treatment. The importance of this group can hardly be overestimated, more particularly in view of a recent paper by Robinson,¹² in which 13 deaths occurred as the result of parturition in the 16 cases studied. Hemiplegia occurred in 5 cases, and death took place while under treatment in 14 cases, but this cannot represent the real mortality, for most of the patients attended the outpatient clinic, and such are frequently lost sight of, and cannot be traced. Poor results of treatment were obtained in 19 cases, presumably on account of extensive myocardial damage, although this was by no means always demonstrable by any diagnostic method—for example, in the exophthalmic goitre group. No digitalis was given to 14 patients, there being little or no sign of cardiac insufficiency.

Cases of typical auricular fibrillation are frequently reported in which the pulse speed is at, or about, 80 a minute, and, although grossly irregular, yet the pulse rise on effort is not great and the capacity of the patient for work is sufficiently high to allow him to continue fairly laborious occupations. It was in this group that no digitalis was used.

In a small number of cases there is a real difficulty in the administration of any digitalis, because the passive congestion of cardiac failure has itself already caused vomiting. It was thought that if the active principle of the drug were a glucoside, and glucose could be readily absorbed by the rectum, it might be possible to administer a massive dose by that route. The calculated massive dose of the tincture was so administered in two cases, but, although the enema was well retained, no effect upon the pulse speed was observed. This result corresponds well with results obtained by the administration of glucose by the rectum, in which no rise in blood sugar could be found, and it is probable that no absorption takes place.¹³

The treatment of auricular fibrillation by digitalis or its allies does not aim at the correction of the abnormal rhythm, nor at the cure of the causative condition, and no such result is attained. The drug is merely a means, and a very valuable one, for defending the ventricle adequately against the onslaught of auricular stimuli of high frequency, by which means the ventricle is given adequate diastole for reasonable filling and reasonable rest; apart from this, complete cardiac breakdown is both proximate and inevitable.

The principle underlying the quinidine treatment of auricular fibrillation is, of course, entirely different. Here a definite attempt is made to restore the normal cardiac rhythm. This line of treatment is not in the least applicable to patients showing any serious grade of cardiac insufficiency. In the majority of cases a preliminary course of digitalis is necessary to re-establish the circulatory balance, and it is usually believed that the high speed pulse is a definite contraindication to quinidine.

The question of potency in the preparation does not arise, since it is a crystalline substance of high purity, and is readily soluble in acid solution in the same way and much to the same degree as quinine.

The success of the drug turns upon the fact that the continuance of circus movement within the auricular muscle depends upon three factors—the length of the circuit, the impulse conduction time, and the refractory period of the muscle.¹⁴ Any considerable change in one or other of these three factors would terminate the circus movement, and quinidine has been shown to prolong the refractory period of the muscle to an extent sufficient to bring the circus movement to an end. Immediately this occurs the cardiac pacemaker comes into action, normal rhythm is re-established, and the auricular muscle performs a definite systole, thus once more filling the ventricle normally. The fact remains, however, that the primary cause of the state of fibrillation still continues, and that, therefore, relapse is almost inevitable ultimately.

It is generally believed that almost all cases of fibrillation can be forced into normal rhythm, provided quinidine be given over a sufficient length of time and in sufficient concentration, but my own experience is that when large doses are required normal rhythm does not remain long.

The present routine in my service is, in the first place, to reduce the pulse frequency to between 80 and 100 a

minute while at rest in bed. Quinidine sulphate is then given in 6-grain doses every two hours for five doses—that is, a maximum of 30 grains. Electro-cardiograms are taken before every dose, and examined, so that, should normal rhythm become re-established, no further quinidine is given that day. The next day the patient is given a mixture containing 1-grain doses of quinidine. This is taken three times a day, and is continued for six to twelve weeks. In my opinion quinidine administration is difficult, and probably should not be attempted, in the absence of electro-cardiographic control. Signs of toxic effect upon the heart are fairly frequent, even with the strictly limited dose detailed above, and although no untoward event has occurred, yet the rise in speed can be very alarming, even when adequate tracings are made every two hours.

In successful cases—those in which normal pacemaker rhythm becomes re-established—the patients themselves very generally recognize the difference, for the continuous palpitation of fibrillation completely disappears. Those that have been regularized more than once can frequently tell the precise moment at which the change from one rhythm to another has occurred.

In spite of the enormous theoretical benefit that should accrue when a fibrillating auricle again resumes a correctly timed and regular contraction, yet a considerable number of regularized auricular fibrillation patients consider themselves no better than they were when under adequate digitalis control. On the other hand, another group of patients will return immediately for further regularization whenever fibrillation recurs, because they recognize very clearly that their capacity for effort is very much higher under pacemaker rhythm than it can ever be during fibrillation.

