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THE NATURE OF ANGINAL PAIN*

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The pain of angina pectoris is considered to be the result of myocardial ischaemia, and to result from the stimulation of nerve endings in muscle by metabolites.

There are, however, certain clinical and experimental findings which appear to suggest that the pain may be a vascular one related to coronary spasm.

Beck[1] has recently brilliantly demonstrated that a shift of the S-T segment is due to electrical imbalance of the heart, resulting from the fact that one area of the heart is anoxic relative to the remainder of the heart. Such a deviation of the cardiac vector must be due to myocardial involvement, the anoxia deflecting the vector from its normal course.

Does such an S-T shift necessarily produce pain? We are familiar with the ischaemic heart, where a permanently depressed S-T segment is often not associated with pain. Similarly prolonged paroxysmal tachycardia or anaemia may produce such changes yet not necessarily be associated with pain.

In view of this I performed exercise tests on two elderly subjects who did not complain of chest pain and was able to produce a depressed S-T segment without pain.

When one considers the high incidence of symptomless coronary atheroma found in individuals dying of other causes, it becomes obvious that, given sufficient exercise, it must be easy to produce an S-T depression.

Paul Wood[2] states that 'very few (less than 10%) electrocardiograms remain normal during or immediately after an attack of true angina *or sufficient effort to induce breathlessness and fatigue* (*in ischaemic subjects*)'.

It would therefore appear to be a reasonable conclusion that relative anoxia producing regional myocardial ischaemia is not necessarily associated with pain.

We are familiar with the fact that an exercise test in individuals with the classical anginal syndrome may be negative in a significant proportion of cases.

Gerlis[3] has recently demonstrated the presence of adventitial infiltrations round the vasa vasorum of coronary arteries which he considers to be the result of vascular spasm causing ischaemia, and concludes that coronary spasm, rather than anatomical change, is responsible for the clinical symptoms of coronary insufficiency, particularly as vaso-dilators relieve the pain.

It has been suggested that the peripheral vaso-dilation induced by trinitrin may reduce the work of the heart (by reducing right auricular pressure) and thus relieve the strain on ischaemic muscle.

However, Paul Wood[4] records the 'paradoxical' relief of anginal pain where the S-T segment has actually been further depressed by a vaso-dilator, while pain has been relieved.

Since individuals suffering from angina are almost always on the ascending limb of the Starling curve it is highly possible that coronary blood flow to an ischaemic area may actually be reduced by the peripheral pooling of the blood. A reasonable assumption, it would seem, is that coronary spasm is relieved and that this is more important than the amount of oxygen delivered to the muscle.

Vascular spasm is known to cause pain.

The myocardium of a normal individual is insensitive to stimulation.[5]

Gerlis found his changes around the larger coronary arteries only, and not round the smaller myocardial branches, and points out that Woollard has demonstrated that the former are mainly supplied by sympathetic fibres and the latter by the vagus.

The precise mode of action of the autonomic nervous system on the coronary arteries is debatable, but Green[6] has shown that profound stimuli from many parts of the body can cause profound vaso-constriction of the coronary arteries.

* A paper read at the first clinical meeting of the Natal branch of the South African Cardiac Society.

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VAN DIE REDAKSIE

STOLLINGSTEENSTOWWE IN DIE BLOEDSOMLOOP

By pasiënte wat aan bloedingssiektes ly ontbreek daar moontlik in die bloed 'n faktor wat noodsaaklik is vir doeltreffende stolling. Ons kan dadelik aan voorbeelde hiervan dink. Daar is byvoorbeeld die afwesigheid van bloedplaatjies by siektes waarby hierdie plaatjies drasties verminder word, die gebrek aan bloedingbestrydende globulien by hemofilie, en die gebrek aan faktor 5 of faktor 7 hetsy as aangebore afwyking, hetsy as later ontstaande defek. Baie ander voorbeelde kan aangehaal word. In die meeste gevalle kan die stollingsabnormaliteit reggestel word deur die toevoeging van klein hoeveelhede normale bloed tot hierdie soort abnormale bloed, of selfs deur die toevoeging van een abnormale bloedsoort tot 'n ander soort abnormale bloed. Laasgenoemde geval word beskou as 'n wederkerige vergoeding vir gebreke, want elkeen van die abnormale bloedsoorte bevat betreklik baie van die faktor wat by die ander ontbreek.

