BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 27 1957

THE AUTONOMIC NERVOUS SYSTEM IN ITS RELATION TO SOME FORMS OF HEART AND LUNG DISEASE*

I. HEART DISEASE

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William Harvey performed several experiments on a son of Count Montgomery, a friend of King Charles I. The poor child had suffered a severe accident which left him with his heart exposed and its beating easily seen. Touching the heart produced no sensation. Therefore it was assumed that the seat of the soul was insensitive. What, then, is the cause of cardiac pain? Is it direct mechanical stimulation or the product of anoxaemia? Before trying to answer this question I should like to remind you of the anatomy and physiology of the cardiac nerve supply.

Anatomy

The sympathetic fibres arise from cells in the inter-medio-lateral grey columns of the first to the fourth or the second to the fifth thoracic spinal segments. They pass as white or mixed rami communicantes from the spinal nerves to the ganglia of the paravertebral sympathetic trunks. Communication with the heart is made by the superior, middle, and inferior cervical nerves. They all send many filaments to form the cardiac plexus, which is situated between the heart and arch of the aorta and between the aortic arch and tracheal bifurcation. The superior cervical sympathetic cardiac nerve also sends fibres to the pre-aortic plexus which overlies the ascending aorta. The thoracic cardiac nerves arise on each side from the second to the fourth or fifth thoracic sympathetic ganglia and enter the cardiac plexus directly, or having united and then parted from other sympathetic fibres destined for different mediastinal structures. Efferent accelerator fibres and afferent pain fibres pass in these nerves.

The parasympathetic nervous supply to the heart is by the vagi which have synaptic connexions in the ganglia of the cardiac plexus or in the intrinsic cardiac ganglia. The cardiac fibres arise in the neck and thorax in three groups—superior, middle, and inferior—which interconnect with sympathetic branches and other nerves (Mitchell, 1956).

From the cardiac and pre-aortic plexuses many branches containing sympathetic and parasympathetic fibres pass to the pulmonary vessels and cavae. Others pass to the coronary arteries, forming plexuses and supplying them. Much smaller fibres leave the vicinity of the coronary arteries and ramify over the surface of

the heart and penetrate the myocardium even as deeply as the subendocardial layer. The foci of impulse formation and the paths of impulse conduction in the heart are well supplied with bundles of nerve fibres. Finally, there are a number of intrinsic cardiac ganglia, especially in the atria and the atrio-ventricular grooves.

Afferent impulses arising in the heart travel centrally by the vagi and sympathetic nerves. There has been much discussion of the proportion of atria and ventricles supplied by each system. Much of the experimental evidence surrounding this discussion has been obtained by ablation experiments and subsequent observation of the site of nerve degeneration. One fairly widely accepted thesis was that of Woollard (1926), who was later supported by Nettleship (1936). It was found that after removal of the stellate ganglion there was considerable degeneration of nerve fibres in the media of the larger coronary arteries, but that there was much less degeneration in the smaller arteries and arterioles. It was thought that the larger arteries were supplied by both sympathetic and parasympathetic fibres. If this is so, it suggests that the parasympathetic mainly supplies the larger vessels of both ventricles but plays little part in the supply of the adjacent myocardium.

Physiology

Reflexes from the Cardiac Wall

Most of the information concerning reflexes from the cardiac wall has been derived from innervated heart-lung preparations or from cross-circulation techniques in which blood flowing through either side of the heart is isolated.

De Burgh Daly and Verney (1926) found that in an innervated heart-lung preparation with constant aortic pressure increasing pressure in the left side of the heart led to cardiac slowing. Subsequent workers have shown that this reflex arises in the left ventricle and is abolished by division of the vagi. Similar experiments on the right heart reveal that increasing right-sided perfusion pressure causes bradycardia and hypotension, which are not necessarily dependent upon each other. This reflex originates in the right auricle and again is abolished by division of the vagi.

It will at once be seen that the view of Bainbridge (1931) that the tachycardia of exercise is due to a rise

*The first Goulstonian Lecture, delivered at the Royal College of Physicians of London on January 17, 1957.

in right auricular pressure is contradictory to these experimental findings. Also, Lagerlöf and Werkö (1948) have shown that during exercise the right auricular pressure rarely rises and often remains the same or even falls slightly. It has been suggested by Kao and Ray (1954), using cross-circulation experiments in which the exercising hind legs of a dog are perfused by a donor animal, that the increased cardiac output of exercise is a neural and humoral mechanism originating from the exercising legs. This state of affairs is not true of diseased hearts, when exercise is accompanied by a rising right auricular pressure. In the fibrillating heart Blumgart (1924) found that exercise produced an initial slowing of ventricular rate followed by a prolonged increase. Atropinization of such patients eliminates these rate changes.

It is becoming increasingly probable that such rate and blood-pressure changes are due to varying pressure transients activating baroreceptors located in many parts of the heart and great vessels.

Reflexes from the Coronary Vessels

Inhibitor and constrictor fibres are said to predominate in the vagus, and dilator and accelerator fibres to predominate in the sympathetic nerves. Gregg (1950) reports that Eckstein *et al.* observed a considerable decrease in coronary inflow when the peripheral vagi were stimulated and in the presence of a somewhat lower blood pressure.

Stimulation of the stellate ganglion increases coronary inflow without necessarily a concomitant change in heart rate or blood pressure. It also increases the vigour of contraction.

