Angina Pectoris: A Validation of the Biopsychosocial Model

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The belief in the biopsychosocial model is fundamental to family medicine and practice. Using knowledge gained from history, clinical experience, epidemiologic studies, pathophysiologic processes, psychophysiologic pathways, and molecular-chemical reactions, angina pectoris is examined to validate the concepts of the biopsychosocial model. This model is one where biological, psychological, and sociocultural factors interact to produce illness or disease through molecular-chemical processes. Angina pectoris is shown to be a valid example of the biopsychosocial model. **J Fam Pract**
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T he major models used in family medicine are biomedical, biopsychosocial, developmental, general and family systems, and epidemiological. This definition of a model includes the major points from a number of sources.[1–3] A *model* is an integrated description (or organization) of a belief system to explain natural phenomena or to visualize something that cannot be observed.

The Biomedical Model

The biomedical model consists of two elements: reductionistic and exclusionistic.[1] The reductionistic aspect explains that all disease is conceptualized in terms of derangement of underlying physiochemical mechanisms, and molecular biology is the basic scientific discipline. The exclusionistic aspect leaves no room for social, psychological, or behavioral dimensions of illness. A corollary is that whatever is incapable of being explained by physiochemical mechanisms should be excluded from the categorization of disease and as such should probably not be the province of physicians or medicine.

The remarkable advances in molecular biology over the last decade are rapidly changing our understanding of previously explained disease processes and have strengthened the reductionistic aspect of the biomedical model.

The Biopsychosocial Model

The biopsychosocial model is "A framework for understanding the integration and interplay of the biological, psychological, and social dimensions of health, disease, and health care."[4] The model also states that for illness or symptoms to occur, at least three requirements are necessary[5]:

1. A stressful event or challenge to the system, eg, exposure to an infectious agent or loss of a family member
2. Physiologic vulnerability, eg, predisposition to bronchial spasm
3. Compromise of one or more pathophysiologic systems: immune, nervous, cardiovascular, etc

This model has been expanded to include the understanding of many pertinent dimensions of the patient's life, including the family, neighborhood, work environment, and community. It also includes the physician-patient relationship and an understanding of the physician's own beliefs, biases, and so on. This definition makes the biopsychosocial model a basic foundation for both the systems and epidemiological concepts of health and disease. As originally conceived, there seemed to be one deficiency in that it did not take "time" into consideration. There was no allowance for changes over time, either in the individual or the environment.

A point of clarification is appropriate at this time. Many people, including the author, wrongfully surmised that the

biopsychosocial model excluded much of the reductionistic aspects of the biomedical model. George Engel (in a personal communication with the author, February 1989) stated, however, that even though some of the writing might be a bit ambiguous, he definitely intended to include the molecular-chemical aspects of the biomedical model within the biopsychosocial one.

The Developmental Model

The developmental model takes this temporal relationship into consideration by examining change occurring over the life cycle of the individual and family as defined by Erikson,[6] Hill,[7] and Duvall.[8] The key concepts of the life cycle model are changes over time and development through sequential phases. Each phase has specific developmental tasks, normal transitions, and often, unexpected crises. