mucin could be extracted from the subcutaneous tissues of these persons. He therefore gave the name of "myxoedema" to supposedly dropsical cases of this type.²⁸ The separation of these cases, which formerly had been classed as a type of dropsy, was further made in 1883 by Kocher, who found that the condition developed after removal of the thyroid gland,²⁹ and by Semon,³⁰ who in the same year suggested the identity of cretinism, myxoedema, and cachexia strumipriva, and whose suggestions on identity of origin were confirmed through an investigation held by the Clinical Society of London in the following year.³¹

In contrast to the helplessness expressed by Gull in 1873 for the betterment of these cases, Murray³² in 1891 used with good result hypodermic injections of glycerin extract of sheep's glands; and, in 1892, the treatment was further improved and simplified by Hector Mackenzie and Fox,³³ who independently and successfully used the administration of sheep's thyroid gland, or its extract, by the mouth in the treatment of myxoedema.

Other forms of dropsy of a localized nature have from time to time been shown to be due to conditions which offer a local obstruction to the circulation of blood or lymph. It is unnecessary to particularize these, but one may simply mention the discovery by Bancroft in 1876 of the filaria which causes elephantiasis and allied conditions that were for long a puzzle to physicians practising in tropical regions.

SUMMARY.

Dropsy from the earliest times was an obvious morbid condition, and was for long regarded as a disease *sui generis*, due to liquefaction of the tissues. The ancient Greek physicians attributed it chiefly to a disorder of the liver, and hardening of this organ was regarded as the principal cause by the Alexandrian School of Medicine. Galen regarded the defective action of the heart, which is often an accompaniment of dropsy, as an effect rather than a cause. In the eighteenth century Morgagni drew attention to the frequency with which the heart is found to show valvular defects and other disorders in cases of dropsy, but he did not carry the matter further. Withering, who introduced the use of digitalis in 1775, recognized that only certain cases of dropsy were amenable to treatment by this drug. He described as the type of case in which the dropsy was chiefly benefited persons showing symptoms which we can now recognize as being those of advanced cardiac disease, although the means of diagnosing valvular disorder was not at the time available to him. In the beginning of the nineteenth century Corvisart, followed by Laennec, placed the diagnosis of cardiac disease on a sure foundation and showed that dropsy was frequently simply a sequel of this type of disease. The recognition of kidney disease as a cause of dropsy was first made early in the nineteenth century when Wells, Blackall, and others pointed out the fact that the presence of albumin in the urine was a prominent feature in certain dropsical cases, and these observations were placed on a sure footing by Bright in 1827. A further group of cases in which neither the heart nor the kidney is found to be at fault was demonstrated by Gull and Ord, in the seventies of last century, to be due to atrophy of the thyroid gland and to be of a different nature from simple watery oedema.

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DISEASES OF THE CORONARY ARTERIES.*

BY

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THE maintenance of an efficient circulation to the heart muscle is of fundamental importance if the heart is to be able to perform its function in health or disease to the best advantage. One of the essential requirements for this purpose is the possession of healthy coronary arteries, and it is to a consideration of diseases of these vessels that I have been asked to direct your attention.

Before embarking on the subject proper it might not be inappropriate to indicate the scope of the discussion in relation to the title. Although diseases that affect the coronary arteries are the same as those that affect arteries in general, discussion of minute points in classification or of pathological details would be unfortunate and probably profitless. One should concentrate rather on the effects produced on the heart by such diseases as receive general acceptance. Again, because of the widely recognized connexion between angina pectoris and these diseases, one must guard against any concentration on the theories of angina pectoris, interesting though that might be in itself, as a detraction from the value of the main subject before us.

Further, coronary artery thrombosis is an important manifestation which has attracted much attention in recent years and will no doubt be freely discussed to-day, but it would denote a narrow outlook if discussion became limited to this condition. There is a danger in any of these directions of overlooking other important considerations.

In so far as special aspects of the subject will be dealt with in detail by subsequent speakers, these opening remarks will best serve their purpose if I survey in a general way some of the essential features of the problem.

HISTOLOGICAL.

Disease of the coronary arteries has been recognized for a considerable time, and its association with angina pectoris as more than a coincidence has been widely accepted, though many have refused to accept the view that coronary disease offers a complete explanation of that condition. Prominent among the latter have been Allbutt,¹ Mackenzie,² Cabot,³ and Vaquez.¹⁶ In recent years, fifteen to twenty at most, prominence has been given to certain symptoms, anginoid in nature, which have been found to be associated with coronary blockage—usually by thrombosis *in situ*. The importance of this syndrome, to which further reference will be made, is undoubted, and has anew directed attention to these vessels. Inquiries into the literature have been made by Hamman,⁵ and more recently by Parkinson and Bedford,¹⁰ and while it would appear that the association of special symptoms with occlusion of the coronary blood supply had been recognized as far back as 1878, it is only during the last few years that it has received intensive study and that a clear distinction has been established between it and the more widely recognized syndrome of typical angina pectoris.

In this country the papers published in 1925 by McNee⁸ and by Gibson³ have helped to focus attention on this subject. It is interesting to note, however, that in 1887

* A paper read in opening a discussion in the Section of Medicine of the Annual Meeting of the British Medical Association, Cardiff, 1928.

Lindsay Steven¹⁵ of Glasgow, whom I had the privilege of assisting in his clinic for a few years, in a lengthy paper on "Fibroid degeneration and allied lesions of the heart and their association with disease of the coronary arteries," made a careful analysis of the literature. One of the earliest cases he noted was recorded by Sir William Gairdner in 1854—"a case of ossification of the coronary arteries with tendinous degeneration of the heart." Steven recorded sixteen cases with clinical histories and *post-mortem* reports, emphasized the relationship existing between disease or obstruction of the coronary arteries and fibroid degeneration, and distinguished in this connexion between this fibrous transformation and chronic interstitial myocarditis due to other causes. It may be mentioned at this point, though somewhat anticipating subsequent remarks, that in two of the cases recorded Professor Coats demonstrated, by injection with Prussian blue, free anastomoses between a pervious coronary artery and the branches of a blocked vessel, and also between branches supplying the two auricles and the two ventricles.

Coincident with this increased attention to the clinical aspects very important anatomical investigations have been made, and to Gross⁴ and his collaborators physicians owe a debt of gratitude. It may be appropriate at this point to mention some of the results of their work. The blood supply to the heart is subject to much variation, but certain main facts ought to be borne in mind.

The right coronary artery emerges between the pulmonary artery and aorta, passes to the right in the auriculo-ventricular groove as the right circumflex branch, and, crossing the acute margin, continues to the posterior aspect of the heart, where it gives off the posterior descending branch in the interventricular groove. It supplies the entire right ventricle except the left third of the anterior wall. It also supplies the right half of the posterior wall of the left ventricle and a strip of the interventricular septum.

The left coronary artery divides, almost immediately after its origin from the left anterior sulcus of the aorta, and under cover of the left auricle, into two branches, the chief branch being the anterior descending branch, which passes down in the anterior interventricular groove to the apex, curves round the apex, and ascends the posterior wall. The other, the left circumflex branch, passes to the left in the auriculo-ventricular groove. The left coronary artery supplies the left ventricle except the right half of the posterior wall, the left third of the anterior portion of the right ventricle, and part of the septum. Thus both vessels supply part of the posterior wall of the left ventricle, the anterior wall of the right ventricle, and the septum. The left aspect of the left ventricle and the anterior papillary muscle of the ventricle are only supplied by the left coronary artery. Further, the right branch of the auriculo-ventricular bundle is only supplied by the left coronary artery, while the left branch is usually supplied by both.

From his studies Gross also concludes that the heart is perhaps the richest organ in the body as regards capillary and precapillary anastomoses between branches of the same artery as well as between branches of both arteries, and, further, that as age advances there is also an anastomosis between the vessels in the epicardial fat and other adjacent parts and the coronaries—a fact which has a certain clinical bearing in explaining some of the features presented by cases of occlusion in later life.

