ANGINA OF EFFORT

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Angina of effort was first described by Heberden in 1768 under the title of "Angina Pectoris." The typical form is a very common syndrome, the diagnosis of which is obvious to the observer with previous experience of the complaint. There are many atypical forms which require much closer consideration to distinguish them from other conditions characterized by chest pain.

Chest pain is the cardinal feature in angina of effort; the pain is induced by exertion, for example, by walking, and is quickly relieved if the patient stands still. Careful consideration must be given to a detailed history with special reference to the pain. It is on the history and the response to treatment that the diagnosis rests rather than on the investigations.

The pain is classically severe, but may be any grade from an ache to an agonizing pain. It is often described as a sense of constriction around the lower or middle chest, "like an iron band" or "like being gripped in a vice." The pain is usually substernal in origin, or a little higher up, and typically radiates to the left arm, running down the inner side, sometimes as far as the ulnar border of the hand and the ring and little fingers. However, it may radiate to the right arm or to the back, when it is usually the right subscapular region which is affected. It radiates sometimes to the angle of the jaw, and rarely to the abdomen. In a few cases it remains fixed in the substernal region without radiating at all.

The pain lasts from a few seconds to thirty minutes, but rarely more than a few minutes unless the movement producing it is continued. It lasts longest when the attacks are produced at rest, which occurs in the later stages of the

disease. As soon as the walking or other movement is stopped the pain begins to pass off, only to be brought on again if the same action is carried out. The patient may notice his pain coming on at approximately the same part of a hill which he climbs each day, or he may notice that the same movement always causes it. The pain may be brought on by excitement, anger, or other severe emotion, but these are never the only factors.

A heavy meal may bring on the pain, especially when followed by exercise. Some patients notice exposure to cold brings on an attack, and heavy smoking has been suggested as a cause. None of these, however, are found alone without muscular effort as an accompanying factor, and if there is no pain on effort, the diagnosis should be reconsidered.

The pain usually stops the patient as he walks or carries out some energetic movement. He stands, pale and anxious, but without shortness of breath, and slowly his pain passes off. There are few accompanying symptoms, and often no accompanying signs. The heart is unaffected clinically, and the pulse rate and blood pressure little altered.

Angina of effort is much commoner in males, especially in those over forty, but can occur at almost any age. When it occurs in young people it may be due to rheumatic heart disease with aortic regurgitation. This causes a poor blood supply to the coronaries and hence angina. This has been the view in the past, but recently American observers have described many cases in young soldiers who are overweight and subjected to heavy strain.

Angina is much commoner in the professional classes and in brain workers leading a sedentary life. The white race is more prone

than the coloured races, who rarely suffer from it. Dock shows an interesting anatomical possibility as a background for these aetiological influences. He states that the coronary arteries of males are thicker in their intima than in females, and that this thickening is markedly found in the more susceptible races who appear to live on a diet relatively rich in cholesterol. As angina is commonly associated with coronary disease and coronary insufficiency, it may well be that the diet of civilization is a strong predisposing factor and that the male, by reason of his coronary intima, is a more likely subject for it.

Angina is becoming an increasingly common disease, probably as the result of the stress and strain of modern existence, and in association with the increased prevalence of arterial disease and early arterial degeneration. It is invariably caused by coronary insufficiency, this in turn arising from atheroma, hypertension or other cardiovascular disease. The commonly accepted theory of the cause of the pain is that coronary insufficiency produces anoxaemia of the cardiac muscle, so giving cardiac pain, although the exact mechanism is in some doubt. The coronary arteries are nearly always abnormal in cases coming to post mortem.

Syphilis predisposes to angina through its action on the aorta and the aortic valve, causing an adverse effect on the blood flow to the coronaries. Anaemias, especially pernicious anaemia, cause anoxaemia sufficient to produce angina when ordinary work is being done. As soon as the anaemia is treated the anginal attacks disappear although the electrocardiographic changes, according to Hunter, may be permanent. Thyrotoxicosis, by unusual demands on a toxic heart muscle, can produce typical pain, but the angina clears up if the thyrotoxicosis is treated. Other infections involving fever and toxæmia increase the heart's work while undermining its efficiency, and may produce angina in a susceptible person. Other conditions which play a part are obesity, diabetes, gout, myxoedema, vitamin B deficiency, and possibly heavy smoking.

