.0%		6.7%	
		47.0%				43.0%							

Clinical statistics from the literature generally show a marked predominance of pure mitral lesions (DeGraf and Lingg[10] 62.5 per cent, Cabot[11] 51.5 per cent, Willius[12] 77 per cent, and Grant[13] 44 per cent). In our previous report,[9] the corresponding figure was 54 per cent. Clinical statistics, however, are apt to overestimate pure mitral lesions and to underestimate minor aortic involvement, which is often discovered only at autopsy. In our present investigation, the figure for pure mitral lesions is 32.5 per cent, which is very close to the figure,

34 per cent, given by Clawson and associates.[14] However, if Group II A (predominant mitral lesions) many of which may clinically appear as pure mitral lesions, is added, the figure is raised to 47 per cent.

Of these 240 patients, twenty-six were shown at autopsy to have cerebral embolism (10.8 per cent). In three cases this was bilateral. According to DeGraf and Lingg,[10] embolism, infarction, and thrombosis are the cause of death in 9.2 per cent of valvular heart disease. Another 10 per cent had arterial embolism with other localization chiefly in kidneys, spleen, the superior mesenteric artery, and the brachial artery. These figures are probably minimum figures, as some of the autopsies were incomplete.

Table II shows the distribution of cerebral emboli in relation to the different valvular defects. Eighty per cent of the emboli were found in cases with a mitral valvular lesion, while emboli in pure aortic lesions were rare. Of these 80 per cent one-half (40 per cent) occurred in the cases of pure mitral stenosis and there was no obvious difference in the distribution on the two hemispheres. Table III clearly demonstrates that the main source of cerebral embolism was found in patients with severe mitral valvular lesions. Embolism was not infrequent below the age of 50 years. There was no difference in the occurrence of cerebral embolism between the sexes.

TABLE II. CEREBRAL EMBOLI IN DIFFERENT VALVULAR LESIONS

LESIONS	♂		♀		TOTAL	
	RIGHT	LEFT	RIGHT	LEFT	RIGHT	LEFT
Mitral	1	2	5	2	6	4
Mitral + aortic						
A. Predominant mitral	3	2	3	4	6	6
B. Both equally slightly affected			1	2	1	2
C. Both equally severely affected	1	1			1	1
D. Predominant aortic						
Aortic		1				1
The rest			1		1	
Totals	5	6	10	8	15	14

The other one-half (40 per cent) was found in the group of combined lesions with predominant mitral valvular lesions (Group II A). Also, this group showed an even distribution of emboli between the right and left sides. As shown in Table IV, this group included some cases of emboli in rather young people.

The remaining 20 per cent also had lesions of the mitral valve, but in combination with lesions in the aorta or in the tricuspid valve (Groups II B, C and Group IV). Only in one case of cerebral embolism was there a pure aortic lesion (Group III).

Most workers agree that surgical treatment is most likely to be of value in patients who are less than 50 years old and where the mitral orifice admits one finger at the most. In our material, five men and eight women (13 patients altogether) belonged to this group. This corresponds to 5 per cent of the total

material of valvular defects or approximately 10 per cent of the patients with clinical mitral stenosis, which very closely conforms with our previous calculations.[9] Of these thirteen patients, not less than five died from cerebral embolism, approximately 40 per cent, a figure which may be relevant to the discussion of the indications and contraindications for the operation of mitral stenosis.

It appears clearly from the tables that cerebral embolism is common in mitral valvular lesions and more frequent the more severe the lesion. No significant differences between right and left cerebral embolism were found in our material.

TABLE III. AGE DISTRIBUTION AND INCIDENCE OF EMBOLI RELATIVE TO SEVERITY OF LESION IN PURE MITRAL VALVULAR DISEASE

AGE (YEARS)	DILATED ORIFICE		NORMAL-SIZED ORIFICE WITH SCLEROSIS		APPROXIMATELY ONE FINGER		LESS THAN ONE FINGER		TOTAL	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
70 and over				5		7(1)	1	2(1)	1	14(2)
60 to 69		1(1)		5		2	3(1)	9(2)	3(1)	17(3)
50 to 59		1	1	1	2	4	1	8(1)	4	14(1)
40 to 49		1				3	2(1)	2(2)	2(1)	6(8)
30 to 39	1		1	1				3	2	4
20 to 29	1				1				2	
10 to 19				2						2
9 and under			5	2					5	2
Totals	2	3(1)	7	16	3	16(1)	7(2)	24(6)	19(2)	59(8)

Figures within parentheses indicate number of emboli.