Recently Kugel,⁶ a co-worker with Gross, has more fully demonstrated that an artery, called by him the "*arteria anastomotica auricularis magna*," which constantly links the right and left coronary arteries, usually passes from the circumflex branch of the left coronary artery to the circumflex branch of the right coronary artery through the interauricular septum. Incidentally this is the artery which sends twigs to the aortic cusp of the mitral valve when that valve is vascularized.

The question of anastomosis has been investigated much earlier and from different standpoints. In more immediate connexion with our discussion one might mention the work of Miller and Matthews⁹ on ligation of the descending branch of the left coronary artery in dogs from which the presence of anastomosis was inferred, and the more recent

and more extensive work of Smith,¹³ who arrived at the same conclusion by a similar method. Smith further correlated certain electro-cardiographic results with ligation of the left descending branch in dogs, and among several clinical cases reports,¹⁴ with electro-cardiographic records, one of a man who had the left descending branch ligatured for the stoppage of haemorrhage from the heart wall following a self-inflicted wound.

MORBID ANATOMY.

When we come to consider the morbid processes which are prone to affect the coronary arteries, we find that these can be classified into four clearly defined conditions. A classification built on minute histological detail is not necessary for the purpose of this discussion, and would probably in any case lead to profitless argument, but unless some uniform and simple classification is accepted confusion is likely to arise owing to the variety of terms that are often applied to the same pathological condition.

The four conditions with which I shall deal are atheroma, arterio-sclerosis, syphilis, and calcareous degeneration. As an example of the need for uniform nomenclature may be cited the cases of three recent papers directly or indirectly dealing with coronary artery disease. Apart from syphilis, in one English paper atheroma is the only term employed to denote lesions of the coronary arteries, while in another English paper the term arterio-sclerosis alone is employed. In an American paper the term arterio-sclerosis is used with hypertension as an added condition, while the term atheroma is not once mentioned. The term athero-sclerosis also occasionally crops up. A definition of the terms proposed to be employed would therefore appear to be necessary.

Atheroma.—The commonest primary lesion in the coronaries is a patchy disease, first affecting the deeper layers of the intima. While there may be proliferation of fibrous elements on the aspect nearer the lumen of the vessel the deeper parts tend to degenerate, and in the later stages deformity is produced, encroaching on the lumen. Whether beginning originally as a fatty degeneration or not it is essentially the same condition as that called atheroma in the aorta, and, though with less frequency in the coronaries than in the aorta, is liable to produce atheromatous ulcer with a special tendency to thrombus formation. Atheroma is the term which I shall employ for this condition, as it affects the coronaries. It is to be noted that not only is the disease patchy in its local manifestation, but that it is also quite irregular in its incidence in different parts of the same body, so that the aorta, the coronaries, or the cerebral arteries may be the seat of well-marked atheroma though the accessible arteries of the body give no indication of its presence.

Arterio-sclerosis.—The second lesion met with is a much more diffuse process, characterized by thickening of the media and intima, probably beginning in the media as a hyperplasia and leading on at times to a certain degree of fibrous transformation of the muscular wall. It is the same as that described as the arterio-sclerosis of high blood pressure, and it may or may not produce any narrowing of the lumen of the vessel. It is much more uniform in its distribution throughout the body than is atheroma, and may be found throughout the vascular system, though certain parts may suffer more than others. The term arterio-sclerosis shall be confined to this type.

Syphilis.—While aortic syphilis is one of the commonest visceral manifestations of that disease its presence in the course of the coronary arteries is comparatively rare. The coronary arteries, however, are liable to be implicated at their orifices in a patch of syphilitic mesaortitis, thus producing narrowing of their lumina where they arise just above the aortic cusps.

