Role of Emotional Stress in the Etiology of Clinical Coronary Heart Disease*

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The concept of any disease arising from a single cause is obsolete and misleading.1 Even if one accepts the view that the plasma B-lipoproteins constitute the etiologic agent in atherosclerosis, there are constellations of interacting factors which may influence not only the concentration of serum lipids, but also the susceptibility of the arterial intima to lipid deposition, and the vulnerability of the myocardium to diminished coronary flow. It has been clearly shown in organ cultures that apparently normal intimal cells from patients with atherosclerotic changes have increased susceptibility as a specific characteristic.2 Thus with similar elevation of blood cholesterol there are considerable variations in the observed severity of aortic and coronary lesions. It is significant that a large proportion of patients with clinical coronary heart disease (as many as 50 per cent or more, depending on one's criteria) show no demonstrable abnormality of the lipid constituents of the blood. Consequently, the susceptibility of arterial intimal cells to lipid incorporation, rather than the dose of the agent, may be the determining factor for disease causation in many patients. In similar manner the vulnerability of the myocardium to diminution in coronary flow rather than the extent of the vascular lesion may be crucial in some cases. Particularly on the abundant diet of Western society, the B-lipoprotein concentration may be a less important variable in causing overt disease in many individuals than such factors as stressful and sedentary existence, hypertension, tortuosity of vessels or hereditary predisposition to the degeneration of vascular connective tissue.

Since atherosclerosis is something more than a nonspecific response to hyperlipemia and is often associated with a vascular metabolic abnormality in the handling of serum lipids, the numerous host and environmental factors which influence not only serum lipid concentration, but also vascular reactivity must be carefully considered in any study of its pathogenesis. Olson1 has presented this broad concept in the following epidemiologic triangle (Fig. 1) from which it is readily apparent that multiple interacting factors contribute in varying degree to the initiation and progression of this widespread disease.

The Coronary Prone Personality

Seventy years ago, Osler1 listed heredity, rich diet and, above all, the "worry and strain of modern life" as the causes of arteriosclerosis and especially of coronary diseases. Although there is almost universal agreement that both heredity and a high fat diet are implicated in the pathogenesis of atherosclerosis in man, continued skepticism exists in many quarters concerning the role of the emotions in the causation of

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this disease. Osler's views were based on an intimate knowledge of the life situation, personality and behavior of patients who develop coronary disability before the age of 60. He described the typical patient with coronary disease as "a keen and ambitious man, the indicator of whose engines is always set at 'full speed ahead.'" Arlow observed, "a compulsive striving for achievement and mastery which never seems to end." Kemple characterized the coronary patient as an aggressive, ambitious individual with an intense physical and emotional drive, unable to delegate authority or responsibility with ease, possessing no hobbies and concentrating all his thoughts and energy in the narrow groove of his career. Wolf has compared the "coronary-prone individual" with the mythologic Sisyphus, "who passed the time in Hades pushing a large rock up a steep hill and never quite getting it there." The candidate for coronary disease, he asserts, is a person who not only meets a challenge by putting out extra effort, but who takes little satisfaction from his accomplishments. An identical behavior pattern, delineated by Friedman and Rosenman, has emphasized the prevalence of intense ambition, competitive drive, sense of urgency, and preoccupation with deadlines among persons predisposed to clinical coronary disease. More than 80 per cent of these subjects, they found, exhibited a behavior pattern characterized by "excessively rapid body movement, tense facial and bodily musculature, explosive conversational intonations, hand or teeth clenching, excessive unconscious gesturing and a general air of impatience.