TABLE IV. AGE DISTRIBUTION AND INCIDENCE OF EMBOLI RELATIVE TO SEVERITY OF LESION IN COMBINED MITRAL-AORTIC LESIONS (PREDOMINANTLY MITRAL)

AGE (YEARS)	DILATED ORIFICE		NORMAL-SIZED ORIFICE		APPROXIMATELY ONE FINGER		LESS THAN ONE FINGER		TOTAL	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
70 and over	1					2			1	2
60 to 69		1				2(3)	1(1)		1(1)	3(3)
50 to 59					1	5(1)	1	2(1)	2	7(2)
40 to 49					3	2(3)	1(1)	2(1)	4(1)	4(4)
30 to 39					2(1)		1	1	3(1)	1
20 to 29		2			2(2)		1		3(2)	2
10 to 19	1								1	
9 and under						1				1
Totals	2	3			8(3)	12(7)	5(2)	5(2)	15(5)	20(9)

Figures within parentheses indicate number of emboli.

PERIPHERAL DISTRIBUTION OF EMBOLI, AFTER INJECTION OF EMBOLIC MATERIAL INTO LEFT HEART OF RABBITS

The vascular characteristics of the aortic arch in man are rare in animals. As far as we know similar conditions exist only in cloacal animals, certain kinds of bats, sirenians, sea cows, and half-apes. The difficulty in procuring such animals necessitated the use of some other experimental animals, for instance, rabbits, in which both the right and the left carotid arteries originate in the innominate artery. The experimental conditions thus are not quite satisfactory; however, this is probably of little consequence. The results obtained in the experiments are in conformity to those of the autopsy findings.

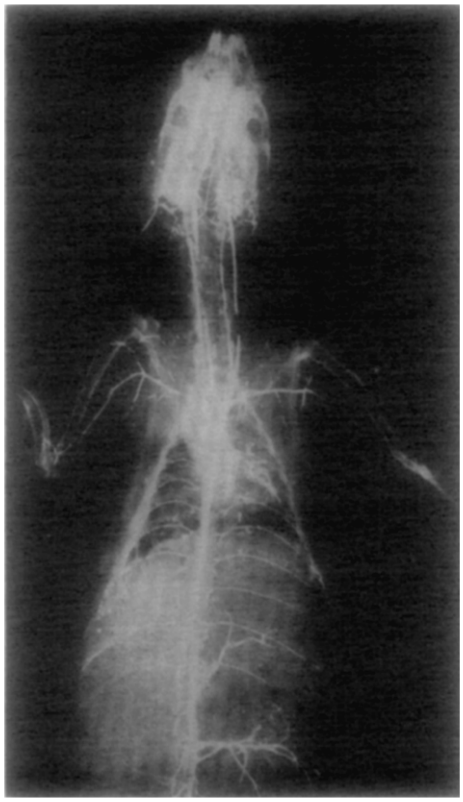

Fig. 1.

The rabbits were about 3 months old and at that age the diameter of the carotid vessels is 1.5 to 2 mm. A rabbit board was utilized throughout and the head of the animal was on the same level as the trunk. Ether anesthesia was used and in a few instances also barbiturates. Heparin was administered prior to the injection of emboli in order to prevent clotting. All injections were made percutaneously into the left ventricle. Identification of the emboli was carried out by means of roentgenograms in several projections. In our first experiments mercury was injected (Fig. 1). In spite of the high specific gravity of this

substance a beautiful contrast picture of the cerebral and other vessels was obtained. However, the mercury did not enter the carotid vessels if the head was raised approximately 60 degrees. Later on, pieces of aluminum (specific gravity 2.7) were injected, of which 30 per cent were traced in the cerebral vessels.

The main part of our experiments was carried out by means of specially constructed "emboli" which were added to a saline solution. The emboli were made from a cellulose sponge with fine pores impregnated with a mixture of lead acetate and glue. The size of the emboli was 0.8 × 0.6 × 0.3 mm. and the specific gravity about 1.5. The number of emboli injected varied from 8 to 65. The percentile recovery varied somewhat in spite of their roentgen opacity. Those which were re-found would be clearly seen and there was usually no difficulty in their identification. There is no reason to believe that the missing emboli were distributed in a manner other than that of those recorded.