Calcification.—The fourth condition met with is calcareous degeneration, and it is frequently found superimposed on either atheroma or arterio-sclerosis, though it may occur as a primary medial degeneration. The deformity it produces in the coronary arteries in association with atheroma makes it a potent factor in diminishing the lumen, either directly or by the formation of thrombus on its surface.

If the purists in pathological terminology will agree to

accept such a classification it will, I am sure, meet all the requirements of the present discussion.

To obtain some idea of the relative frequency of these lesions of the coronary arteries, through the courtesy of Professor Muir, I took the figures from 1,000 consecutive *post-mortem* examinations made in the Western Infirmary, Glasgow, using only the routine reports of the naked-eye findings. It will be understood, therefore, that the figures will be below, rather than above, the actual, because the state of the coronary arteries was not mentioned in every report, and, further, the coronary arterioles did not come under observation.

Under these conditions I was surprised to find that out of 1,000 consecutive *post-mortem* examinations made, there were 371 cases in which note was made by naked-eye observation of a lesion, whether trifling or severe, of the coronary arteries (see table). Of this number the average

Lesions of Coronary Arteries, with Accompanying Muscle Defects, Found in 1,000 Consecutive Post-mortem Examinations.

Coronary Lesions.	Number.	Fibrosis, Patchy or Diffuse.	Fibrosis and Fatty.	Fatty Only.	No Fibrosis or Fatty.
A.	162	63	7	26	66
A. and A. S. ...	96	52	1	12	31
A. and C.	26	18	3	1	4
A. and S.	8	2	0	0	6
A., A. S., and C. ...	6	6	0	0	0
A., A. S., and S. ...	1	1	0	0	0
A. S.	60	30	1	8	21
A. S. and C.	4	1	0	1	2
A. S. and S.	1	0	0	0	1
C.	4	3	0	0	1
S.	3	2	0	0	1
Total lesions found	371	178	12	48	133
No lesion	629	68	—	—	—

A.=Atheroma. A. S.=Arterio-sclerosis. C.=Calcification. S.=Syphilis.

age of the patients was 55.4, the youngest being 13 and the oldest 85 years, and the causes of death were about as varied as one gets in any general hospital. Of these 371 cases, 238 showed a definite lesion of the myocardium; 178 presented fibrosis, either patchy or diffuse; 12 fibrosis with fatty change; 48 fatty change alone; and in 133, or 35.9 per cent., no obvious change was present or there was only simple or brown atrophy or hypertrophy. Thus the predominant lesion present was fibrosis, as it was found 180 times (51.2 per cent.) in 371 cases with coronary artery lesions. In the remainder of the 1,000 cases in which no lesion of the coronary arteries was noted fibrosis occurred in only 68 (10.8 per cent.), the average age being 48.4 years. The lesions found in these 371 cases, with the percentage incidence of fibrosis, were as follows:

Atheroma...	299 (80.6%),	with fibrosis in 153 (51.2%)
Arterio-sclerosis	168 (45.3%)	" " 92 (54.7%)
Calcification	40 (10.8%)	" " 31 (77.5%)
Syphilis (at or near an orifice)	13 (3.5%)	" " 5 (38.0%)

Using fibrosis, then, as an index of the effect of the various lesions of the coronary arteries, we found that calcification when present was the factor most likely to produce a lesion of the myocardium. It was usually found in association with atheroma or with atheroma and arterio-sclerosis.

There were 97 cases in which the lesion of the arteries was specially noted as producing definite narrowing or actual blockage of the lumen:

Atheroma was present	in 85,	with fibrosis in 82 per cent.
Arterio-sclerosis	... in 31,	" " 84 "
Calcification	... in 33,	" " 85 "
Syphilis	... in 7,	" " 57 "

Fibrosis was present in 78, or 80.5 per cent. of the 97 cases, in contrast with 51.2 per cent. of the whole group.

Thus, it may be inferred that when a lesion is sufficiently severe to narrow the lumen, no matter what the lesion, fibrosis is the natural result.