While a significant proportion of our young coronary patients did manifest some or all of these characteristics, we consider this description to be a caricature rather than a portrait of the average coronary patient under the age of 40 in our series. The majority did not exhibit such easily recognized outward behavior characteristics. In fact, most of the young patients under observation have shown a striking degree of self control, dignified reserve, and outward complacency during interrogation. In most of these, psychologic factors would have remained unrecognized had a special inquiry not been made regarding their presence. The most characteristic trait of the young coronary patient was his restlessness during leisure hours and his sense of guilt during periods of "relaxation." As a consequence, he rarely took vacations, and such leisure time as he did possess was frequently regimented by obligatory participation in an assortment of social, civic or educational activities. Impressive as these observations all appear to be, they suffer from a common weakness arising from retrospective analysis of values which can only be qualitatively estimated. Strong support for their validity, however, can be found in the careful prospective studies of Rosenman and associates. These authors have shown that possession of the specific behavior pattern, which they have so clearly described, appears to accelerate the advent of manifest coronary heart disease. Moreover, the exhibition of this behavior pattern furnished the most important single predictive entity of all suspected pathogenetic factors. The mechanisms by which behavior may be associated with a higher prevalence of coronary heart disease have not been clearly identified. Any assessment of the etiologic role of a specific personality type presents the same problems as are currently encountered in the evaluation of the pathogenetic significance of tobacco

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**Figure 1—Etiologic Factors in Atherosclerosis**

*(Derived from R. E. Olson)*
smoking. Both factors may be "causative" or merely associated with an underlying genetic predisposition to the disease. Nevertheless, since emotional stress is, on the one hand, an inevitable by-product of compulsive behavior and, on the other, a major determinant of excessive indulgence in tobacco, this common denominator must continue to be held suspect in coronary disease etiology.

**Emotional Stress**

Much evidence now suggests that most of the lethality of a high fat diet in Western society may actually be dependent on the "catalytic" influence of stressful living. While behavior patterns may generate "stress" independently of the demands of the job, there is good evidence to indicate that occupational responsibilities may be directly related to coronary heart disease prevalence rates. In a study of 100 young coronary patients, 25 per cent had been holding down two jobs and an additional 46 per cent had worked 60 hours or more per week for long periods immediately preceding the onset of symptoms. Although prolonged emotional strain associated with job responsibility had preceded the attack in 91 per cent of these 100 cases, similar stress was observed in only 20 per cent of the controls. Thus, psychic stress of occupational origin appeared to be far more significant in the etiologic picture of coronary disease than did a positive heredity, a prodigiously high fat diet, obesity, body build, tobacco consumption or exercise ('Table 1'). Buell and Breslow have confirmed a greater mortality risk from atherosclerotic-coronary heart disease among occupational groups working more than 48 hours per week. Similarly, a survey of 12,000 professional men in 14 occupational categories showed that the marked gradient in distribution of the disease appeared to be unassociated with heredity or diet, but strikingly related to the relative stressfulness of occupational activity (Fig. 2).

It has been argued that racial groups in various geographic areas (Korea, China, Japan and Yemen) who subsist on relatively low fat diets have appeared to exhibit a distinct immunity to coronary disease despite obvious emotional stress in their patterns of life. Since this immunity seems to be lost when high fat diets are ingested, the role of the emotions has been relegated to a position of secondary significance by some observers. It cannot be denied that the lethality of emotional stress is strongly mitigated, if not nullified, by subsistence on a diet low in fat. Snapper, in studying the Chinese population under the severe stress of Japanese invasion, long ago concluded that stress has little or no effect if the diet is poor in animal fat. Nevertheless, there is good evidence to indicate that the atherogenicity and lethality of a high fat diet in Western society is greatly compounded by the influence of stressful living.

**Pathogenetic Interrelationship Between Emotional Stress and Dietary Fat**

Groen and associates' findings in a study of Benedictine and Trappist monks provide insight into the role of fat as related to stress in the genesis of coronary disease. Both groups live in rural areas removed from the stresses of urban life and, in the monastic environment, are free from economic

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**Table 1—Incidence of Various Factors in Patients who Had Coronary Attacks and in Control Groups**