Whether these are true reflex mechanisms remains unknown, and it is quite possible that they are chemico-metabolic responses. Similarly, despite a great deal of experimental work, there is no definite information that the autonomic nervous system plays an important part in the cardiogenic shock of coronary occlusion. After reviewing the available evidence Aviado and Schmidt (1955) state that: "The management of myocardial infarction is influenced by judgment as to the state of the heart and peripheral circulation. Those who regard a primary reflex vasodilation from cardiac receptors as a protective mechanism to reduce heart work while regarding a secondary reflex vasoconstriction from the low pressure in the carotid sinuses as harmful have proposed two procedures; veratrum alkaloids intravenously and procaine block of carotid sinuses. Those who regard the state of hypotension as harmful because it further reduces coronary blood pressure have proposed the use of pressor amines. These diametrically opposite therapeutic interventions epitomize the unsatisfactory state of existing evidence bearing on the significance of coronary reflexes."

Cause of Coronary Pain

The circumstance causing cardiac pain appears to be a disproportion between the inflow of the proper quantity of coronary blood of adequate quality, and the work of the heart. It remains unknown whether it is oxygen deficiency in coronary arterial blood which is directly responsible for stimulation of pain-carrying afferent nerve endings or whether oxygen deficiency alters myocardial metabolism, leading to nerve stimulation by excessive or abnormal metabolites. It is not disputed that relative anoxia is essential for the production of pain, but it must be realized that the metabolic effect of myocardial ischaemia is slight or absent if the oxygen supply and demand are proportionately reduced, as in hypothermia. When the oxygen-carrying capacity of blood is reduced as in anaemia, angina pectoris is likely, especially if there is pre-existing coronary narrowing. Breathing such a mixture as 10% oxygen in nitrogen is likely to provoke attacks of angina in those subject to them, although I do not wish to suggest that I regard such a manoeuvre as a test of coronary integrity, because I do not. Experimental occlusion of a coronary artery leads to myo-

cardial necrosis. It is therefore probable that myocardial anoxia of less intense degree and of briefer duration is invoked in the pain of angina pectoris. The pain of myocardial infarction is sometimes improved by inhalation of oxygen, even in the absence of pulmonary oedema and central cyanosis, presumably by increasing arterial oxygen tension and plasma oxygen content. When myocardial anoxia becomes extreme ventricular fibrillation is very likely, and, as Bing (1955) has pointed out, the metabolic changes within the heart muscle are then very extensive. The glucose, pyruvate, lactate, and potassium concentration in coronary-vein blood are elevated above those in arterial blood.

The problem of coronary spasm is also unsolved. The evidence in favour of its occurrence is the occasional attack of angina at rest unaccompanied by tachycardia; sudden death without evidence of major coronary arterial occlusion; and as an explanation for the mechanism of action of small doses of nitroglycerin when it is effective in relieving pain without alteration in cardiac output or blood pressure. The evidence against the occurrence of spasm is that tachycardia is far from universal even when coronary occlusion is known to have occurred; that properly authenticated reports of sudden cardiac deaths without arterial disease are very rare, especially if injection studies are made; and that, as described below, there is another explanation for the action of nitroglycerin. Coronary flow does vary greatly and is altered by various reflex mechanisms, but whether these changes are associated with primary changes of arterial calibre or are due to altered cardiac output on coronary arterial filling pressure is not known. I feel that, while spasm of any tube in the body may occur, until it is proved to me I regard it as a resort of the diagnostically destitute.

To this maze of contradiction and conjecture I should like to add further conjecture of my own.

A Curious Example of Anginal Pain

Mackenzie's hypothesis of segmental and extrasegmental sensory irradiation is used to explain the wide somatic reference of anginal pain and may extend to include any or all dermatomes from the third cervical to fourth thoracic, and the occurrence of facial pain indicates a very widespread irradiation. In rare patients in whom the peripheral site of the pain affects chiefly the temple, cheek, and jaw but spares the nose and central parts of the face, it suggests that there is a central origin and is consonant with excitation of the lower part of the sensory nucleus of the fifth nerve, which extends into the cord as far as the second cervical segment. Cardiac pain may be accompanied, or even replaced, by erythema or sweating in the area of pain reference. Also at the height of the pain there may be excess salivation, colour changes, and polyuria. Succeeding the pain there may be disordered muscle function and trophic skin changes. All these phenomena can hardly be explained otherwise than as viscerosensory reflexes excited by irradiation from cardiac ischaemia.

In 1945 Dr. Henry Miller and I had a patient under our care who demonstrated some of these things most dramatically (Miller and Daley, 1946).

An officer aged 48 was well until August, 1943. At this time, and at the end of a strenuous ten-day battle course, he was climbing a high wall when he had a sudden attack of severe gripping pain in the chest accompanied by breathlessness. At 3.30 the next morning he was awakened by a severe pain in the left elbow and forearm. Later exertion produced well-defined pain and tingling in the ulnar forearm and fingers, and if the exertion was continued the pain spread to the radial side of the hand and to the thenar muscles.

