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THE PATHOLOGY OF CORONARY ARTERIAL DISEASE*

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The present report is based on the study of 200 autopsies on cases of obstructive disease of the coronary arteries encountered among a total of 1750 autopsies. The data gathered in this work form too great a bulk to be presented in detail in a preliminary report such as this, and will have to be given in a series of articles in special journals devoted to pathology. The purpose at this time is to call attention to the high incidence of this group of conditions in clinical practice, and more particularly as a cause of sudden death. At the same time a general conception can be furnished of the range of pathologic change found in the series.

Longcopé remarks, probably with justification, that the typical picture of coronary occlusion is not commonly found. The fact that we are able to report 200 instances of advanced coronary obstruction in 1750 autopsies is undoubtedly explained by the source of these autopsies. Our department has performed all postmortem examinations for the Multnomah County Coroner for the past four years. The rules of that office have required that in cases of sudden death and all fatalities without recent attendance of a physician, the body must be examined to determine the cause of death, and the result has been that about one thousand cases of sudden or unexplained death have come to our attention. This procedure has furnished us with a type of cases not commonly seen in the hospital or even in private practice, 137 out of 200 being coroner's cases.

The effect of this regime on the diagnosis of coronary obstruction in Portland has been noteworthy. Up to the time when we undertook this work four years ago, the clinical diagnosis of coronary thrombosis was almost, if not quite, unknown in this city, but since the pathologist has so frequently reported cardiac infarcts, aneurysms and ruptures, the interest of the clinician has been attracted to the subject to the extent that these cases are now frequently diagnosed and usually correctly. Last year several of our graduates interned in Multnomah County Hospital, and these young men usually worked out their coronary cases most accurately.

Of the 200 cases only 40 died following hospital admission, as far as can be determined. It follows that most of the remaining 160 were instances of sudden death, although brief accounts of previous complaints have been obtained from a physician or from members of the family in a large percentage of these. In a certain proportion no history whatever was obtained.

It has been learned that 14 died in bed without immediate preceding illness. Eight died in their chair, one while playing cards, 11 others were found dead in their rooms. Nine dropped dead at their work, 15 fell dead on the street, two more while driving an auto, and two following exercise. One had his fatal attack while on the golf course, and one each died in ambulance, on train and in the barber shop. Several died while straining at stool.

Other facts in symptomatology will help to give a visual picture of the clinical types included here. Varying degrees of anginoid pain were encountered. Eleven were said to have the complex of symptoms constituting typical angina pectoris. This figure of course may be too low. Twenty-nine are known to have suffered pain of a more persistent nature, usually characterized as status anginosus. Fourteen complained of persistent or intermittent pain in the abdomen.

The symptoms may be summarized as follows. Sudden death without forewarning may be the only symptom, as already recorded by various authors. About one-fourth of our cases apparently belong in this category. Others complain intermittently of attacks, such as Gorham[2] refers to as "a sudden attack of severe pain over the heart, radiating to the arm, lasting for several hours, unrelieved by

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morphine and nitroglycerine, and succeeded by a feeling of soreness for several days. Flatulence, slight nausea, restlessness, and some dyspnea are present; fever 99° to 100°, leukocytosis 18,000. Three days after the onset a localized to-and-fro pericardial friction rub is heard (perhaps for a few hours only) in the fourth left interspace near the sternum. Tachycardia, feeble heart sounds, falling blood pressure are accompanied by signs of edema of the lungs and chronic passive congestion of the liver and, twenty days after the onset, the patient may suddenly fall back on his pillow dead, or may make a partial recovery, depending upon the amount of damage to the myocardium * * *. There is only one physical sign which may be taken as almost absolutely diagnostic of coronary thrombosis, i.e., pericardial friction rub * * *. Unfortunately the friction rub is not always present."

In several members of our series the patient complained only of gastric distress or "dyspepsia," as some of them termed it. One elderly man was subjected to laparotomy for supposed intestinal obstruction; autopsy a few days later revealed coronary thrombosis, old and recent, with cardiac aneurysm. Another had a cholecystectomy, and at least two other coronary cases were diagnosed as acute cholecystitis.

Several of our cases complained particularly of choking sensations, sometimes without pain, and in a few instances difficulty in swallowing was a prominent symptom. One aged patient habitually compressed the tongue with a spoon-handle to facilitate swallowing.