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>Heridity (Positive)</th>
<th>High-fat Diet</th>
<th>Stress and Strain (Occupational)</th>
<th>Obesity</th>
<th>Tobacco (30 Cigarettes, Plus)</th>
<th>Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary group</td>
<td>100</td>
<td>67%</td>
<td>53%</td>
<td>91%</td>
<td>26%</td>
<td>70%</td>
<td>58%</td>
</tr>
<tr>
<td>Control group</td>
<td>100</td>
<td>40%</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
<td>35%</td>
<td>60%</td>
</tr>
<tr>
<td>Ratio</td>
<td>1.7:1</td>
<td>2.7:1</td>
<td>4.6:1</td>
<td>1.3:1</td>
<td>2:1</td>
<td>1:1</td>
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</tbody>
</table>
and family problems. The Benedictines have a diet substantially the same as other Europeans, while the Trappists do not eat fish, meat, eggs or butter. Although there is a much higher average level of blood cholesterol among the Benedictine monks, no striking differences were observed in coronary heart disease prevalence and not a single instance of significant disease was encountered under the age of 65 in either group. Moreover, both groups showed a far smaller incidence of coronary disease than the general population. It appears significant, therefore, that although the "unstressed" Benedictine monk eats as much fat as the greatly harassed general practitioner of medicine, he suffers only about one-fifth as frequently from clinical coronary disease. Of the many variables which undoubtedly participate, none appears more decisive than psychic stress. Similarly, it is noteworthy that Somali camel herdsmen appear to be relatively free from clinical symptoms suggestive of atherosclerosis although they subsist on a high fat diet derived from approximately 5 liters of camel's milk per day. While many theories may be advanced to explain this paradoxic immunity, a major factor in these persons, whose pastoral and patriarchal way of life has remained unchanged for centuries, could be their relative freedom from serious psychologic stress. Although physical fitness as a result of vigorous activity has been reported to protect the Masai despite a diet rich in animal products and dairy fat, freedom from clinical disease in this East African pastoral people could also be, in the main, an outcome of the simplicity of their way of life. In like manner, the unusually low incidence of death from myocardial infarction reported for the Italian-American community of Roseto, Pennsylvania similarly suggests that the way of life may be an important determinant of the atherogenicity of a high fat diet. Consequently, while habitual diet and stressful living both appear implicated in the pathogenesis of clinical coronary disease, there is mounting evidence to suggest that each is dependent upon the other for pathologic significance.

**Figure 2—Coronary Prevalence by Age and Stress Group**

*Classification of occupations according to stress is as follows: low: dermatologists, orthodontists, patent lawyers and periodontists; medium: oral surgeons, other lawyers, pathologists, security analysts, and trial lawyers; and high: anesthesiologists, general practice dentistry, general practice law, general practice medicine, and security traders.
EMOTIONAL STRESS IN CORONARY HEART DISEASE

Influence of Stressful Living in Animals

Inasmuch as dietary habits among various population groups reflect profound differences in patterns of living, "diet cannot be readily isolated from the matrix of man's total transaction with his environment." In the animal kingdom, however, major environmental factors have been identified and controlled far more readily and completely than is possible with the corresponding factors in human society. For example, in mammals and birds at the Philadelphia Zoo on a constant diet, there has been a ten-fold increase in arteriosclerosis of the coronary arteries during the last decade. This increased susceptibility to vascular degenerative lesions has been ascribed to psychologic disturbances evoked by social interactions attending increased population densities in the zoo. Man's response to population density appears to correspond closely to that of other animals. This is reflected in the significantly higher death rate from clinical coronary heart disease that has been found in metropolitan communities as compared with rural areas.

Stress and Atherosclerosis in the Experimental Animal

Experimentally, the profound but dependent role of "stress" in atherogenesis has been clearly confirmed. Thus, it has been shown that hypercholesterolemia and aortic atherosclerosis in cholesterol-fed rabbits may be either augmented or reduced by drugs which stimulate or depress the central nervous system. Similarly, greater degrees of hypercholesterolemia and coronary atherosclerosis have been evoked in rats fed an atherogenic diet and exposed to a particular form of stress than in their unstressed controls. Additional experiments were needed, however, to determine whether such stresses alone are capable of initiating atherosclerosis when the diet is low in fat. Clear answers were provided by the careful studies of Gunn and associates in rabbits. These authors found that on a cholesterol-rich diet, hypothalamic stimulation, like other forms of stress, increased the atherogeneity of diet alone. More important was the observation that hypothalamic stimulation in controls on a low cholesterol diet left the vascular system unimpaired. These experimental studies appear to correlate with epidemiologic data obtained in man. Thus, like "stressed" animals in the laboratory, "stressed" humans have manifested no increased susceptibility to atherosclerosis unless the composition of the diet had been relatively high in animal fat.