One day in October he was cycling uphill and already feeling rather breathless, when he suddenly became aware that his left eye was running and that tears were streaming down his face on this side. He attributed this to the cold wind, and when he dismounted his bicycle five minutes later there was a burning pain on the left side of his face affecting chiefly the temple, eye, cheek, and angle of the

lower jaw. At the same time he noticed that his left face felt warm and sticky. He lectured for nearly an hour in this condition, and was then suddenly seized by a severe pain which was mid-sternal and involved the whole of the left forearm and hand simultaneously.

From this time on all the severe attacks began in the same way—with watering of the left eye, followed by pain in the left face, which was observed to be warm, congested, and moist to the touch. He noticed that if he sat down at the onset of lacrimation the subsequent chest pain was much less severe.

He continued thus until mid-December. One afternoon, just as he was recovering from an attack of postprandial exertional pain, he had his photograph taken. When this picture came back from the printers he noticed that his left eye was practically closed. This was the first occasion on which ptosis was noted, and after this time he observed a gradual drooping of the left lid simultaneously with the onset of the other ocular symptoms in every attack. The ptosis was such that in a severe attack he could not see except by raising the lid manually.

When he inhaled amyl nitrite the chest and arm pain gradually disappeared over a period of time up to about fifteen minutes, depending on their severity. The pain in the face disappeared simultaneously, but the drug had no effect on the weeping or the ptosis. Careful inquiry showed that the weeping and ptosis were always accompanied by mild mid-sternal discomfort and dyspnoea, and always followed by facial pain, and then by chest and arm pain unless he rested absolutely at the onset.

The following observations were made during the half-hour preceding the onset of chest pain. The pulse rate showed no change, but the blood pressure rose. There was flushing of the whole of the left face with hyperhidrosis, extreme conjunctival congestion, left pupillo-dilatation with retention of normal pupillary reactions (evident only in a dim light and therefore sympatheticonic), striking dilatation of the retinal veins on ophthalmoscopy, and left ptosis of moderate degree and gradual onset. Electrocardiography during an attack showed inversion of T II. Conjunctival instillation of one drop of 1/1,000 adrenaline, carried out at his suggestion, revealed left sympatheticonia as shown by left pupillo-dilatation, the right pupil being unaffected. Radiological examination of the skull was normal.

The phenomena described above as preceding and accompanying the patient's attacks of angina pectoris are not easy to explain. The features shown in the face and eye appear to comprise two clearly defined components. First, there is evidence of irritation of the cervical sympathetic in lacrimation, hyperhidrosis, vasodilatation, pupillo-dilatation, and abnormal pupillary response to adrenaline. Secondly, there is evidence of a partial paralytic lesion of the third cranial nerve, in ptosis and paresis of the superior rectus muscle, producing diplopia.

Wide irradiation of different impulses in the spinal cord might be related to the first group of symptoms, but would not explain the second. Of intermittent pressure from a dilated or aneurysmal vessel within the skull the reverse is true. Yet the constant association and close time-relation of the two components of the syndrome indicate the probability of an equally close relation in their mode of production.

The sympathetic pupillo-dilator fibres originate in cells of the posterior hypothalamic nuclei, having connexions there with cortical levels, and they pass down through the medulla and cervical spinal cord in close relation with the pyramidal tracts, to terminate in the cilio-spinal centre situated in the lateral horn of grey matter at the levels of the eighth cervical to the second thoracic segments. Here pre-ganglionic fibres originate, and, passing out with the lowest cervical and upper two thoracic anterior roots, make their way via the white rami communicantes to the inferior cervical (stellate) ganglia. These fibres course up the sympathetic chain to the cell-station in the superior cervical ganglia, where post-ganglionic fibres arise to be distributed

to the eye by way of the coat of the internal carotid arteries and their branches. The sympathetic supply to the other parts concerned in Horner's syndrome—the tarsal muscles, the muscle of Müller, the facial sweat glands, and blood vessels—follow a similar, if less clearly defined, route.

These two pathways, the one afferent and the other efferent, therefore have part of their course (between the stellate ganglion and the spinal cord) in common, except that the bulk of the afferent fibres probably pass in the posterior, and the bulk of the efferent fibres in the anterior, roots of the same segments. More significantly, their cell-stations within the spinal cord are in close proximity. The cilio-spinal centre lies in the lateral horn of the grey matter between the eighth cervical and second thoracic segments, with the related sympathetic efferent cell-stations close by, while the synaptic connexions between the cardiac visceral afferents and the cells of origin of the spino-thalamic tract lie at the base of the posterior horns at the same levels of the cord.

In the present case, therefore, it is suggested that the sympatheticonic phenomena were due to central irradiation within the spinal cord. The nature of the recurrent partial paresis of the oculo-motor nerve indicates a peripheral lesion, recoverable and probably involving only the superior ramus of the nerve that supplies the two muscles involved (levator palpebrae superioris and superior rectus). The delayed onset and slow recovery of the third-nerve signs support a mechanical causation, and it is suggested that the paresis may have been due to local pressure on the superior ramus of the nerve by a dilated artery. The anterior site of the third-nerve involvement, and the failure to elicit any evidence of impaired function in the first division of the fifth nerve on repeated testing during and between attacks, suggest that the ophthalmic artery or one of its branches rather than the internal carotid was responsible, and in its distension both the widespread sympathetic vasodilatation and pre-anginal rise in blood pressure may have played a part.