The last group I extracted from this series was that of 58 cases in which the patients died suddenly from coronary artery disease, or in which there was definite occlusion of a coronary artery or main branch. The average age in this group was likewise 55 years. Of the 58, atheroma was present in 49, or 84 per cent.; arterio-sclerosis in 13, or 22 per cent.; calcification in 20, or 34 per cent.; and syphilis in 11, or 19 per cent. It is important to note that while this group is a little less than one-sixth of the total, about one-sixth of the cases of atheroma are found in it, one-half of the cases of calcification, three-fourths of the cases of syphilis, but only one-twelfth of the cases of arterio-sclerosis. This supports the view that atheroma, the commonest lesion, is also a serious one, while calcification or syphilis materially increases the gravity of the case in the direction of promoting occlusion of the vessel. Fibrosis was present in 48 of these cases, but there were 10 in which there is no note of any fibrosis in the heart muscle.

These cases present striking instances of the adaptability of the anastomotic channels in suitable circumstances, one of the conditions being slowness of the constricting process. The average age of the 10 patients was only 41. Space alone forbids details of these patients, all of whom died suddenly; all had well-marked, often extreme, old coronary lesions, and yet presented no gross fibrosis. More than half the cases had syphilis. One case must serve as an example: A female, aged 40, had suffered from angina for five years. At autopsy the right coronary artery was completely occluded with arterio-sclerosis, and there were syphilitic lesions in the aorta. The left coronary artery was small. There was no gross fibrosis and no recent thrombosis.

From this study, in addition to the general information regarding the frequency of the lesions and their effects, three points emerged which are worthy of note: (1) severe coronary artery narrowing may be present without obvious lesion in the myocardium; (2) old-standing severe arterial lesions and actual occlusion with fibrosis may be present with no clinical history of its occurrence; (3) patients may die with symptoms suggesting coronary artery occlusion in which no such lesion is found.

GENERAL EFFECTS OF CORONARY ARTERY DISEASE.

In general it may be said that there is a tendency for disease affecting the coronary arteries to produce diminution of their lumen. Rupture of a coronary artery, a condition analogous to that producing cerebral haemorrhage, must be very rare. Undoubted embolism causing blockage was not noted in this series.

The effect of the narrowing is to produce starvation atrophy in the parts supplied, followed by replacement fibrosis, or, if sudden complete occlusion is produced, infarction results, which may show necrosis and at a later date fibrosis; or sudden death may occur before either is manifest. The infarction is usually smaller than the area supplied by the blocked artery and is generally found to affect the middle or inner two-thirds of the heart wall. Fibrosis may, if sufficiently general, lead to dilatation of the chamber affected, or, if more localized and sufficiently severe, to aneurysm of the heart wall. As the descending branch of the left coronary artery is the vessel most commonly involved, the fibrosis is usually most marked towards the apex of the left ventricle, in the anterior papillary muscle of the left ventricle, and in part of the inter-ventricular septum.

If one takes a sufficiently wide outlook of the subject, it will be apparent that there can be no diagnostic symptomatology which will cover all cases of coronary artery disease. Thus it may be remembered that in the series of cases to which I have alluded the disease did not progress so far as to interfere appreciably with the blood supply in 133, or 35 per cent. of the cases; at least no gross lesion in the muscle was apparent. In the remaining 238 cases only 58 could be said to have died as an immediate result of coronary artery lesions. In some of these a preliminary diagnosis, which would have been of value as

a guide to treatment, could not have been made, as the terminal event was the first indication of ill health. In an unknown proportion of the remainder, the coronary artery narrowing was no doubt a factor which promoted a fatal termination in the disease from which the patient chanced to die. In some patients death was due to ordinary cardiac failure, with or without dropsy, without any special symptoms or signs which might distinguish them from those dying with myocardial degeneration from other causes. In cases of arterio-sclerosis with high blood pressure, or in cases with evidence of atheroma in peripheral vessels, one might surmise that fibrosis of the myocardium due to these lesions in the coronary arteries was the cause of disease, if no other obvious cause was present. In some of them no doubt a more careful inquiry into the history during life might have directed the attention to the coronary arteries and made a diagnosis possible in view of the symptoms and signs that we now know occur in typical cases.