At present, there is no clear understanding of the manner in which emotional stress may hasten the advent of clinical coronary artery disease. Elevation in blood cholesterol level, metabolic changes in the vascular wall leading to an increase in its lipid receptiveness, augmentation of myocardial oxygen requirements, and increase in the coagulability and viscosity of the blood all appear to be implicated. Thus, prolonged emotional stress acting through the cerebral cortex and hypothalamus via neurohormonal and hormonal mechanisms may contribute not only to the initiation and progression of atheromatosis but also to its clinical complications.

Influence of Emotional Stress on Homeostasis

Numerous investigators have shown that stressful life experiences are capable of evoking hypercholesterolemia despite constant diet and exercise. Bogdonoff and associates have also shown that emotional episodes cause rapid mobilization of nonesterified fatty acids from the body tissues into the circulation and have obtained similar results with infusions of epinephrine and arterenol. Steinberg and Shafir and others have demonstrated in animals that it is cortisone which enhances the ability of epinephrine to trigger sharp blood lipid increases under the influence of psychic stress. They observed a marked and almost immediate rise in the nonesterified fatty acids followed by a slower but definite rise in serum cholesterol. According to Sabin, free fatty acids are irritating and, in excess, may cause subendothelial hemorrhage and
small mural thrombi. Whatever the exact mechanisms underlying such responses may be, hyperlipemia so evoked is believed to “provide metabolic substrate for the aroused organism.”

As a result of stress, sympathetic adrenergic effects on vascular tissue metabolism, by primarily damaging the intima, may prepare the soil for subsequent lipid depositions. Prolonged vasoconstriction could reduce blood flow in the vasa vasorum and produce vascular wall ischemia leading to increased permeability and intramural edema. Raab and Humphreys have shown that catecholamines also diminish myocardial efficiency by wasting oxygen in a disproportionate fashion. Through this action, the hormones are capable not only of increasing myocardial vulnerability in the presence of coronary atherosclerosis, but also of inducing severe, potentially necrotizing myocardial hypoxia in animals with perfectly normal coronary vessels. Indeed, Raab and associates have recently produced myocardial necroses in rats solely by subjecting these animals to sensory and emotional stresses. Groover and others have also reported myocardial infarction without demonstrable atherosclerosis in baboons subjected to the emotional storm induced by trapping and caging. It seems probable, therefore, that occult disease in man may surface to clinical view solely or prematurely as a result of stressful life experiences.

The blood clotting elements have also been found to be susceptible to emotional stresses. Dreyfuss and Czaczkes measured the clotting time and found it to be accelerated in 36 medical students the morning of a final examination in medicine. Still and Heifter demonstrated sharp increases in viscosity mediated through action of the sympathetic nervous system as the result of emotional stimuli in animals. More significantly, stress-induced platelet elevation with reduction in blood clotting time has been reported in human subjects. Such changes appear to be part of an adaptive response to combat, designed to prevent blood loss. When this mechanism reacts excessively over a prolonged period of time, blood with increased coagulability and decreased fluidity may slow sufficiently in passing through narrowed coronary or cerebral arteries to produce thrombosis.

**Atherosclerosis as a Maladaptation Syndrome**

Wolff has stated that, “Man, feeling threatened, may use for long-term purposes devices designed for short-term needs. They are not designed to be used as lifelong patterns and when so utilized may damage structures they were designed to protect.” In many instances, therefore, atherosclerosis and coronary heart disease may represent a maladaptation syndrome in which the organism already oversupplied with metabolic substrate remains in a chronic state of mobilization for “fight or flight” as a result of stressful life situations. While mechanisms so evoked appear innocuous in “immune” groups subsisting on a low fat diet, these adaptive devices may greatly augment the atherogenicity and lethality of excessive ingestion of fat and hypercholesterolemia.