This patient, of course, had most florid and unusual symptoms, but the following are more common. Facial pallor and sweating are often seen in patients suffering from myocardial infarction. At times the sweats may be drenching and sometimes precede by several hours the time when the infarction, as judged by other means, is believed to have occurred. On other occasions sweating is limited to the left shoulder or to the hand and arm, which is painful. I have seen a patient who had severe angina pectoris at rest in bed, and when it developed the painful left hand became as white as the sheet on which it lay and left a pool of moisture. The painless right hand remained pink and dry. Within a few minutes of the cessation of pain both hands become normal and alike. These phenomena are presumably sympathetically mediated.

The stiff and painful shoulder which may follow myocardial infarction, usually several weeks after the attack, is always more severe in the shoulder to which the pain is referred and hence is more common on the left side. The symptoms may vary from only mild stiffness to complete inability to use the shoulder, the so-called "frozen shoulder." They have a natural tendency to remission, as do "frozen shoulders" unaccompanied by heart disease, but this may take up to two years, and even then recurrence is likely.

When cardiac pain is particularly severely felt in one or other arm it has been followed by swelling and stiffness. At a later stage there may also be pain and swelling of the small joints of the hand with glossy skin, purplish-red discoloration, irregularity of the nails, trophic ulceration of the hand, and even a Dupuytren-like contracture.

The aetiology of these "shoulder-arm-hand" syndromes is far from clear. One theory has been that disuse of the shoulder has exaggerated a mild pre-existing periarthritis. Also, disuse has been blamed for the arm changes analogous to the changes in an arm after prolonged encasement in plaster. Such explanations are not satisfactory, because it

is not a feature of patients with coronary infarction to keep their arms still, and it is well known that angina pectoris is not precipitated by arm movements as in bench workers. An alternative theory is that as cardiac pain produces vasoconstriction the changes are due to anoxia. This, of course, does not adequately explain the occasional delayed onset, often several weeks after the cessation of cardiac pain, or that when "shoulder-arm-hand" stiffness and pain do accompany cardiac pain nitroglycerin relieves the latter and not the former.

As in so much of medicine, aetiology may be suggested by therapeutic response, and in this instance, while physiotherapy in its more conventional forms may alleviate, a most successful form of treatment is repeated stellate ganglion block. The aetiology which this suggests is no more than an implication of the sympathetic nervous system, but it is a beginning of understanding.

Excessive flatulence, bloating, and belching are well known to occur frequently with myocardial infarction or angina pectoris. Two examples of this stand out in my mind. The first, an obese middle-aged squadron leader at the end of the war was given a farewell demobilization dinner. At the end of the evening he had painless uncontrollable belching. He later had a sleepless night with a feeling that "I want a flue brush to clear my swallowing tube." He had a posterior infarction. The second patient did not have an infarction or even chest pain on exercise, but at the long second hole of his golf course he began to belch, and this recurred for about half the round before he literally lost his first wind. The occurrence of decreasing anginal pain on continued effort has, of course, been described before. Some months later the electrocardiogram became abnormal, revealing the cause of his disability.

This gas can clearly reach the stomach only by air-swallowing. The situation is somewhat comparable to the belching which often accompanies paroxysmal tachycardia. I have watched two patients who have developed paroxysmal tachycardia while being observed on the x-ray screen, and, as the paroxysm continued, so did the stomach fill with air. In them it was not excessive gastric distension which precipitated the attack but that during the attack uncontrollable air-swallowing occurred. This is regarded as a further example of a visceral-reflex mechanism.

Some Other Examples of Visceral Cardiac Reflex Mechanism

I should like here to discuss the relationship between the knuckle form of hiatus hernia and angina pectoris. The pain of such a hernia is usually felt beneath the lower sternum and may radiate to the back. Sometimes it may differ from this pattern and be identical with the pain of angina in that it is felt higher in the chest, radiates to the throat or one or both arms, and is provoked by effort. When it does this, successful repair of the hernia often cures the pain although it may recur several years later. There are two possibilities to account for this type of radiation of pain provoked by an oesophageal lesion. One is that oesophageal pain actually does so radiate; the other is that the pain originates in the heart and is induced by a disordered oesophagus. Support for the latter possibility comes from animal experiments: a balloon inflated in the lower end of the oesophagus in healthy anaesthetized dogs causes reduction in coronary artery flow as great as 50%. It could therefore be that, if coronary flow is already reduced by atheromatous coronary arterial narrowing, further reflex reduction in flow might cause anginal pain. I have actually never seen a hiatus hernia in a young person cause typical anginal pain with arm radiation, and believe that coronary arterial narrowing is necessary for its occurrence. This would explain why surgical repair of the hernia will produce relief of anginal-like pain for several months or years but the pain ultimately returns as coronary disease progresses, without the hernia having recurred. I understand that this is not always the experience of others, but one can only discuss what one sees.

There is considerable discussion concerning the relation of the gall-bladder to cardiac pain. I do not wish to discuss here the relationship between high serum cholesterol levels, gall-stones, and coronary atheroma, or the fact that pain from cholelithiasis can aggravate cardiac pain as can any pain anywhere else in the body. The sympathetic supply of the gall-bladder is usually via the fifth dorsal ganglion. If the supply happens to be too high or there is spread of impulses within the cord it is quite likely that gall-bladder disease may cause pain very similar in distribution to anginal pain. There is, however, another explanation. Just as the ingenuity of man has led to inflation of balloons in the oesophagus, so it has led to mechanical stimulation of the extrahepatic bile ducts (Allegrì *et al.*, 1956), and the effect on coronary flow appears to be identical. Once again there is a reduction in coronary blood flow, albeit with a concomitant reduction in systemic blood pressure. Which-ever explanation is used, the improvement in angina following removal of a diseased gall-bladder is often dramatic. The most interesting case of Friedberg (1951), in which infarction of a gall-stone coincided with myocardial infarction, does support the contention that there might well have been a sudden reflex diminution in coronary flow when the stone impacted.