CORONARY ARTERY OCCLUSION.

When the blockage is abrupt, as from thrombosis on an atheromatous or calcified patch, certain features are present with such regularity as to make diagnosis reasonably sure. Even when coronary artery thrombosis is recognized it must be understood that the result is still variable, depending on the size of the artery blocked, the actual branch that is affected, and the age of the patient. Hamman,⁸ in his review on the subject, has divided cases of coronary artery thrombosis into six classes, according to the course of events—namely: (1) Cases of sudden death. (2) Death in a few hours or days. (3) Continued myocardial insufficiency, with death in weeks or months. (4) Recovery after grave symptoms. (5) Cases that are not grave but recognizable. (6) Mild or uncertain cases.

The clinical features and diagnosis of coronary artery thrombosis will be dealt with in detail by subsequent speakers. The features that demand attention in coming to a diagnosis, and which I trust will be fully discussed, are, among others, the duration and situation of the pain, the associated symptoms such as collapse, vomiting, respiratory and mental distress, such signs as the rate and rhythm of the heart, the fall of blood pressure, pericardial friction, fever and leucocytosis, and the information that may be derived from electro-cardiograms.

I forbear to say more on these points than to repeat what emerged from the pathological inquiry. In a few cases old organized thrombosis may be present at autopsy without a history of antecedent acute illness; or there may be what appears to be a typical history and no thrombosis is found. The diagnosis must therefore be carefully assessed or it may readily overstep the truth.

PROGNOSIS.

Once the diagnosis has been made the outlook is uncertain, and even the immediate prognosis can only be assessed after time has elapsed to gauge the response to treatment. In almost all cases the ultimate prognosis is bad, particularly in view of the absence of any evidence that arterio-sclerosis, atheroma, or calcification can be influenced materially by any known line of treatment. Gradually increasing cardiac weakness and sudden death at a subsequent date are not uncommon features. Until the diagnosis of minor manifestations is more accurate the number who recover cannot be stated. Judging from the old lesions found at autopsy those who make a good recovery, at least temporarily, must be fairly numerous.

TREATMENT.

In considering treatment one must clearly distinguish between treatment of the actual disease which is affecting the coronary artery and treatment of a complication that may arise in the course of that disease, such as thrombosis.

It may be advisable to speak first of treatment of a case of coronary artery thrombosis. When the patient is struck down with such a catastrophe the first indication is to relieve the pain. The pain presents a striking contrast, in respect of its response to treatment, to that of true angina pectoris, where vaso-dilators may give instant relief. In this condition morphine is required, and often in large

doses. It may be stated that in cases of persistent anginoid pain, or of low blood pressure, amyl nitrite is seldom effective and is usually dangerous. Morphine also aids in giving to the patient the mental and physical rest that is so essential. Some find digitalis of great value when the heart rate is accelerated, and in cases with auricular fibrillation the indication is obvious. Cases that rally from the initial attack, but present in time the ordinary signs of cardiac failure, should be treated along the usual lines for that condition.

I have for some time been impressed with the value of glucose in strengthening the heart in cases of myocardial weakness, but I have not been able to follow a sufficiently large series of cases to make any dogmatic statement. The dose I have employed has been half a pound daily, and I should like to have the views of others who have adopted this line.

In considering treatment of the actual disease of the coronary arteries one must admit that the ideal stage at which to deal with it is the stage before it has produced any effects on the heart, and the treatment resolves itself ultimately into the prevention of such conditions as atheroma and arterio-sclerosis. This implies a knowledge of etiology that is far from efficient.