However brilliant the results of quinidine administration may be in a small proportion of patients, it yet remains obvious that the routine treatment of auricular fibrillation must be carried out with digitalis.

This paper will have attained its object if it helps in any way towards an appreciation of the underlying processes of fibrillation, the objective of digitalis treatment, and, above all, an adequacy of dosage.

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Remarks

ON

THE CAUSATION OF ANGINA PECTORIS:

WITH A REPORT OF THE RESULTS OF SOME EXPERIMENTAL AORTIC LESIONS.

BY

R. CUNLIFFE SHAW, F.R.C.S.,

MANCHESTER.

THE failure of medicine to supply a consistently satisfactory method of treatment for angina pectoris renders necessary the careful investigation of any new procedure for which a claim of cure, or even amelioration of the symptoms, has been advanced. Such is presented by the introduction of surgery into this field, as instanced by the successful operations of Jonnesco, or of Coffey and Brown. On the correctness of the theoretical view of the causal lesion depends the justification for surgical intervention; if it be in the heart or aorta it is beyond the present scope of such procedure, but if the anginal syndrome is attributable to a nerve lesion or depends on the integrity of a nerve path, this line of treatment merits more serious consideration.

Any explanation must take into consideration two essential factors—the neurological element as shown by the operative results, and the cardio-aortic lesions as evidenced by their frequency. Theories that view angina as a neuralgia or paroxysmal neurosis are too nebulous to carry conviction; to disregard the almost constant vascular lesions is to ignore one of the principal features of this condition. On the other hand, to attribute the disease solely to derangement of heart action due to myocardial incoordination or insufficiency is to disregard the very definite neurological factor and the results of surgery. Hence the necessity for some link which will combine these two factors in an interpretation of the disease. With this objective in view, I carried out an experimental investigation the results of which form the basis of the theory of this paper. The details of this have been reported elsewhere;¹ it will suffice here to give a summary of the work.

Following up a line of thought suggested by the work of Todd and Stopford, who have shown that irritation of the peripheral nerves by injury or anatomical abnormalities such as cervical rib produces vascular degeneration in the distribution of the affected nerve, it was decided to apply similar conditions experimentally to the cardio-aortic nerves. For this purpose rabbits were selected and a number of experiments performed in which these nerves in the neck were subjected to chronic irritation, the animals being killed after intervals of several months. It was found that approximately 80 per cent. of the autopsies exhibited inflammatory plaques in the first part of the aorta, either near the valves or near the commencement of the innominate artery; further, the results showed that different stages of aortitis were represented, from early proliferation of the intima to the formation of atheromatous abscesses and the sloughing of the vessel wall in one case and to a diffuse aneurysmal dilatation in another. Generally speaking, the most advanced stages were observed in those animals that had lived the longest after operation. The most frequent lesion was a fairly well defined plaque due to proliferation of the intima and media; there was an increase of cellular elements and hypertrophy of elastic and muscle tissues, and frequently a slight fatty change in the intima. These experiments were controlled by a number of necropsies on rabbits that had been operated on under general anaesthesia with other objects, and had been kept under like conditions. In none of these cases were similar lesions found. In the heart, changes chiefly of a fatty nature were commonly present, but in a few instances there were other degenerative changes. The value of this latter evidence is unfortunately affected by the frequency of fatty degeneration in normal hutch-fed rabbits. In all the *post-mortem* examinations it was noted that the nerves operated on were firmly embedded in a small mass of scar tissue which it was the objective to produce, so as to have a slowly acting irritant increasing in its severity and thus to simulate the human lesions.

Manouélian has experimentally produced atheromatous plaques in the pulmonary artery and in the abdominal aorta by removal of the nerve supply, whilst the experimental results mentioned above prove that disturbance of the normal conductivity in the cardio-aortic nerves likewise results in pathological lesions, at first slight, but later gross, of the aorta and probably in the heart, though the evidence for the latter is not quite conclusive. Here, then, we have a connecting link between the nervous system and the cardio-aortic lesions. The hypothesis may now be stated: that angina pectoris is a group of symptoms primarily invoked by a nervous lesion, located either in the upper dorsal or lower cervical cord, its associated ganglia or their connexions, and that such lesion secondarily invokes inflammatory and degenerative reactions in the aorta and possibly the heart. These become progressively worse, thereby inducing a vicious cycle of irritation, which on the principles of induction and facilitation of synaptic resistance produces hypersensitivity of the sensorimotor mechanism of the heart, especially the vagal element, commonly resulting in sudden death in severe cases.