Attempts to Relieve Cardiac Pain by Surgery

Two main approaches have been made in order to try to relieve cardiac pain by surgery. The first is by severance of the pathways of the afferent sympathetic pain. The second is in attempts to revascularize ischaemic areas.

Sympathectomy and Revascularization

Sympathectomy has suffered many vicissitudes, mainly because early attempts were too limited and removal of the stellate or cervical ganglia alone produced substantial pain relief only on very rare occasions. The credit for extending the operation to include not only the stellate ganglion but also the second, third, fourth, and sometimes fifth is given to White and Smithwick. The original suggestion that sympathectomy of some sort would help anginal patients came in 1899 from François-Franck, who was then professor of physiology in Paris. Pioneer operations were carried out by Jonnesco (1923) in Bucharest. Because of the variability of results Sir James Mackenzie in 1924 said that discussions on the painful mechanisms involved in angina pectoris were usually futile, as they simply consisted of the replacement of one speculative hypothesis by another. The pessimism of Sir James has not stood the test of time, and upper dorsal ganglionectomy is now a standard and satisfactory procedure. I have heard of unilateral operations producing pain relief when pain was strictly limited to one side of the chest or to one arm, and have been intrigued by reports of successful operations for right-sided angina in patients with dextrocardia, but the patients whom I have had operated upon myself have all required a bilateral operation. It is interesting in this connexion that Wyburn-Mason (1948) believes that the heart, embryologically, is a midline structure and has nervous connexions with the two sides of the body which correspond to its right and left components.

Following adequate sympathectomy there is usually complete relief of chest and arm pain, but the "warning" of angina is not abolished, as there is left mild, and not too unpleasant, pain under the jaw provoked by the circumstances causing the pre-operative true angina. This pain must be vagally mediated.

With this form of sympathectomy there is no suggestion that the calibre of coronary arteries is increased by the release of some sort of coronary spasm. What is dramatic at times is the decrease in heart rate, especially at the conclusion of operation on the second side. The heart, nevertheless, still has the ability to increase in rate after exercise, although not to the same extent as before operation. This must be due to vagal inhibition.

The second form of operation has many variations, but the common principle is revascularization. Such work was pioneered in this country before the last war by Laurence

O'Shaughnessy (1935). He brought a piece of omentum through the diaphragm and attached it to the scarified epicardium. In the United States of America Claude Beck has devoted many years to the problem, and one of his more recent ideas has been retrograde perfusion of the myocardium by introducing an arterial feed into the coronary sinus. Other methods have been the attachment of any adjacent structure to the heart such as pectoral muscle or lung, the adherence of the pericardium to the epicardium by the insertion of irritant material, and the fixing of the central bleeding end of one of the internal mammary arteries into a myocardial tunnel.

How do these operations produce relief of cardiac pain—and without doubt the majority of them do? With the O'Shaughnessy cardio-omentopexy it is probably from the records, which I have compared with those of Lindgren's (1950) extensive series of sympathectomies, that the expectation of life was not increased by the attempt to increase the vascularity of ischaemic areas of myocardium, although the great difficulties of assessing results must be stressed. The late Professor Barnard told me that only on very rare occasions was he able to demonstrate significant anastomotic channels between the omentum and the myocardium. In other anastomotic operations, such as stitching the lung or pectoral muscle to the myocardium, no adequate anastomoses have ever, to my knowledge, been shown when there have been adequate post-mortem injection studies. These remarks do not apply to the insertion of the proximal end of the internal mammary artery into a myocardial tunnel (Vineberg, 1954), for in this operation there is experimental evidence in its favour, and in any case it is too new for adequate assessment of long-term results.

Similarly, there have never been any proper post-mortem studies which clearly show collateral blood vessels between the pericardium and epicardium after the insertion of various substances into the pericardial sac.

Phenol and Talc

In an attempt to explain why pain relief is not accompanied by demonstrable increased cardiac vascularity I must make a short digression. In 1948 Mr. Norman Barrett, at St. Thomas's Hospital, had devised an operation to increase the vascularity of the lungs in children suffering from cyanotic congenital heart disease and inadequate pulmonary blood flow. He stripped the upper two-thirds of the pleura and inserted powdered asbestos in order to produce vascular adhesion between the chest wall and lung. These operations have, in the course of time, been shown to produce good clinical results.

However, on one occasion, instead of using asbestos he painted the lung with phenol. Three months later the patient returned to hospital, and a registrar thought that he would show, by artificial pneumothorax, that the lung was firmly adherent to the chest wall. The lung collapsed without any evidence of adhesions, but it was noticed that the original operation had resulted in Horner's syndrome. The presumption was that the sole effect of the introduction of phenol was to paralyse the dorsal sympathetic chain. Acting on this idea, Mr. F. B. Cockett successfully sympathectomized a number of dogs by painting sympathetic ganglia with phenol. Is this method of sympathetic ablation applicable to the cardiac nerves? Judging by a few recent reports such as that of Harken *et al.* (1955), and by some of our own patients at St. Thomas's, it is a satisfactory procedure, and direct painting of the epicardium with phenol prevents anginal pain in patients with ischaemic heart disease. In one of our patients, who subsequently died several months after this operation of a myocardial infarction, there were no vascular adhesions and his infarction was painless.

