TWO major theories of causation of coronary atherosclerosis are now popular. One relates the pathology to an abnormal lipid level in the blood, either total lipid or some fraction of lipoprotein. The other, that of the school of Rokitansky¹ and Duguid,² considers the cholesterol deposit to be secondary to the damage from repeated thrombotic injury ineffectively neutralized by normal fibrinolytic mechanisms. It is possible that both of these may be related in some way to abnormalities of fat metabolism in that thrombotic episodes appear to be more common in populations with high fat intakes.

There seems to be some pressure, by those psychosomatically oriented, to admit the camel of atherosclerosis into the spiritual tent, even though, up to now, his nose is the only part even suggestively inside. By this I mean that emotional stress is being proposed as the agent through which lipids appear in coronary vessels, and that is why coronary disease is increasing in what is supposed to be an unusually anxious age in world history. Just how this happens we are yet to be told.

This point of view presents dangers. It is an easy way out because it almost precludes scientific investigation. No one can prove that our age is more troubled than many before it. No one can measure emotional stress, since it has no meaning except in relation to him who is stressed. Furthermore, it creates the belief that emotional stress is a bad thing. Therefore, not only are pain, anxiety, grief, fear, anger, and frustration undesirable, but so also must be joy, pride, success, striving, and love.

I confine this discussion to the question of the fundamental etiology of coronary disease, not wishing to enter the murky area concerned with the events purported to initiate an isolated acute myocardial infarction.

What are some of the facts? Cannon and Mendenhall³ from their work of over 40 years ago, are the authorities quoted to indicate that normal reactions to emotional stimuli are protective but may be deleterious. For example, blood coagulability is increased by pain and therefore this leads to coronary thrombosis. Yet, from a practical standpoint, not one of the many tests of blood coagulation has been able to show that a patient suffering from either an overt myocardial infarct, or prolonged anginal pain, has increased clotting of his blood.*

Perhaps I am reversing myself, since I said that no one can measure emotional stress, yet there are situations that almost everyone would consider indicative of spiritual disturbance. One of these is suicide. It is reported that in Japan hypertension is prevalent, and so is suicide, but coronary disease is rare.⁴ Manic depressive psychosis shows, in both its agitated and depressed phases, severe

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*McDonald and Edgill (Lancet 278: 457, 1957) report "increased coagulability of the blood has been demonstrated between a group of patients with ischaemic heart disease and healthy controls." However, this was true in respect to statistical comparison only of both groups and in only some of the total battery of tests employed. No patients with recent cardiac infarction were included. There was considerable overlapping of results in the two groups and in some patients with ischemic heart disease the coagulability was actually less than in the controls by some tests.
turmoil, and yet these patients, if properly fed and nursed, do not succumb to coronary disease to any greater extent than does the general population; indeed their life expectancy is the same. Neurocirculatory asthenia, which many agree is an anxiety neurosis, does not lead to coronary disease nor to "hypertension, peptic ulcer, asthma, ulcerative colitis or thyrotoxicosis, which some authors have speculated are caused by 'anxiety.'" Pris-

oners in Federal penitentiaries had the lowest incidence of new coronary disease of all groups in the lipoprotein study. The incidence of fatal coronary attacks was reduced in the oc-

upied Scandinavian countries in wartime—certainly a stressful period. Primitive races with oppressive tabus, terrifying witchcraft, and "uncivilized" customs are not prone to coronary disease.

Anxiety appears either to have no influence on blood coagulation or it may favor fibrinoly-
sis—"a protective enzymatic response. It is re-

ported that in patients with recurrent thrombophlebitis, stressful situations produced attacks. In hypertensive patients in whom stressful interviews caused a rise in blood pressure there was slight increase in blood coagulability and viscosity but not in other hypertensive patients nor in people suffering from other "stress" diseases.

It seems likely that emotional tension re-

sults in compulsive eating, drinking, and smoking in many individuals as compensation for anxiety, and I believe that it is through this indirect mechanism that stress has its influence on coronary disease. In addition it contrib-
utes to the failure to achieve daily physical exercise by promoting fatigue and by forcing a man to make so many commitments that no time is found for exercise, such as walking.

The danger of attributing cardiovascular disease to emotional tension is that it makes everyone fearful lest he find himself in a situa-
tion of anxiety, and it fosters a belief that struggle and achievement are lethal, whereas they are probably healthy. It plays into the hands of those who would have us believe that work causes heart disease. Authoritative opinion denies this.

Stress is not new. What is new is coronary thrombosis. Over one hundred years ago Thoreau wrote "The mass of men lead lives of quiet desperation" but these men were ap-

parently not dying of coronary disease in great numbers in 1854.