By sekere siektes bestaan hierdie toestand nie. Die pasiënt kan 'n stollingsdefek en 'n kwaai bloedingssiekte hê. Maar nie alleen word die bloed slegs onvolkome gekorrigeer deur die toevoeging van normale bloed nie, maar die normale bloed word boonop abnormaal gemaak. Hierdie omstandighede dui gewoonlik op die aanwesigheid van 'n stollingsteenstof in die bloedsomloop. 'n Vergelykbare toestand sou bestaan as 'n stollingsremmende stof soos heparien *in vitro* bygevoeg word. In seldsame gevalle kan heparien-agtige werksaamheid selfs aangetoon word by natuurlik voorkomende siektes,[1, 2] of dit kan voorkom ná die gebruik van stikstofmosterd of ioniserende bestralings.[3] Maar die stollingsteenstof is in die meeste gevalle nie heparien, of selfs heparien-agtig, nie.

Daar is drie groepe siektetoestande wat verantwoordelik is vir die meeste gevalle waar stollingsteenstowwe in die bloed voorkom:[3–6] (*a*) kompliserende kondisies by hemofilie en christmas-siekte; (*b*) kondisies na swangerskap; (*c*) 'n verskeidenheid slepende siektes.

Voorbeelde van hierdie komplikasie by hemofilie en christmas-siekte word vandag meer dikwels as in die verlede uitgeken. Dit is ongetwyfeld deels te danke aan beter diagnose, en waarskynlik ook deels aan die groter gebruik van bloed- of bloedplasma-oortappings. Daar is reeds aanspraak gemaak daarop,[7] en dit is moontlik bevestig,[8] dat natuurlik voorkomende hemofilie geheel en al òf gedeeltelik te wyte is aan 'n oormaat van 'n stof wat 'n stollingsremmende werking het. Maar baie

EDITORIAL

CIRCULATING ANTICOAGULANTS

Patients suffering from bleeding diseases may lack a factor in their blood which is necessary for adequate coagulation. Examples of this readily spring to mind. One may mention the absence of blood platelets in thrombocytopenic states, the deficiency of anti-haemophilic globulin in haemophilia, and the lack of factor 5 or factor 7 either as a congenital anomaly or an acquired defect. Many more examples could be quoted. The coagulation defect can, in most cases, be corrected by the addition of small proportions of normal blood to this kind of abnormal blood, or even by the addition of one abnormal blood to a different variety of abnormal blood. The latter instance is regarded as a mutual correction of defects, since each of the abnormal bloods contains a relative abundance of the factor which is lacking in the other.

In certain diseases this state of affairs does not exist. The patient may have a coagulation defect and a severe haemorrhagic state. Yet not only is the blood not fully corrected by the addition of normal blood but the normal blood is rendered abnormal. These circumstances usually imply the presence of a circulating anticoagulant. A somewhat comparable state of affairs would exist if an anticoagulant substance such as heparin were added *in vitro*. On rare occasions, heparin-like activity may even be demonstrated in naturally occurring disease[1,2] or may follow the use of nitrogen mustard or ionizing radiations.[3] But in most cases the anticoagulant is not heparin or even heparin-like.

Three groups of conditions account for the bulk of cases in which circulating anticoagulants have been encountered:[3–6] (*a*) conditions complicating haemophilia and christmas disease; (*b*) conditions following pregnancy; and (*c*) a variety of chronic diseases.