Is it possible that other operations in which the epicardium is injured cause relief of pain mainly because of nerve destruction? I believe that this is very likely. A study of patients operated upon by Mr. Kent Harrison who have had talc dusted into the pericardial cavity have often lost their anginal pain, but instead of being halted by pain they are

halted by dyspnoea. Electrocardiograms taken before and after operation show exactly the same depressions of the ST segment after equivalent amounts of exercise, and, interestingly, now dyspnoea rather than pain is relieved by nitroglycerin. If this idea is correct, then other conditions in which there is presumably firm attachment between the pericardium and epicardium should not be accompanied by the symptom of angina pectoris. This is in the main true, and while it may occur I have never seen a patient with constrictive pericarditis suffering from angina pectoris. Similarly, before operation about 10% of patients suffering from mitral stenosis have in addition angina pectoris. After operation, angina is exceedingly rare. Two of our patients who lost their anginal symptoms after mitral valvotomy became increasingly dyspnoeic two and three years respectively after operation, and cardiac failure and pulmonary hypertension compelled further operation. Neither had a recurrence of angina and both had adherent pericardiums and considerable mitral stenosis.

Patients suffering from aortic or pulmonary stenosis nearly always lose their angina after valvotomy, and I should like to submit that, independent of how satisfactory the valvotomy may have been, opening of the pericardium and the resulting haemopericardium can destroy sympathetic pain fibres.

I should like to quote two examples of the talc and phenol operations.

A crane repairer aged 55 developed typical angina pectoris in 1950. The pain spread across the chest and down the left arm to the wrist. It gradually became worse, so that by the end of 1954 he could walk 600 yards before meals, but only 10 yards afterwards. The pain never occurred at rest and was promptly relieved by nitroglycerin. There were no abnormal physical signs and the blood pressure was 140/90. In the electrocardiogram there was a little depression of the ST segments in leads V_1 and V_2 , which became more pronounced when he exercised until he had pain. In January, 1955, Mr. Kent Harrison performed a thoracotomy and put two teaspoonfuls of talc into the pericardial sac, which was free from adhesions. Since that time the patient has not used a nitroglycerin tablet and climbs to the top of cranes without difficulty. The electrocardiogram is unchanged and the ST-segment depression occurs after the same amount of exercise as before, but now is accompanied by dyspnoea.

An epileptic man aged 50 had an anterior myocardial infarction in 1950 which was followed by increasing angina pectoris until early in 1954; the distance which he could walk was only about 30 yards. The pain was felt across the chest and in both arms and the jaws. The blood pressure was 150/90 and there was loud presystolic triple rhythm. The electrocardiogram confirmed the old anterior infarction. In March, 1954, Mr. John Pullan performed a bilateral upper dorsal sympathectomy from thoracic ganglia one to four on the right, and one to five inclusive on the left. After the operation the patient lost the chest and arm pain, but his walking distance was not increased because of the persistence of jaw pain. As he insisted that something more must be done for him Mr. Norman Barrett, in January, 1955, performed a thoracotomy, opened the pericardium, and painted the coronary artery with phenol. This removed his jaw pain without altering his physical signs or electrocardiogram, but again he can walk no further than before, because he now has dyspnoea and right-leg claudication after 30 yards. I think that he must have had one of the most complete cardiac sympathectomies ever carried out.

This explanation of the mode of action of these operations does not mean that they should not be performed, because dyspnoea is a much less unpleasant symptom than angina pectoris. It has not happened to our patients yet, but it is conceivable that they might exercise "through" the dyspnoea and harm themselves. They should be warned to be careful.

Effect of Nitrites on Coronary Pain

While the effect of nitrites on coronary pain may not strictly come under the heading of some effects of the autonomic nervous system on the heart, the subject is worthy of discussion for the very reason that the mode of action of nitrites may not be via the autonomic nervous system. It is a remarkable state of affairs that so little is known

about the action of nitrites, although it was as long ago as 1867 that Lauder Brunton introduced amyl nitrite. As Gregg points out, the innumerable studies carried out with nitrites and other drugs on the isolated heart, the fibrillating heart, and the heart-lung preparation are not really significant, because not only can a drug have different effects on the hearts of two different preparations, but also the extra-cardiac effects may be so profound that they themselves alter the cardiac load or vasomotor state so that the local coronary effect is overshadowed. The only really valid experiments are those performed on the heart *in situ*.

In all experiments it appears that nitrites exert a vasodilating effect on the coronary vessels, but, as Gregg again states: "The fact remains, however, that alterations in coronary blood flow in the intact animal may differ significantly in extent and even in direction from what would be anticipated as a result of active changes in the size of the coronary vessels because of varying degrees of extravascular compression by the contracting cardiac muscle, changing cardiac output (mechanical, reflex, and metabolic effects), and alterations of blood pressure." The vasodilating effect could be a direct action on the coronary vessels, but it could be brought about by an alteration of cardiac metabolism or work.