Libman[3] and others have referred to the peculiar leaden or ashy or earthy color of the skin in chronic coronary thrombosis subjects. This is almost diagnostic of obstruction of the coronary arteries, although one member of our series, because of the cutaneous pigmentation and low blood pressure, was mistaken clinically for a case of Addison's disease.

One of the most valuable symptoms in the more serious cases has been the drop in a blood pressure which had previously been high. The drop in pulse pressure has frequently been an even more prominent feature. Other symptoms are fatigue on exertion, pain from distant embolism in the brain, lungs, spleen, kidneys, or intestine, and arrhythmias.

Fever, usually moderate, but occasionally high, and leucocytosis ranging from 10,000 to 25,000 or even more, occur in most instances of cardiac infarction during the early stages, and again in the aneurysm stage, due to the development of a mural thrombus in the ventricle. These symptoms have by some been attributed to inflammatory agents, but are usually considered as due to absorption of necrotic material.

Having described briefly the symptomatology of all grades of the very severe and moderately severe types, we should mention the most favorable examples of coronary arterial disease. There is no question that extensive coronary obstruction is sometimes attended by only a transient flurry of precordial pain, and we have even found complete thrombosis of a main coronary artery in subjects who, it is safe to assume, had experienced no noteworthy discomfort therefrom.

Herrick and others have established beyond peradventure that extensive coronary obstruction is not always promptly fatal. Many individuals survive the attack only to suffer subsequent similar accidents, until finally the damage to the myocardium becomes too great to be tolerated. Complete recovery undoubtedly occurs occasionally in even the most extensive lesions, with death later in life from other conditions.

CONGENITAL AND ACQUIRED ANOMALIES OF THE CIRCULATION IN THEIR RELATION TO CORONARY OBSTRUCTION

In tracing out the life history of coronary disease we must extend our investigation backward to early life, and even to the time of birth. Thus we are concerned with the role of certain congenital anomalies.

One of the commonest of these is the variation in number of coronary artery orifices, and in addition we have similar conditions in the acquired sense. We had one case in which the right coronary orifice was congenitally absent. In comparison with this we have had six examples of complete closure of one or other orifice, due to scarring of the

adjacent aorta, all syphilitic. In 23 other cases one or both orifices have been so constricted by disease as to produce possibly serious effects on the action of the heart. In one heart, both orifices were in the same sinus of Valsalva.

The presence of supernumerary coronary orifices is a factor which is of frequent occurrence and yet has received little attention. It appears from our series that this anomaly is much commoner among cases of coronary arterial disease than in general. Forty-three of our 200 have supernumerary orifices.

The pathogenesis of supernumerary orifices is still open to some doubt. In most instances it probably represents a mere congenital anomaly. Again, it may be produced by the contraction of scar tissue in the aorta, drawing one of the early branches of the coronary arteries into the aortic lining. A third possibility is that a capillary or arteriole arising in the aortic lining may under emergency become enlarged to form an accessory coronary artery. It is obvious that a multiplicity of coronary orifices might seriously affect the fate of a heart condition.

Attention has been called recently to the importance of the position of the coronary orifices. It has been argued that these should lie within the sinuses of Valsalva, and that, when they lie above the margin of the aortic cusp, they are more exposed to the deforming influence of syphilitic scars of the ascending aorta.

The most important anatomic factors, however, are the distribution of the coronary arteries of the heart and their anastomoses. For centuries much controversy has centered on the question whether the coronary arteries are true end-arteries without ample anastomoses. This, as Gross[4] has pointed out, concerns three considerations: (1) whether anastomoses exist between the right and left coronary arteries; (2) whether branches of one coronary artery anastomose among themselves; (3) whether anastomoses exist between the coronary arteries and vessels of adjacent organs.

Thebesius[5] in 1708 was probably the first to demonstrate by dissection that anastomoses exist between the coronary arteries, and later Haller[5] proved the variety and richness of these connections.

In 1810 Caldani[6], the Venetian, in his Atlas based on careful dissections, described and reproduced the course of one of the important anastomoses about the conus arteriosus. Many others since Caldani's time have described anastomoses in various parts of the heart.

In spite of all these anatomic proofs Hyrtl[7] in 1865 on the basis of injection experiments denied the existence of anastomoses between the coronary arteries, and in 1866 Henle[8] corroborated his findings. As late as 1881 Cohnheim and von Schulthess-Rechberg[9] supported the same view by dog experiments. They concluded that clamping of either main coronary artery in a curarized dog caused cessation of the ventricular action within two minutes. This view was confirmed by many observers.