Angina was found in 43 out of 1,560 cases of pernicious anaemia by Willis and Griffin, but certain differences were noticed. The pain was seldom the presenting symptoms, and

when present, remained relatively fixed and did not radiate as in angina of effort. Many writers have denied that anaemia can give angina by itself, but post mortems on anaemias with angina, do not always disclose coronary arterial disease. Out of 34 cases of mixed anaemias described by Hunter, 8 had angina, and successful treatment of the anaemia cured the pain in all. This is the usual finding, and serves to distinguish angina of effort from angina secondary to anaemia.

Similarly, angina arises in thyrotoxicosis, but tends to occur only in the early stages of the disease, and again tends to be more localized in site, and responds dramatically to effective treatment. This forms the basis for the suggested form of treatment by surgery, which will be discussed later.

Diabetes mellitus predisposes to angina of effort because of the relative frequency of atheroma and hypertension. Treatment of the diabetes tends to improve the angina, but the arterial changes are largely irreversible, and therefore the angina cannot be effectively altered, even with control of the diabetes. Gout also causes arterial disease with resulting angina through the consequent coronary insufficiency. Any other disease leading to widespread arterial damage will work similarly through coronary disease. Examples of these are Buerger's disease, chronic lead poisoning, and Paget's disease.

Paroxysmal auricular tachycardia may initiate or increase attacks of angina, but auricular fibrillation and angina rarely appear together, and seem to be antagonistic.

Excess of smoking has been blamed by many for angina of effort, and appears to play some part in its causation. It has been shown experimentally to constrict the coronary arteries, but how often this occurs in the human being is open to some doubt. Patients often state that their attacks are less severe and frequent when their smoking is curtailed.

Friedman has described an interesting type of angina associated with abnormal sensitivity of the carotid sinus. In this syndrome a typical anginal pain is experienced on sudden movements of the head, whether associated with other actions or not. The case described felt faint and had a fall of blood pressure, and syncope as a late effect, these symptoms being

reproduced by experimental massage of the carotid sinus.

Another cause of angina is hypoglycaemia in susceptible subjects with labile blood sugar levels and sensitivity to changes. In these people, starvation followed by exercise, not only produced faintness, but also an angina indistinguishable from ordinary angina of effort.

The degree of disease underlying the symptom angina of effort may be very variable, some patients having a much greater sensitivity to pain than others. Thus one will experience frequent severe pain and limit his activities early in the course of the disease, while a less sensitive subject will persist with his muscular efforts as he experiences little or no pain.

The course of the disease is variable, but the attacks tend to get more frequent and come on with less and less effort as time goes on. The patient may die in his first attack of pain or live for thirty or forty years after it. Commonly up to ten years will be the expectancy of life, depending largely on how the patient orders his life.

The course of the disease cannot be estimated by the degree or frequency of the pain unless the symptoms are progressive, as the patient suffering the minimum of pain, and having a short history, may have the maximum underlying disease, and may drop dead in an early mild attack. The prognosis is, therefore, a difficult one, and the wise physician is guarded in his outlook, being guided by the signs of underlying disease if present, and the progress of the patient, and his ability to live a restricted life with advice and treatment. The prognosis is better in the nervous or sensitive patient, as he will be more likely to live within the capabilities of his heart, and will stop muscular efforts before over-exerting himself. There is always the possibility of some complication such as coronary thrombosis occurring, but on the other hand, there is also the possibility that anastomotic vessels will bring collateral circulation into being, and so increase the coronary flow and cause the angina to disappear or lessen. Death of an area of heart muscle may cause the pain to cease—this occurs as the result of a coronary thrombosis.

The prognosis is also determined by the

temperament and wishes of the patient. He may desire to live a shorter but more active life on one hand, risking curtailment for a more enjoyable or profitable existence.

Angina which arises at rest is an adverse factor in the prognosis. This occurs on lying down and is usually seen in patients who have got frequent anginal attacks with the minimum of effort. Relief from the pain is gained on sitting or standing up, the cause of the pain while lying down being due to the increased work the heart has to do in the prone position, and to the lower blood pressure, with consequent poorer coronary circulation. Another factor, in the prone position, is the rise of the abdominal contents with consequent pressure on the heart.

Rest and adequate treatment can influence the course of the disease considerably, but there is some dissension of opinion as to whether a period of complete rest is beneficial or not. Most observers advise a period of complete rest, when the symptoms first manifest themselves, in the hope that the coronary circulation may recover sufficiently to allow of relatively normal activities.