Dr. Richard Gorlin (1955, personal communication) has allowed me to quote the results of his experiments with nitroglycerin in men. He found that the cardiac output remained essentially unchanged, but as the mean blood pressure fell there was a decrease in peripheral vascular resistance. The pulmonary capillary, pulmonary artery, and right auricular pressure usually decreased, and more strikingly in the more abnormal patients. There was no instance when the fall in right auricular pressure was greater than that in the pulmonary capillary; thus there was no change in pulmonary vascular resistance. Hence the work of the left ventricle may decrease but not that of the right as a result of nitroglycerin.

There is now, as a result of other experiments, a strong suggestion that nitroglycerin greatly alters myocardial metabolism. Bing (1955) produced coronary occlusion in dogs by injecting plastic microspheres coated with gum acacia. Apart from a drop in blood pressure he found that glucose and lactate appeared in increased concentrations in coronary-vein blood. Nitroglycerin is known to reverse these metabolic effects in man.

Therefore, nitroglycerin produces coronary vasodilatation and almost certainly has a metabolic effect, and the two may be related. The speed of action of nitroglycerin does not necessarily infer any reflex nervous path, and it can be agreed that other drugs such as adrenaline can produce a very rapid metabolic response.

Role of Sympathectomy in Cardiac Arrhythmia

Sympathetic efferent nerve impulses are concerned with cardiac acceleration, while vagal impulses are mainly concerned with slowing of heart rate, although Okinaka *et al.* (1951) believe that some of the vagal fibres are accelerator. Kuntz (1953) found that stimulation of the right vagus slows both auricles and ventricles proportionately and hence suggests that it may have its main action on the sino-auricular node. Stimulation of the left vagus did not appear to have much effect on the auricles but might produce partial heart-blocks. It is our experience in anaesthetized dogs that stimulation of either vagus reduced sino-auricular and hence ventricular activity. Stimulation of the sympathetic on either side in man or anaesthetized dogs causes cardiac acceleration with apparently equal facility.

Unlike the effect on most other blood vessels in the body, sympathetic stimulation leads to coronary vasodilatation and vagal stimulation to vasoconstriction. This is teleologically satisfactory, as with increasing heart rate there is increased vasodilatation. Knowing these facts, it is hardly surprising that upper dorsal sympathectomies have been tried for uncontrolled rapid heart-beating. I do not think that anybody has great experience of these procedures, but

they have been practised since, at least, 1928, when Leriche reported the successful treatment by stellate ganglionectomy of two patients suffering from paroxysmal fibrillation. One of these remained in normal rhythm for over four years. Since then infrequent reports have been published of the effect of sympathetic ablation on auricular tachycardia and fibrillation. White, Smithwick, and Simeone (1952) state that they think that alcoholic interruption of the sympathetic chain is not satisfactory and that attempts to predict the results of ganglionectomy by previous paravertebral injections of procaine are not accurate. Most surgeons now agree that the most satisfactory procedure is removal of the upper four or five thoracic ganglia, and they vary only in their technique concerning whether the stellate ganglia are removed or isolated. If these operations are successful the heart rate is satisfactorily reduced, but still has some, although less, ability to increase on exercise, and is probably due to vagal accelerator fibres.

There are three groups of patients in whom upper dorsal ganglionectomy may be reasonably considered. The first is in children with paroxysmal tachycardia which does not respond to usual therapeutic measures. Many of these children have no structural heart disease, and, provided they can be tided to puberty, have a strong tendency to spontaneous remission. Meanwhile, if they develop heart failure their life may be in jeopardy. The second is in adults with frequent recurrent paroxysmal auricular tachycardia, often considerably aggravated by emotion. This is clearly not a dangerous condition, but it can be most disabling, and at times the emotional storm may be so strong that pills even in poisonous dosage cannot quieten the turmoil and maintain normal rhythm. The third is in a few patients suffering from mitral stenosis and auricular fibrillation in whom digitalis is quite unable to slow the ventricular rate.

In the first group I have seen two children in whom sinus rhythm returned at the end of the operation and at least several months later the ectopic focus had not again become master. In the second group I have no first-hand knowledge of successful surgery, but in two such patients drugs have completely failed and surgery is seriously contemplated. In the third group of fibrillating mitral stenotic patients I have personal experience of four and am grateful for a report on a fifth. In my patients the ventricular rate was always between 120 and 160 a minute; it was not possible to revert them to normal rhythm with quinidine, and digitalis was ineffective in slowing the ventricles; failure persisted, as left ventricular diastolic filling time remained inadequate. In two patients a ventricular rate could be maintained after operation between 80 and 90 without digitalis. In the other two the fall in rate was not dramatic, but it became possible to control it with digitalis for the first time. Mr. Belsey and Dr. Davies, of Bristol, have kindly allowed me to report the following case.

A woman of 39 had the symptoms and signs of mitral stenosis following an attack of rheumatic fever. Fibrillation was occurring with a ventricular rate at rest of about 112 a minute. When any member of the medical staff appeared in the ward this increased to 170 or higher. Digitalis had no effect in controlling this, and at the time it was thought that she was quite unfit for mitral valvotomy. A bilateral upper thoracic ganglionectomy was performed which reduced her ventricular rate to the region of 80 and eliminated the tendency for the pulse to rise on the slightest emotional provocation. Her condition improved considerably, and eighteen months later a successful mitral valvotomy was carried out. Several years later she was still well and was doing a full day's work.