Instances of this complication of haemophilia and christmas disease are being encountered more frequently than in the past. This is no doubt due in part to better diagnosis and also probably to the greater use of blood or plasma transfusion in those diseases. It has been claimed,[7] in

Exercise and emotional stress induce sympathetic stimulation and vagal inhibition, and resting reverses this process.

If electrical imbalance *per se* were the cause of pain it should appear in a higher percentage of exercise tests. The fact that it does not appear would depend on whether collateral circulation to the involved muscle was sufficient to prevent regional ischaemia or whether, particularly with a rigid artery, the pain was due to spasm of more plastic vasa vasorum.

It is obvious that anatomical coronary change and myocardial ischaemia must be closely associated, but if anginal pain was functional, and vascular or perivascular in origin, it would be possible to have spasm without regional anoxia of muscle.

If this hypothesis were accepted it would cast serious doubts on the value of the exercise test, for a positive test could represent the effects of anatomical change rather than a vascular spasm. One has long felt, particularly where pain has not been quite typical, that the mere depression of an S-T segment is not proof of the existence of the syndrome of angina pectoris.

Beecher[7] has relieved anginal pain in over 30% of cases by the administration of a placebo, and Russek[8] refuses to acknowledge the mere relief of pain as proof of the efficacy of a drug tested for angina.

Since the coronary vessels are under autonomic control, and thence under cortico-hypothalamic control, it is possible that the supposedly inert placebo may effect changes in the autonomic balance which would tend to influence favourably the effects of exertion or emotion on the coronary circulation.

The person who suffers from angina is commonly a tense, anxious and frightened individual, who by his reactions to his symptoms may well condition the balance of his autonomic nervous system in the direction of a more easily induced vascular spasm.

Russek[8] has condemned alleged remedies for angina because they have not favourably influenced S-T depression, but such remedies may simply be less potent than trinitrin or Peritrate yet may sufficiently relax a contracted coronary artery to relieve pain.

A concept of vasospasm would allow of a diagnosis of reflex vasospasm from, say, gall-bladder or diaphragmatic hernia which, one feels, we all see from time to time as an alarming event.

The recent demonstration by Brewster *et al.*[9] that the ultimate effects of the thyroid hormone involve an increased adrenaline output would then account for some relief of anginal pain by total thyroidectomy.

Raab and Gigee[10] have shown that in diseased hearts, including those due to coronary sclerosis, there is an alteration in the normal concentration of noradrenaline and adrenaline with an increased concentration of the latter in these hearts.

Noradrenaline has a fairly generalized vaso-constrictor effect on blood vessels (*except on the coronaries, which it dilates*).[11] Adrenaline is not considered a potent vaso-constrictor, merely having a transient and slight initial effect on the diastolic pressure, but when one seeks some enlightenment on the control of the calibre of the coronary vessels one finds hypotheses, many in direct conflict with one another, from which it is easy to pick one to suit one's own opinion. Suffice to say that a hormonal and autonomic imbalance, in the presence of anatomical change, may create conditions favouring vascular spasm.

As regards pain in myocardial infarction, with or without thrombosis, it is obvious that slow tissue-death is involved, and this alone may produce pain, but it seems more reasonable to postulate that coronary spasm of an irreversible nature is present in both cases as an accompanying factor, than to state that relative anoxia beyond a simple anatomical narrowing is sufficient to produce so devastating an effect.

CONCLUSIONS

Coronary atheroma is a common condition and is often symptomless.

Clinically it is commonly detected with the electrocardiogram when it produces an electrical imbalance of the heart.

Such an imbalance may be associated with the anginal pain but is often painless. On the other hand anginal pain may occur without demonstrable electrical imbalance.

Anatomical coronary changes can produce painless myocardial ischaemia, and functional vascular spasm could produce pain without myocardial ischaemia.

Undoubtedly a combination of the two factors is the most commonly encountered disturbance, but it is tentatively suggested that vascular spasm rather than myocardial ischaemia is the factor which decides whether pain is present or absent.

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