The diagnosis of angina of effort rests almost entirely on a close consideration of the history and the progress of the case. There are no typical concomitant signs, although the heart is usually enlarged and various irregularities of rate or rhythm may be present. Frequently, atheroma of the arteries may be detected in the peripheral or retinal vessels.

The electrocardiograph shows no typical changes, but certain changes occur relatively frequently and may arise when the patient exercises enough to induce an attack of angina, or when he is subjected to an atmosphere with an artificially reduced oxygen content. Typically one or more of the T waves in the limb leads is inverted during the attack, if not in between attacks, and the R.T. segment is often altered in its take off. It can also be shown that the electrocardiograph changes do not occur with the same amount of exercise if a suitable drug such as one of the nitrites is given beforehand.

The differential diagnosis is often very difficult without a clear history and needs a period of observation. It involves a consideration of other forms of chest pain. The most

difficult conditions to distinguish are the so-called pseudo anginas associated with neuro-circulatory asthenia, effort syndrome, or the type found in females nearing the menopause. In all these latter, there is a cardiac neurosis, a fixation of ideas on the heart and its functions, and a pain experienced, irregularly, on varying degrees of effort, and on occasions without exercise. The pain is almost invariably fixed and localized to the apical area where the patient imagines her heart to be. It is relieved equally by drugs other than nitrites, and is open in some degree to improvement or otherwise by suggestion. It is usually accompanied by many other symptoms, chiefly palpitations, dyspnoea, faintness, and a feeling of ill-health. These conditions have no physical signs other than a fast pulse rate and a poor general physique. There is a good response to sedatives, rather than to nitrites.

Angina of effort is to be distinguished from chest pain due to congestive heart failure or other cardiac disease. These latter pains are all relatively fixed and more constant and longer in duration, and respond to different treatment. The pain of coronary thrombosis is relatively easy to distinguish as it is more severe and prolonged, and more fixed to one site, and is usually accompanied by lowered blood pressure and some symptoms of shock and collapse. It may also radiate through to the back or upwards to the jaws in coronary thrombosis, but it nearly always begins at rest or after a heavy meal. It does not respond well to nitrites. Pain due to ectopic tachycardia has already been mentioned as a cause of similar pain, although again the response is to different treatment. In a series of 77 cases of angina of effort described by Harrison, none had sharply localized pain, but on the other hand, only 50 per cent. of them originated in the substernal region.

Other causes of chest pain have to be distinguished from angina. Dyspepsia is so often associated or confused with it, that careful consideration must be given to any case of pain in middle aged people which does not have a definite intestinal origin. Thus cardio-spasm, or spasm of the oesophagus, may closely simulate angina in type of pain and distribution, but it is not produced by effort or relieved by rest. Radiological investigations

of the intestinal tract should distinguish them if there is difficulty with the history, and response to treatment is also helpful. Pain originating in the stomach may simulate true angina in its radiation and intensity, but it is usually relieved by alkalis and has relation to food rather than to exercise. Stimulation of the stomach may cause constriction of the coronary arteries and true angina, in those already liable to attacks, and sometimes a combination of conditions is present. Pylorospasm, aerophagy, herniation of the stomach and 'cascade stomach' are all gastric conditions which may give rise to difficulties in differential diagnosis.

Cholecystitis or other forms of gall bladder disease may initiate attacks of angina reflexly, and this has to be distinguished from radiation of gall bladder pain alone. Sometimes angina of effort is improved or temporarily 'cured' by cholecystectomy. On the other hand, spasm of the muscle of Oddi after cholecystectomy may mimic angina closely (Clark).

Many other conditions such as tabes, herpes zoster, aneurysm or osteoarthritis of spine may lead to initial confusion, but the history usually differentiates them relatively easily, and investigations make the diagnosis definite. Carcinoma of the bronchus must always be considered as a cause, and a radiogram of the chest taken.

It only remains to consider the treatment of angina, which resolves itself largely into an organization of life and habits so as to prevent pain, and the use of one or two well-tryed drugs. There is little dissension in the former, but fresh drugs are constantly being tried in an effort to find one which will meet all the requirements. The attack of angina itself brooks of no delay in treatment and a sufferer quickly establishes his own measures for temporary relief. He learns that a certain amount of exertion will bring on a spasm of pain, and that standing still will enable the pain to pass off. Soon he knows just how much effort he is capable of taking without initiating further attacks, or at any rate, without having frequent attacks, for so many imponderables affect the onset that he will probably have some attacks in spite of all efforts to prevent them. A period of complete rest in the early stages of angina pectoris may well keep the condition at bay

for a considerable time, as collateral channels of coronary circulation may then be opened up.