From the surgical standpoint the compatibility of this

hypothesis with the results obtained is sufficiently obvious. That Jonnesco's operation has gained the most success, judged purely on its effect on the angina, is readily understandable if the lesion is in the area supposed; that Coffey and Brown's operation alleviates but does not cure may likewise be explained, in that the more channels for the conduction of irritant impulses that are eliminated the more likelihood is there of the diminution of the severity of the symptoms; a cure in this way could not, however, be expected.

Some of the corroborative clinical evidence for this hypothesis may be briefly stated.

I.

In a number of cases the angina is accompanied by very definite signs of disturbance of function in the somatic nerves, more especially in the left arm, affecting the motor, sensory, and trophic elements. In the first-named category come paresis of arm or hand muscles, or transitory paralysis, as in the case reported by Bretschneider, or those mentioned by Allbutt, of increased myotatic irritability and exaggeration of reflexes such as the supination and triceps jerks. Under the sensory heading hyperaesthesia, analgesia, and anaesthesia have all been reported. In one most striking case recorded by Gibson all three sensory changes occurred in the left arm, and, what is more noteworthy, in the order which has been described by Stopford as characteristic of the syndrome of nerve compression. Under the last-named group muscle wasting, necrosis of the superficial layers of the dermis in the hand as reported by Salvini, herpetiform eruptions, and even lichen planus have been found in anginal cases. With regard to herpes an especially interesting case which I saw may be briefly mentioned, for it illustrates not only this condition but the occurrence of strongly neuritic prodromal symptoms in a classical case of angina.

A lady, aged 43, in an important executive position attended with much anxiety, complained in 1915 of pain and weakness in the left arm; in 1919 there was severe pain on the same side in the neck, post-occipital region, and arm; about March, 1920, she was troubled with breathlessness, tachycardia, and flatulence; severe pain came on in the fifth and sixth dorsal areas in the left side, followed by an outbreak of herpes. At this time the patient was subjected to increased mental strain and worry. In May of the same year, following a long and tiring motor drive, pain occurred in the left arm, and following dinner that evening she was struck with a sudden sense of constriction in the left side of the chest, followed by an inspiratory gasp, and then a severe stab-like pain in the back of the chest, which was in turn followed by a twisting and tightening sensation over the heart. The patient was doubled forward, unable to move or speak, and obsessed with the fear of death.

II.

In many cases, as discussed by Head, there is a dissociation of the symptoms, crises of peripheral neuritic pains, or of intrathoracic pain and sensations of cardiac oppression alternating with classical attacks of angina. If a nerve lesion be the cause it is conceivable that irritation of a particular group of fibres or cells might occur, occasionally producing either peripheral or visceral symptoms, whereas if all neuritic symptoms be the secondary effects of cardio-aortic disturbance it is difficult to see why at times such a lesion does not manifest itself clinically when the supposed secondary effects, the pain crises in somatic nerves, are very much in evidence.

III.

A nerve lesion located in the region presumed in this theory might be expected to exhibit clinical signs of irritation characteristic of the sympathetic—as, for example, in the vasomotor fibres, on the sweat excretory mechanism, on the ocular path, or, again, on the cardiac acceleratory mechanism. With respect to the latter it must be remembered that the rate of the heart beat must represent the algebraic sum of two antagonistic influences—the sympathetic and the vagus, with the latter normally predominating. The close association in the medulla between the accelerator and inhibitory centres might conceivably result in irritative impulses from the cord or ganglionic lesion stimulating either centre or both to equivalent degree, resulting in acceleration, inhibition, or no change in the rate of the heart beat. The severer the attack, the presumed great degree of irritation, the more probable is the

¹ *Quart. Journ. of Med.*, vol. 19, No. 74, 1926.

spread of the stimulus to both controlling centres, preventing change or even slightly augmenting the vagal inhibition. The same may be said of the vasomotor phenomena; the reciprocal innervation of vascular areas and their intimate adjustment by the principal and subsidiary centres in the medulla and lateral horn of the spinal cord would tend to prevent great extremes of vascular tone. In some cases the great variations in the volume flow of blood through the arms during a crisis, especially in the left, are well shown by plethysmographic tracings. With respect to the other nerve paths excessive sweat excretions and pupillary changes have been reported; these were specially noteworthy in Gibson's case, where the left pupil dilated and the eye became more prominent during an attack; and in the case Allbutt records, where "profuse sweating always preceded the attacks by half an hour." In several instances increased tonicity of the skeletal muscles is recorded; in Hunter's the attacks commenced with rigidity of the facial muscles. Alterations in muscle tone are especially interesting in view of the recent evidence relating this with the nerve terminals of Boeke and Agduhr, which are sympathetic in origin, possessing trophic cells in the sympathetic ganglion of the lateral chain.

IV.