Arterio-sclerosis of the hypertensive type has been much discussed for many years. As we have seen, it is a widespread condition as a rule, and so may be recognized before it has produced any effect on the cardiac muscle. Since the introduction of the sphygmomanometer some useful and much useless speculation has been printed. In certain cases it would appear that the thickening of the arterial wall is a direct result of hyperpiesis without kidney disease, while in others disease of the kidney appears to produce both. Over twenty years ago W. Russell¹¹ enunciated the view that arterio-sclerosis was due to the putrefaction of protein bodies in the intestine, and a few years ago Batty Shaw,¹² in his work on hyperpiesis, gave further support to that view. Treatment directed against the causes of hyperpiesis may then be of some value. The association of arterio-sclerosis and hard physical labour has not been clearly defined, though all conditions that tend to raise the blood pressure, even intermittently, over a long time may be expected to play a part.

Atheroma is more elusive even than arterio-sclerosis; there need be nothing in the patient to give a clue to the condition. Irregular in its distribution as it usually is, and not infrequently confined to inaccessible vessels, no history of its presence may be forthcoming till an accident, such as cerebral or coronary thrombosis, occurs. Its predilection for the aorta should direct attention to a careful assessment of all points that might assist in a diagnosis. It causes a weakening of the elastic tissue and leads to fusiform dilatation, which may be detected by x rays, by percussion over the manubrium, by palpation in the episternal notch, or by accentuation of the aortic second sound, these being of most value when the blood pressure is low and the Wassermann reaction negative.

With regard to the causes, one title—that of senile atheroma—suggests that it is a natural process associated with old age. Though resident physicians have been known to index cases as senility and enter them on dismissal as cured, the prospect is not so hopeful for those who have had a little more experience in their profession. It is scarcely possible to assign any cause for the condition in the present state of knowledge. It is essentially a degenerative process. Age, physical strain, infections, and disorders of metabolism have all been assigned as causes in different cases. The special susceptibility of the coronary arteries has suggested that one of the factors may be the constant buffeting they receive from the contracting ventricles, and it has been suggested that the relative predisposition of the descending branch of the left coronary artery might be explained by the position of the vessel in relation to the sternum.

In these remarks I am afraid I have only presented what are to me the difficulties, and have not added anything constructive to the treatment of these diseases. It is important, however, to face the facts, and not to rest content with merely treating what are, after all, the accidents superimposed on the primary condition. I have

attempted, and have only very imperfectly managed, to present you with the broad aspects of the subject. Diseases of the coronary arteries present a varied picture, and certain of the more dramatic aspects are apt to blind one to the fundamental condition. These remarks, however, will have been justified if they lead to a very general discussion this forenoon.

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THE ETIOLOGY OF GLAUCOMA.*

BY

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FROM the days when ophthalmology was first a science the etiology of glaucoma has given rise to investigations and discussions innumerable; to-day, although our knowledge has advanced, we are still quarrelling over the matter. I do not imagine for a moment that we have solved the problem, or that we have ended our quarrels; it is more likely that we are starting them afresh. But I would suggest that the trend of modern thought is throwing some new light upon the subject, and is introducing us to a completely new aspect of it. For too long the attention of investigators has been focused upon the gross pathological changes which have been observed in eyes excised for established glaucoma. The findings in these have almost invariably been interpreted as the essential causal factors in the disease, while it is more than possible that they may have been merely subsidiary causes, or even results. The essential cause is almost certainly something deeper and more subtle, and to discover its nature we shall have to go more deeply into the problem. Before we are in a position to understand pathological changes in the tension of the eye we must investigate first of all the more fundamental question of the maintenance of the intraocular pressure at its normal level and the variations to which it may be subjected under physiological conditions.