The patient will have to lessen his general activities, and avoid precipitating factors. This means he will have to avoid strenuous exercise, large meals, or exercise soon after meals, undue exposure to cold, or exposure to cold following a meal, and excitement or excessive emotion of any description. Excessive smoking should also be avoided and only a minimum allowed, as patients have found that smoking in any amount does tend to increase the frequency of attacks. Certain experimental evidence is in favour of this, as nicotine is shown to cause some constriction of the coronary vessels.

A holiday away from all the usual energetic occupations may well be beneficial in the early stages of the condition, and a complete physical and mental relaxation may benefit the underlying condition by enabling the heart to become adjusted to its altered arterial supply.

Any underlying or associated disease capable of treatment such as anaemia or thyrotoxicosis should be treated energetically, and this may in turn benefit the angina enormously.

After consideration of general measures, drugs for the attack, and drugs for prevention of the attack, need to be considered. Little advance has been made in this treatment except in a negative direction, as one drug after another has been tried and found of little use. Stokes states 'Glyceryl trinitrate has had no equal in the relief and prevention of the anginal attack,' and with this statement few observers would quarrel. The nitrites have an established place by themselves in the treatment of angina. Evans and Hoyle compared the effects of a wide range of drugs in the prevention of attacks, and in the reduction of the pain, and showed that none could be relied on when compared with controls or the use of placebos.

Several nitrites have been tried, ranging from the rapidly acting amyl nitrite to erythrol nitrate, but the intermediate glyceryl trinitrate has been found best for common use. Amyl nitrite (m, 1-3) in capsules works very quickly, but the effects pass off equally quickly. It is put up in small ampoules which are crushed and the contents sniffed. The result is vasodilatation which also affects the coronaries,

but produces unpleasant banging in the head and other side effects. The ampoules are expensive when used frequently.

Glyceryl trinitrate is used in tablets of gr. 1/100, gr. 1/120, or gr. 1/200. The tablets should not be allowed to get old and hard, and should be quickly absorbed from under the tongue. It has less severe side effects than amyl nitrite, is longer lasting, cheaper and easier to carry. A tablet can be taken before any effort which has to be carried out, and which has previously produced attacks of angina. One or two daily may be taken prophylactically or reserved for special efforts. No bad effects seem to arise from using them habitually and in frequently repeated doses.

Erythrol nitrate (gr. $\frac{1}{4}$ - $\frac{1}{2}$) is a slower acting and longer lasting drug of the nitrite series, taken in tablet form by the mouth. It lasts several hours and takes about half-an-hour to act.

All other nitrites are of little use clinically, and in practice, glyceryl trinitrate is invariably the drug of choice. If it is not available in an emergency, a few ounces of whisky or brandy will soon ease the pain, but rest will usually do this equally well, and there is always the risk of chronic alcoholism if the drug is used and found to work. Inhalation of ether used to be used, but has been given up owing to its slow action and its side effects. Other sedative drugs are useless for the pain, but help to control the excitement or nervous element which may help to set off an attack. It is thus customary to take a small dose of phenobarbiton, for example gr. fs. b.d.

The next most useful drugs, a group of purine derivatives, act by dilating the coronary arteries over a period, and increasing the blood flow to the heart, and thus lessening the chance of anginal attacks. Not all observers have agreed on the extent of their efficiency, but they appear to act symptomatically in many patients, and the small group of hypertensive angina patients do particularly well on these drugs. Theobromine and theophylline, and their derivatives are the chief members of this group. The most commonly used in this country are cardophyllin, aminophyllin, and diuretin, and they are prescribed in tablet form over a long period. Unpleasant side effects are seldom experienced, but flushing

and nausea have been described. Steinberg and Jensen gave theophylline a clinical trial and came to the conclusion it had little effect on the acute attacks, but it remains as a factor in treatment over a long term period.