The American Heart Association has recently listed the chief risk factors in coronary heart disease as hypercholesterolemia, overweight, high blood pressure, lack of exercise, cigarette smoking and diabetes. It is well recognized that emotional tension may result in compulsive eating, drinking, and smoking in many persons as compensation for anxiety. Moreover, it does frequently contribute to the failure to achieve daily exercise by promoting fatigue, creating a sense of time urgency, and decreasing motivation. Nervous strain of occupational, cultural, social or domestic origin is known to elevate blood pressure, to increase the tendency to obesity, to contribute to excessive smoking and lack of exercise, to participate in hypercholesterolemia, and to aggravate diabetes, through psychic influences and alteration of the functional characteristics of the mode of life. Consequently, even such indirect effects of emotional stress, barring all others, must elevate this
factor to a position of considerable significance in the etiologic picture of coronary heart disease.

**Summary**

The concept of any disease arising from a single cause is obsolete and misleading. Much evidence now suggests that most of the lethality of a high fat diet in Western society may actually be dependent on the "catalytic" influence of stressful living. Indeed, while habitual diet and psychic stress both appear implicated in the pathogenesis of clinical coronary disease, there is mounting evidence to suggest that each of these factors is dependent upon the other for pathologic significance. Observations in the animal kingdom, in the experimental laboratory, and in epidemiologic surveys all attest to the validity of this pathogenetic interrelationship. Like "stressed" animals in the laboratory, "stressed" humans have manifested no increased susceptibility to atherosclerosis unless the composition of the diet had been high in animal fat. Contrariwise, numerous examples are now at hand to indicate the low atherogenicity of a high fat diet when there is relative freedom from serious psychologic stress.

Despite the profound effect of "stress" on homeostatic mechanisms this factor has been largely ignored by most authorities in the field of coronary artery disease. Major emphasis has been placed on hypercholesterolemia, overweight, high blood pressure, lack of exercise, cigarette smoking and diabetes. Nevertheless, nervous strain is known to elevate blood pressure, to increase the tendency to obesity, to contribute to excessive smoking and lack of exercise, to participate in hypercholesterolemia, and to aggravate diabetes, through psychic influence and alteration of the functional characteristics of the mode of life. Consequently, even such indirect effects of emotional stress, barring all others, must elevate this factor to a position of considerable significance in the etiologic picture of coronary heart disease.

**Resumen**

El concepto de que las enfermedades se originan de una sola causa es anticuado y erróneo. Gran parte de la evidencia acumulada parece indicar que el efecto perjudicial de una dieta rica en grasa en la sociedad occidental puede de hecho depender de la influencia "catalítica" del vivir en tensión. Si bien la dieta habitual y la tensión psíquica parecen estar relacionadas con las manifestaciones clínicas de las enfermedades coronarias, el peso de la evidencia disponible indica que cada uno de estos factores depende del otro en cuanto a su significación patológica. La observación en el reino animal, en el laboratorio experimental y en las encuestas epidemiológicas, confirman la validez de esta interrelación patogénica.

A pesar del profundo efecto de la tensión sobre los mecanismos homeostáticos, su papel ha sido en gran parte desestimado por la mayoría de los investigadores autorizados en el campo de las enfermedades coronarias. El énfasis mayor ha recaído en la hipercolesterolemia, el sobrepeso, la hipertensión arterial, vida sedentaria, el consumo de cigarrillos y la diabetes. Sin embargo, es bien sabido que la tensión nerviosa aumenta la presión arterial, propicia la obesidad, la vida sedentaria y la diabetes, induce a fumar con exceso, participa en la hipercolesterolemia y agrava la diabetes a través de influencias psíquicas y modificación de las características funcionales del genero de vida.

En consecuencia aun los efectos indirectos de la tensión nerviosa, aparte de todos los otros, confieren a este factor una alta significación en la etiología de las afecciones coronarias.