At the outset of any problem which concerns itself with the intraocular pressure the first matter to be settled is the nature of the processes controlling the formation of the aqueous humour; for these essentially must play the most predominant role in the determination of any pressure conditions, and, until agreement can be reached upon this, we can never arrive at a satisfactory or generally acceptable theory of the etiology of glaucoma. This is, indeed, the most fundamental question in the physiology of the eye, and, strangely, it is a question on which there is, as yet, a great diversity of opinion. To it I propose to suggest a very definite answer: the aqueous is not a secretion, nor is it, in normal circumstances, a transudate. It is, on the other hand, a dialysate of the capillary blood, formed by the same processes as the other tissue fluids, the only difference being that the process is modified by the relative impermeability of the ocular capillaries in order to allow the physiological requirements of the eye to be met. If the eye is to be an efficient organ of vision it is essential that its fluid contents be kept clear and practically free from colloidal micelles to allow the light to pass through undisturbed, and this is accomplished by making the capillary walls relatively impermeable. If the dioptric apparatus of the eye is to be kept properly adjusted it is essential that

the various elements in the refractive system be kept each accurately in its own proper position, a condition which is brought about by making the eyeball tense and filled with fluid under pressure; this again is accomplished, as we shall see later, by the same process of making the capillary walls relatively impermeable. The permeability of the capillary walls varies within wide limits throughout the body from organ to organ, and, in each organ, from time to time, adapting itself to suit the requirements of each peculiar case; thus, for example, in order that the functions of the liver may be carried out efficiently, the capillaries here are extremely permeable. By a modification of the same universal physiological process in the opposite direction, the eye has become biologically adapted as an organ of vision; no more simple means could have been chosen, and I know of no more beautiful example of the purposive and teleological activities of the living organism.

The argument which has led me to adopt this view would take too long to go into in detail. It is essentially a physico-chemical one, and in essence it is as follows: A dialysate in equilibrium with its parent fluid must have a very precise and definite chemical composition, it must have a very definite osmotic pressure, a definite reaction, a definite electrical potential, and there must be a definite relationship between the hydrostatic pressure at which it is maintained and that of the parent fluid.

During the past few years we have analysed the aqueous humour chemically, comparing it with the arterial and venous blood. We have measured its osmotic pressure, its electrical potential, its reaction, and determined the pressures in the chambers of the eye and in the arteries and veins. We have done it in normal conditions and in experimental variations from the normal, taking minute precautions against sources of error, and we have satisfied ourselves that the aqueous in all conditions is in complete thermo-dynamical equilibrium with the plasma—chemically, osmotically, electrically, and hydrostatically.

It must be remembered that these relationships are very complicated and very precise, and if the aqueous shows all these very complex properties, it seems illogical to deny that it is a dialysate in the absence of any definite reason to the contrary. There is no evidence, experimental or otherwise, which I know, or which I can find in the literature, and which will bear legitimate criticism, which can detract from this conclusion; to my way of thinking, at any rate, we are forced to accept it. Indeed, I think that the physico-chemical evidence which we have put forward is the most unequivocal obtainable. In the last resort the formation of the aqueous humour is a physico-chemical process. In a case such as this, anatomical evidence must be subservient to physiological findings. In much of the physiological work which has been done upon the eye confusion has arisen from a failure to appreciate the ease with which the normal equilibrium is disturbed, and many of the results lay themselves open to the criticism of reasoning from the abnormal to the normal. From this criticism a physico-chemical method of inquiry is almost entirely free. We can separate the aqueous from the influences of the complex changes which beset it *in vivo*, and in the isolation of the test tube we can determine with a very great degree of precision what the normal really is. Similarly, after introducing abnormal conditions, we can repeat the same process, and by comparison construct a coherent picture of the train of events as they have actually occurred.

The second fundamental question to be answered is that of the circulation of the aqueous humour. It is to be remembered that although I have used the word "equilibrium," the meaning is a dynamic and not a static equilibrium. All vital equilibria are of this nature. Three factors enter into the circulation of the fluid in the eye. There is in the first place a continuous metabolic interchange between the blood and the aqueous humour through the capillary walls, on either side of which the balancing hydrostatic and osmotic pressures are continually fluctuating, conditioning a flow of fluid now in one direction, now in another, so that the whole is continually renewed. Secondly, there is an internal thermal circulation caused by convection currents in the anterior chamber. More important, there is a through-and-through pressure circulation. We measured the pressure in the intrascleral

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