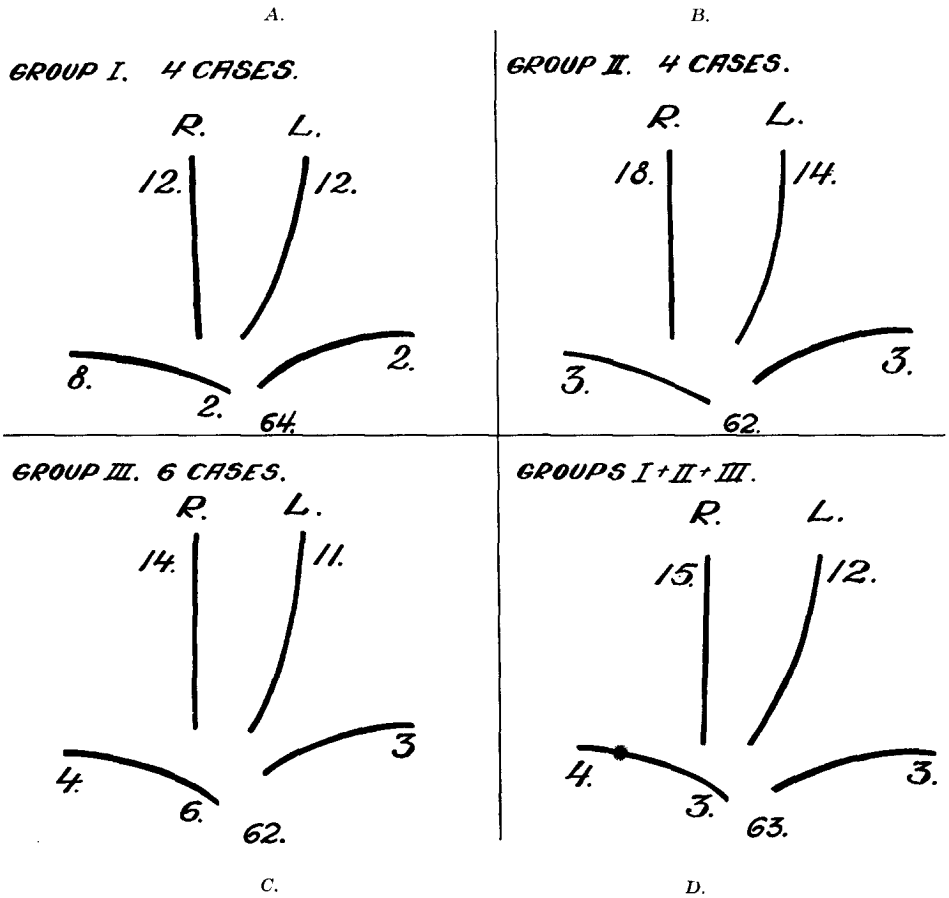

Fig. 2.

Our material is comprised of fourteen successful animal experiments. They were divided into three groups according to the number of emboli found. Group I consisted of four animals. In two of these all emboli were found and in the other two all but one. Groups II and III were comprised of four and six animals;

the number of emboli not traced varied in the second group between 11 and 20 per cent, and in the third between 22 and 53 per cent. The results appear from the sketches (Fig. 2, *A* to *D*), where the figures denote the percentage of emboli in whole numbers. Group I (*A*) showed an even distribution on the two hemispheres, 12 per cent; 8 per cent were found in the right subclavian artery, 2 per cent in the innominate artery, and 2 per cent in the left subclavian artery. In 64 per cent the emboli were spread within the arterial system below the heart. Groups II and III (*B* and *C*) showed a slight predominance of the right hemisphere with 4 and 3 per cent, respectively. In the second group no emboli were observed in the innominate artery but in the third group there were 3 per cent. The fourth sketch (*D*) is a summation of the fourteen experiments. The difference per cent between the right and the left hemisphere was shown to be 3. There appeared furthermore to be a slight predominance of the right subclavian artery as compared to the left. The 3 per cent localized to the innominate artery must be regarded as potential right-carotid emboli since most emboli were situated above the origin of the left carotid artery. However, the difference between the right and left hemispheres was so small that it lends support to the clinical observation of an equal distribution on the two sides.

The total number of cerebral emboli in the three groups was 24, 32, and 25 per cent, the mean being 27 per cent. These figures were somewhat too small in view of the emboli which were located in the innominate artery. The percentage of emboli found in the caudal parts of the vascular system agreed remarkably well in the three groups, thus corroborating the assumption that the emboli not traced were distributed in the same way as the ones traced.

These results are presented as a complement to the autopsy investigation. They will, furthermore, be used as a normal material, forming a starting point for experiments intended to show how the occlusion of one carotid artery affects the distribution of the emboli. Such studies are in progress and the results will be published later. At present, it may be assumed that successful temporary occlusion of one of the carotid arteries will probably reduce the number of cerebral emboli to one-half. Occlusion of one vessel may, however, force the emboli to choose a neighbor vessel, and it may be that occlusion of the right carotid artery will give a somewhat increased embolization through the left carotid artery or through the vertebral arteries.

SUMMARY

Investigations have been carried out on autopsy material, and experimentally on rabbits, in order to ascertain whether cerebral emboli are equally distributed in the right and left hemispheres. Both the autopsy material and the experiments showed that the distribution is even and that no significant predominance of one vessel to the other exists.

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