Another drug to be tried widely is nicotinic acid. Stokes conducted a clinical trial of this in comparison with nicotinamide, glyceryl trinitrini and placebos. His conclusions were that there was no appreciable effect with any except glyceryl trinitrini, and unpleasant side effects such as flushing, fainting and drop in blood pressure, occurred with nicotinic acid. If the nicotinic acid was used in large dosage it did, in some cases, prevent the irregularities of the R.T. segment and the T waves occurring, which otherwise arose on exercise or artificially produced anoxaemia. It did not, however, keep the electrocardiograph normal as long as with the nitrites, and the side effects were much more unpleasant.

Gray investigated the use of papaverine hydrochloride and found that large intravenous dosage (200 mgm.) had to be given for a limited temporary effect to allow exercise to be taken. By mouth there was no appreciable result and unpleasant side effects arose with the intravenous dosage.

Recently, sex hormones have had a vogue, and there is still conflicting evidence on their efficacy. Strong and Wallace report 20 cases of angina due to arteriosclerosis, six of which they claim showed marked improvement, 11 only moderate, and the rest, none. They had treatment with 25 mgm. of testosterone propionate daily by injection for four to five days in the males and 5 mgm. of oestradiol daily in the females. Their conclusions were drawn from the amount of glyceryl trinitrini necessary, and the frequency of attacks with hormone treatment compared with nitrites alone. Various tissue extracts have also been tried, but found of little use.

Many other drugs have been tried, but none have survived to become of use in the patient with angina.

Surgical measures have been tried for some time and are still being developed. There are none of proven worth as yet, but increasing use is being made of some of the operations.

Surgery offers three modes of attack on the problem. First thyroidectomy has been tried

in an effort to reduce the basal metabolic rate, and the blood requirements of the heart muscle, and so allow the diseased coronaries to suffice for their work. It is a severe operation and apart from the initial risk and the questionable result on the heart, the myxoedema resulting may produce still further arterial disease.

Recently thiouracil has been given in an attempt to lower the basal metabolic rate, and so directly relieve the pain. As it has to be given over a long period, to a person with a normal basal metabolic rate, to produce a fall, the risks of toxic effects are greater, and therefore its use is only permissible in severe anginas in whom other measures have failed, or where there are contra-indications to other methods. If thiouracil is given, the dosage should be small, in the region of 100/mgm. daily, and frequent blood counts should be undertaken to preclude leucopenia and agranulocytosis.

The second approach is to give a better blood supply to the heart by anastomosing other tissues, to bring in a collateral blood supply. Thus cardio-omentopexy aimed at bringing blood from the abdomen to the heart muscle, and Beck joined the subpectoral muscle to the heart with a similar idea. Neither of these operations have been widely practised and are big undertakings. Further evidence of their success will have to be produced before they can be advised.

The third surgical measure is to attempt to relieve pain, and possibly increase the coronary circulation, by cutting out the sympathetic nerve supply. This has been practised for 30 years by means of different techniques and approaches, and various operations have been devised for sectioning different parts of the sympathetic system thought to control the heart and coronary flow. Recently a big stimulus has been received by the work of Smethwick and others in America using extensive operations involving thoracic and abdominal approaches. The operations have been devised and used primarily for the treatment of hypertension, but sufferers from severe angina who can be judged to have good enough general health to stand up to such a severe operation, have also benefited from it in carefully chosen cases. This seems a

promising field of surgical therapy in the future for relief of pain, but apart from the surgical mortality, there remains the danger of 'painless coronary thrombosis' or other cardiac complications if the warning signal of angina is removed. Many patients will carry out tasks too great for their deficient coronary circulation, and without any warning of danger, will incur severe cardiac complications.

Finally, a word may be said for the minor surgical manoeuvres. The injection of novocaine into the pectoral muscles may, in some not clearly understood way, prevent the attacks of angina for a considerable time, and the injection of local anaesthetic or alcohol into the dorsal intervertebral roots often has a marked effect in the reduction of pain. In successful cases the anginal attacks cease altogether, but the danger remains, as in sympathectomy, that the patient will do more than his cardiac condition can support.

These injections are a much safer method of therapy for the intractable case than the major

surgical manoeuvres. They should be tried in cases experiencing frequent severe attacks, who are not given a comfortable existence by medical treatment, and whose general health will stand the necessary amount of interference. It is also preferable to choose cases who will follow a regime of after treatment, and will be content to live a restricted life within the bounds of their hearts' capabilities.

This paper cannot be concluded without recording how many of its ideas have been gained from the teaching of Dr. T. Jenner Hoskin.

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