Recently a report from the Air Force indi-

cated that certain officers under stress had elevated serum cholesterol levels, but it should be noted that 75 per cent of these returned to

a normal range when the subjects were placed on a regimen of more rigid diet and exercise. Similarly, a claim has been made that stress raised serum cholesterol in a group of patients who reacted by a lowering of the lipid under a proper "physician-patient relationship." Dutch investigators have contributed to

this by combining observations on diet and "stress." They state, "A 'reaction pattern' was described which seemed to occur both in infections and in physical and emotional forms of 'stress.' During or immediately after the infection, exertion or emotional tension, the serum cholesterol tended to fall; when the 'stress' period was at an end, i.e. during convalescence, usually after three or four weeks, there occurred a rise of the blood cholesterol, which often exceeded the original value and persisted for two or more weeks."

After discussing the possible significance of elevated serum cholesterol in the genesis of atherosclerosis they say, "Finally by demon-

strating the influence of both nutrition and stress on the serum cholesterol our observa-
tions might bridge the gap between those authors who have regarded atherosclerosis as of nutritional origin only and those who have pointed out its frequent occurrence among pa-

tients who have labored under strain."

In any event, it seems to me that the normal reactivity of serum cholesterol under many influencees makes it extremely difficult to draw conclusions about any one individual. Popu-

lation studies showing a correlation between coronary and thrombotic disease, serum cho-

lesterol level and diet are impressive. No other
variable in the complex atherosclerotic equation seems to me as yet so suggestive.

The defense mechanisms in Cannon’s emotional cats were explained as mediated through epinephrine discharge producing shortening of clotting time, but it must be remembered that epinephrine, or severe physical effort as its activator, is also a potent inducer of fibrinolysis. Duguid, indeed, believes that acute coronary thrombosis is not due to a general hypercoagulable state, since he finds fluid blood in the coronary vessel distal to the occluding thrombus.

Psychiatric analysis of our group of young coronary victims resulted in this conclusion: “No one yet has demonstrated in humans that stresses of a magnitude compatible with a ‘normal’ life can influence the deposition of cholesterol material in coronary vessel walls.”16 The authors noted possible effects of increased heart rate and output, rise in blood pressure, shortened clotting time, and increased blood viscosity but stated “We simply do not have evidence, however, that anxiety or other emotional stress is related to the genesis of the atherosclerosis.”

Even in a field perhaps more contentious than that of the etiology of coronary atherosclerosis, namely, hypertension, we find a very wise psychiatrist saying, “The fact that acute emotional excitement may result in transitory elevations of blood pressure should not be used as a basis for the inference that long standing emotional states or conflictive situations can act as precipitants to chronic vasomotor constriction.”17

I believe we should leave it there at present. Undoubtedly much of the wishful thinking about work and stress being evil is an Old Testament guilt that labor is part of the penalty for original sin, which is not successfuly nullified by the Puritan concept of the nobility of struggle and ambition. We hope that work and anxiety are bad for us so that we can avoid them, or blame them for ills brought upon us by our own vices. But Adam and Eve were expelled from the Garden of Eden not because they had eaten the fruit of the Tree of Knowledge, and therefore had to work for a living, but because of the Lord’s fear that they might also eat the fruit of the Tree of Life and live forever in spite of stress.

Corvisart,18 150 years ago, attributed all heart disease to two principal causes, “from the action of the organ and from the passions of man.” He believed that the heart could be injured (among other things) by crying in infancy, wrestling, fencing, playing wind instruments, laughing, weeping, reading, declamation, and “every kind of effort;” as well as by “anger, madness, fear, jealousy, terror, love, despair, joy, avarice, cupidity, ambition [and] revenge.” But he quite honestly avers that “to conceive man without passions, is to conceive a being without his attributes.”

The complexity of man makes etiologic dogmatism untenable in any disease and we all admit the influence of an acute emotional stimulus upon endocrine mechanisms, but I consider that the following is currently correct: “No technics have been developed as yet for use in this field which permit conclusive observations concerning the exact relationship, if any, of life situations, and emotion-provoking situations to this disorder [neurocirculatory asthenia] or which allow for a definite statement as to whether an illness is or is not on a ‘psychogenic’ basis.”16

It would be a good thing if more people really knew what Selye means by “stress” and if they would read the inscription in the front of his book The Stress of Life, which he says is “dedicated to those who are not afraid to enjoy the stress of a full life, nor too naive to think that they can do so without intellectual effort.”19

Howard B. Sprague

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The authors evaluate the primary data of an indirect study reported in 1953 that led to the assumption of a strong association between the percentage of calories available as fat in the national diet and the national death rates from arteriosclerotic and degenerative heart disease. The apparent association is greatly reduced when tested on all countries for which data are available instead of the 6 countries used by the investigator. The presumed association is not "specific" for fat in the diet or for diseases of the heart. The suggested association between national death rates from heart disease and percentage of fat in the diet available for consumption cannot at the present time be accepted as valid. It is suggested that in indirect studies of association it is the responsibility of the investigator to report the basis on which the primary data were selected, their limitations, any qualifying conditions or considerations, and the method used for testing the validity of the results.

HARRIS
Editorial: Emotional Stress and the Etiology of Coronary Artery Disease
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