Certain other concomitant symptoms are distinctly favourable to a neurological theory. The sense of cardiac oppression common to anginal attacks is reported by Lauder Brunton as being voluntarily produced in the case of Professor Cernak, who could compress his vagus against a cervical exostosis, when he experienced a sense of "Beklemmung" (oppression) in the chest. Several instances of pathological compression are recorded by Skoda, Allbutt, and others. Closely allied to this symptom is the sense of impending dissolution, the *angor animi*. Its affinity to angina has been noted by writers who support the aortic theory, and the rarity of this psychical phenomenon in other heart conditions, accompanied by lesions just as grave, is a singular fact. Mott records a case of cerebral tumour, accompanied by this feeling; does not this suggest that its anginal incidence is the result of irritation of higher cerebral centres?

Salivation is another symptom frequently encountered. The secretion of an abundant watery saliva is dependent on impulses passing through the chorda tympani, the geniculate ganglion, pars intermedia, to the nucleus of the fasciculus solitarius; there is a connexion thence with the upper part of the glosso-pharyngeal vago-accessory nucleus. The occurrence of salivation is readily intelligible if we suppose a nervous lesion in the lower cervical region sending irritant impulses to the medullary sympathetic and vagal centres. The occurrence of gastric disturbance is likewise to be expected in many cases; just as it has been shown that different sympathetic paths are stimulated so also are the vagal. Again, the relief of gastric distension by the passage of an oesophageal tube, as Verdon practised, would tend to prevent a vicious cycle of increased irritation from that region.

V.

The association of angina with mental irritation is a well known fact; the effects of nerve irritation on non-nervous structures have been described—what might be the effects of irritant impulses from the cerebrum on similar structures or on lower nerve centres?

VI.

Lastly, two cases may be mentioned illustrative of the relation between the nerves and the heart here propounded. In the first, reported by Tenier, a man sustained injury to the cervical spine, spondylo-arthritis developed and coincidentally the right heart became dilated, there was arrhythmia and a loud systolic murmur, all of which disappeared as the vertebral trouble subsided. In the second case, reported by Klippel, a man developed cyphoscoliosis, and gradually there came on complete hemiparesis of the left side, with sweating and dilatation of the capillaries, and loss of thermal sense on the right side of the body. During these changes there were four definite attacks of angina distributed over two years.

CONCLUSIONS.

Evidence has been given from the clinical side in which it has been shown that there are reasons for supposing the anginal syndrome to be principally the sum of irritation of several nervous paths, and that certain features indicate direct organic interference with those paths. From experimental pathology it has been found that a primary irritation of the cardio-aortic nerves is capable of exciting in the region they supply pathological lesions identical with those commonly found in angina. Finally, pioneer work in surgery has proved that complete extirpation of the left cardio-aortic sympathetic nerve and connexions may abolish the anginal syndrome.

It is therefore concluded that angina pectoris is probably due to a nervous lesion located in the region of the lower cervical or upper dorsal cord, the associated ganglia or their connexions, exciting secondary pathological changes in the cardio-aortic region; and lastly, that surgical intervention in suitable cases is justifiable from the theoretical standpoint.

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CHRONIC RHEUMATISM.*

BY

A. T. TODD, M.B.ED., M.R.C.P.LOND.,

HONORARY ASSISTANT PHYSICIAN, BRISTOL ROYAL INFIRMARY;
DEMONSTRATOR OF PATHOLOGY, BRISTOL UNIVERSITY.

By chronic rheumatism is meant the presence of aching pains and stiffness affected by changes of the weather. Excluding the subacute arthritis of young adults and children, with sudden onset, some pyrexia, and, as a rule, an obvious septic focus, and also the relatively rare cases of primary myositis and neuritis, we are left with three clinical types: (1) arthritic, osteo-arthritic, or rheumatoid; dominant; (2) muscular, with latent arthritis, commonly termed fibrositis; (3) neuritic, with latent arthritis, commonly termed neuritis.

Transitions are presented from case to case, and in any given case, so that they may be considered to be different manifestations of one disease. Exception may be taken to this classification—neuritis is regarded as a common disease. The non-arthritic neuritis is eased by rest and made worse by warmth and congestion; in secondary, or arthritic, neuritis the converse holds. Nine of every ten cases diagnosed as neuritis show latent arthritis. The same is true of the muscular type, and in both the most effective treatment is directed to the joints. In an arthritic case examination will frequently show that some of the joints are of the rheumatoid and others of the osteo-arthritic type.

It may occur in young subjects; patients aged 17 and 19 are being treated at present. It is more common in women, probably on account of their larger infectable surface and more rapid endocrine upheavals. A family history of gout or rheumatism is frequent. In the personal history contact with lead, hard work, exposure, poverty diets, humidity, and damp houses appear important, but are inconstant and therefore have a secondary value.

* A paper read before the West Dorset Division.