**Resumé**

La conception d'une maladie provenant d'une cause unique est périmée et trompeuse. De nombreuses preuves suggèrent maintenant que l'essentiel de la gravité d'un régime alimentaire riche en graisses dans une société occidentale peut actuellement dépendre de l'influence "catalytique" d'une vie tendue. En effet, alors que la régime habituel et la tension psychique sont l'un et l'autre impliqués dans la pathogenie de la maladie coronarienne clinique, il y a des preuves nettes suggérant que chacun de ces facteurs dépendent de l'autre, pour sa signification pathologique. Des observations dans le régime animal, dans le laboratoire d'expérimentation, et des études épidémiologiques attestent toute la validité de cette inter-relation pathogénique. Comme des animaux de laboratoire "stressés",
les humains "stressés" ne manifestent pas de pré-dispositions particulières à l'athérosclérose à mains que la composition du régime soit forte en graisses animales. Au contraire de nombreux exemples sont maintenant là pour indiquer le faible pouvoir athérogène d'un régime riche en graisses, quand l'individu est relativement libéré d'un stress psychologique sérieux.

Malgré le profond effet du stress sur les mécanismes homéostatiques, ce facteur a été largement ignoré par beaucoup de chercheurs dans le domaine de la maladie coronarienne. On a beaucoup insisté sur l'hypercholestérolémie, la surcharge pondérale, l'hypertension artérielle, le manque d'exercices physiques, l'usage du tabac et le diabète. Néanmoins, on sait que la fatigue nerveuse élève la pression artérielle, augmente la tendance à l'obésité, contribue à l'abus de la fumée et au manque d'exercices, joue un rôle dans l'hypercholestérolémie et aggrave le diabète, par l'intermédiaire d'influence psychique et d'altérations des caractéristiques fonctionnelles du mode de vie. En conséquence, l'effet du stress émotionnel, même indirect, ayant primauté sur les autres, évalue sans doute ce facteur et lui donne une signification considérable dans l'étiologie de la maladie coronarienne.

ZUSAMMENFASSUNG


Trotz des tiefgreifenden Einflusses eines "stress" auf die homoeostatischen Mechanismen wurde dieser Faktor weitgehend vernachlässigt von den meisten maßgebenden Persönlichkeiten auf dem Gebiet der Erforschung der Kranzgefäßerkrankungen. Es wurde vielmehr besonderer Wert gelegt auf eine Hypercholesterinämie, Übergewicht, erhöhter Blutdruck, mangelhafte Bewegung, Zigarettenrauchen und Diabetes. Trotzdem ist aber die nervliche Beanspruchung als blutdruckerhöhennder Faktor bekannt; sie erhöht die Tendenz der Fettleibigkeit, trägt zu exzessivem Rauchen und Mangel an Bewegung bei, sowie zu einer Hypercholesterinämie und verschlechtert einen Diabetes-dank psychischer Einflüsse und Störungen in den funktionalen charakteristischen Merkmalen der Lebensführung. Als Konsequenz müsself selbst ein solcher indirekter Einfluss eines emotionalen stresses, abgesehen von anderen Umständen, diesen Faktor vervielfachen bis zu einer Position beträchtlicher Signifikanz bei dem ätiologischen Bild von Herzkranzgefäßerkrankungen.

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AFFECTION OF THE HEART IN PRIMARY RHEUMATISM IN ADULTS

In 104 adults with primary rheumatoid carditis, the author revealed affection of the heart in the majority of cases with the prevalent involvement of the myocardium. Lesion of the endocardium was found at later periods of the disease. The presence of myocarditis could be established on the basis of the patients' complaints of pain in the region of the heart, dyspnea on exertion, tachycardia and objective data: enlargement of the heart, alteration of the nature of heart sounds, as well as the results of x-ray investigation. Important diagnostic signs of myocardial affection are the third and fourth heart sounds which on the phonocardiogram were represented by medium frequency fluctuations. Phonocardiographic study in patients with primary rheumatism enabled the revelation at the apex of the heart a weakening, splitting prolongation of the duration of the first sound, systolic and mesodiastolic murmurs. In ECG investiga- tion, myocardial involvement is manifested by a prolongation of the electric systole, disturbance and deceleration of intratrial conduction, impairment of intravitreal conduction, pathologic change of the T wave and S-T segment, rarely prolongation of the afterventricular conduction.