It was later proven by numerous experiments in the hands of various workers that a coronary artery could be tied off without death ensuing or, in many cases, without even serious harm. W. T. Porter's[10] figures may be taken as the type of these results. In his experimental closure of the circumflex branch of the left coronary artery in dogs, stoppage of the heart resulted in 64 per cent; the anterior interventricular 28 per cent; the right coronary 14 per cent; and ligation of smaller branches failed to cause arrest. Porter has also demonstrated that the tying of a single vessel causes a rise of diastolic pressure, without a corresponding increase of pressure in the coronary arteries. In other words, the coronary arterial pressure is lowered, while the pressure in the auricles and coronary veins is increased. Thus it becomes difficult for these arteries to propel their blood. It is probable that sudden blocking of the nutrient arteries of the human heart by an embolus or thrombus often causes death in some such manner.

More direct evidence for anastomosis has been furnished by the injection of coronary arteries as performed by Jamin and Merkel[11] in 1907, and by Spalteholz[12] the same year, and later by Gross and others.

We must conclude that an extensive anastomosis of the coronary arteries has been demonstrated.

In the human, spontaneous obstruction of the coronary arteries forms the commonest cause of

sudden death and a still commoner cause of cardiac pathology. Porter's conclusions from his dog experiments, valuable as they are, do not apply entirely to the human for two main reasons: (1) variation in the coronary circulation in man, (2) the etiology of coronary obstruction.

If the coronary arteries were definitely end-arteries, as was formerly supposed, sudden obstruction must necessarily result in infarction. Fortunately, however, the old view in this regard is not quite literally true. It has been proven that there are connecting twigs which form anastomoses between the various arterial branches. These anastomoses are extremely variable in different individuals, and the outcome of an obstruction will depend on whether this particular individual is fortunate enough to possess adequate collateral circulation. Herein lies the importance of congenital variations in the blood supply of the heart.

But in spite of the anastomoses in the coronary arteries in the human, these vessels, and especially their branches, are in a limited sense end-arteries, and it must not be supposed that man could tolerate a ligation such as Porter performed in the dog. Immediate death or infarction would generally occur.

But the obstruction in man is usually not so sudden as to be comparable to a ligation. In most instances a gradual narrowing occurs from arteriosclerosis, a process which as a rule extends over a period of years. This narrowing is so slow, in fact, that the circulation has ample time to adjust itself. New channels form by the hypertrophy of smaller vessels. If the left coronary artery becomes seriously narrowed, the right and its branches enlarge to take over the additional burden, and form adequate anastomoses with the left. Sclerotic narrowing alone rarely if ever produces serious effects. It is only when some sudden event finishes closing a vessel that infarction or other grave results ensue. This sudden event is generally a thrombus which forms on the rough calcareous lining of a sclerotic vessel. If the thrombosis had occurred in a normal healthy heart, serious harm would have immediately followed, but the previous narrowing by arteriosclerosis has had at least one beneficial effect. It has given the circulation a chance to form collateral channels, so that when the occlusion finally occurs the blood from the obstructed vessel can be diverted.

In summary we may say, then, that gradual narrowing may occur from arteriosclerosis, but that the sudden obstruction which can cause infarction or death is by a thrombus forming in a vessel already narrowed by arteriosclerosis. Embolism occasionally accounts for an acute obstruction. Syphilitic arteritis may, like arteriosclerosis, narrow a vessel, even to the extent of occlusion, or may be followed by thrombosis or embolism. But the commonest sequence of events is gradual arteriosclerosis, leading to final sudden thrombosis.

The fate of a thrombus is of interest. If prompt death does not supervene, the thrombus organizes, producing a fibrous plug in the lumen. Blood channels burrow often through this and reestablish the circulation through the obstructed vessel.

TYPES OF INJURY CAUSED BY CORONARY OBSTRUCTION

Because of the variability in the circulation in the heart of different individuals, and owing to the fact that the obstructions may be sudden or gradual, we find various results in man.

1. The heart may promptly stop. This occurs mostly in those instances in which a thrombus suddenly develops in an artery which has not been gradually narrowed by arteriosclerosis, permitting the establishment of an ample collateral circulation. Even though collateral channels are present, thrombosis may prove promptly fatal, if the anastomoses likewise suffer occlusion.