Another use of cardiac denervation procedures suggested itself to us a year ago for the treatment of Stokes-Adams attacks when the condition of the coronary arteries appeared to be reasonably good. In the absence of structural heart disease recurrent Stokes-Adams attacks are presumably due to vagal overactivity. Severance of the cardiac vagal fibres is not possible except in the region of the heart, because so many branching fibres are distributed to the heart from as high as the neck. Removal, therefore, of the cardiac plexuses involves removal of both sympathetic and parasympathetic systems. It is unlikely that sympathetic denervation

at that level has any positive disadvantage. The doubt only remains that denervation of the cardiac plexuses can be so complete that it is effective.

The following case report suggests that it can be.

A man aged 41 had repeated Stokes-Adams attacks for five years. Several of these lasted intermittently for up to seven hours at a time. The electrocardiogram showed complete heart-block, and during attacks there was ventricular arrest. The attacks could not be prevented or treated by ephedrine, atropine, adrenaline, or intravenous lactate. He was operated on by Professor Kimmonth, and the left antero-lateral side of the arch of the aorta was cleared of connective tissue and nerve fibres from before backwards. Further pieces of nervous tissue were removed behind the aorta and the pulmonary artery. The impression was gained that the superficial, deep, and para-aortic plexuses had been removed. Before the operation the heart rate was 34 a minute; at the conclusion he was in normal rhythm at 90 a minute. Eleven months later he had had only one attack of giddiness, but his doctor reported that his pulse rate had never been below 60 a minute. He was then back at work.

Summary

The autonomic nervous supply of the heart pursues a diffuse and complicated course in both its afferent and its efferent components. Its role is often in doubt, but slowly it is becoming clarified.

The nature of cardiac pain is discussed and the metabolic changes consequent upon myocardial infarction are stressed. Coronary "spasm" has no factual evidence to support its occurrence.

A case is described in which the patient suffered a variety of autonomic disturbances when he developed cardiac pain; they are best explained by central radiation within the spinal cord.

The "shoulder-arm" syndrome and excessive flatulence, sometimes associated with coronary artery disease, are probably concomitant autonomic phenomena.

The association between cardiac pain, gall-bladder disease, and hiatus hernia may be more than reduction of pain threshold, and either condition may cause reduction in coronary arterial blood flow.

The evidence is that most operations designed to re-vascularize ischaemic hearts diminish pain by destroying sympathetic afferent pain fibres.

Upper dorsal sympathectomy and direct denervation of the heart may well have a place in uncontrollable auricular fibrillation and sometimes in repeated Stokes-Adams attacks.

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TREATMENT OF COMPLETE PROLAPSE OF THE RECTUM

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The conflicting reports on the results of treatment of complete prolapse of the rectum have caused confusion, and this is reflected in the large number of operations which have been advocated for the condition. Dickson Wright (1949) was able to find 51 procedures described in the literature up to 1949, and more have appeared since. In this report we describe the two types of operation we have performed since 1951 and record the progress results; we have endeavoured to correlate this experience with published reports.

In complete prolapse of the rectum there is a peritoneal sac extending distally between the vagina (or prostate) anteriorly and rectum posteriorly. As such a peritoneal sac may be present without rectal prolapse it is probable that the latter appears only when the pelvic fascia and the muscles surrounding the pelvic aperture are defective.

Present Series

Since 1951 we have operated on 30 patients suffering from complete prolapse of the rectum. In each case the rectum prolapsed at least 3 in. (7.5 cm.) and in some cases as much as 9 in. (23 cm.). There were 28 females whose ages ranged from 27 to 87 years (average 54), and 2 males aged 36 and 40 years. One patient was very obese and another very thin from malnutrition; one patient had long-standing cardiopasm with secondary nutritional changes; a fourth patient had severe rheumatoid arthritis with almost complete fixation of the hip-joints; a fifth had had an amputation of an arm and a leg in the past for an obscure vascular disease.

The series has been divided into two groups according to the type of operation. In group 1 are 17 patients who were operated on between July, 1951, and November, 1955, and in group 2 are 13 patients who were operated on since January, 1956.

Treatment of Patients in Group 1

Each of the 17 patients in group 1 was subjected to a synchronous combined operation. The patient was placed on the Lloyd-Davies lithotomy-Trendelenburg leg-pieces. Through a lower midline incision the abdomen was opened and the small intestine displaced from the pelvis into the upper abdomen. The fundus of the peritoneal sac, having been freed by the perineal surgeon, was grasped from above, invaginated into the peritoneal cavity, and amputated. The pelvic peritoneal cavity was obliterated as completely as possible with multiple encircling purse-string sutures and the abdomen closed.

The perineal surgeon exposed the fundus of the sac through an incision placed between the vagina (prostate) and rectum. After pushing it through to the abdominal surgeon a perineorrhaphy was performed by suturing the puborectalis and pubo-coccygeus muscles and related fascia together with chromic catgut size 2, anterior to the rectum. In 14 of these patients additional reconstruction was carried out behind the anal canal. A longitudinal incision behind the anus was deepened through the coccygeal attachments of the external sphincter and levator ani muscles and the fascia of Waldeyer to enter the presacral space. The rectum and