2. Infarction (nearly always in the left ventricle) occurs in a large percentage of those individuals who do not die immediately following occlusion. Death may subsequently occur in the next few hours or days, due to rupture of the ventricle into the pericardial sac or even through the interventricular septum into the other ventricle. More often, however, death results, not from any such gross mechanical accident, but from myocardial impairment. Dilatation is found at autopsy in a minority of cases, but the usual nature of the fatal event can be better surmised from the animal results of Lewis[13], who observed rapid successions of ven-

tricular extrasystoles, followed by attacks of ventricular tachycardia at rates of 140 to 400 beats per minute in dogs in which a coronary artery had been ligated. In some instances the ventricles went into fibrillation and the dogs died. Lewis' observations have been confirmed by F. M. Smith[14].

3. Infarcts, even though extensive, frequently heal with scar formation of one of the following types:

(a) Myofibrosis: scattered patches of scar tissue, frequently encountered at autopsy, but always to be differentiated from the myofibrosis resulting from healed inflammation and other causes.

(b) Large circumscribed cicatrices.

(c) Aneurysms resulting from thinning and bulging of a scarred ventricular wall. Rupture occurs in this stage, but not as commonly as in fresh infarcts.

4. Thrombosis of the ventricle often occurs in connection with infarcts and even more frequently in aneurysms and other extensive cicatrices. In a large percentage embolism to distant parts of the body, and even to the coronary arteries, may result.

5. A few infarcts heal permanently, with restoration of the normal function of the heart, as in our subject who died of disease of the pancreas five years after infarction of nearly half of the left ventricle. In most instances, however, healing of an infarct is followed by fresh coronary thrombosis and new infarct formation. Most of these coronary accidents, then, are eventually fatal.

Thus we see that in the great preponderance of cases there is a definite interrelation or sequence between coronary sclerosis (senile and syphilitic); coronary thrombosis; infarction of heart; fibrous plaques of myocardium; cardiac aneurysm; rupture of the heart; and intraventricular thrombosis. This relationship is clearly expounded in René-Marie's[15] noted thesis in 1896.

SUMMARY OF OBSERVATIONS ON OUR 200 CASES

This series embraces 200 instances of advanced coronary obstruction, selected from a total of 1750 autopsies, about 1000 of which were done for the county coroner.

In a total of 145 hearts emboli or fresh thrombi or old thrombi or combinations of these were demonstrated.

In 94 hearts fresh thrombi were present in one or more coronary arteries or branches. The criterion employed in demonstration of these was in nearly every case microscopic examination of a section through the occluded portion of the artery. Only 40 of the 94 contained either definite infarcts or cardiac aneurysms, although a few more contained patchy necroses. Thus 54 had fresh coronary thrombosis without infarction or aneurysm and it is probable that the most of these represent death in the first attack before an anatomic infarct has had time to form. In general these are the individuals who have dropped dead on the street or in their chair or under similar circumstances, without forewarning in the way of serious preceding symptoms.

In 70 hearts the coronary arteries contained either old obliterative or recanalized thrombi or types of obliterative endarteritis closely simulating these. Aneurysms of the left ventricle occurred in 19 and healed infarcts without formation of aneurysm in 11 more.

Embolism contributed 14 instances of coronary occlusion, 9 of which resulted in infarction. The other 5 comprise cases which resulted fatally before the anatomic evidences of infarction could manifest themselves.

The total number of acute infarcts collected is 46; healed infarcts 11; and cardiac aneurysms 19; total (after deduction for four duplications) 72 infarcts and aneurysms.

Definite indisputable aortic syphilis was present in 35 or 17.5 per cent of the 200. Examination of the myocardial and coronary microscopic sections has revealed a considerable number of additional syphilitic involvements of these tissues, but this tabulation is not completed and will be presented later. One important observation is, however, that syphilis accounts for all of our six instances of complete closure of a coronary orifice, all left. Among the 35 hearts accompanied by a definitely syphilitic aorta, 10 manifested acute coronary thrombosis, 5 old coronary occlusions, and 6 contained infarcts. Patchy necroses were more frequent than infarcts,

but the number of such cases is not yet determined. Our data on syphilis are far from complete, but we are convinced that this infection plays a role in coronary thrombosis and infarction.

Rupture of the heart, always of the left ventricle, occurred in 14 of our cases, exactly one-half of which fall in the definitely syphilitic class. One ruptured through the septum interventriculorum into the right ventricle, the others into the pericardial sac. Acute infarcts caused 7, syphilitic myocarditis 3, rupture of a syphilitic coronary with resulting myocardial apoplexy one, and rupture of dissecting coronary aneurysm one.

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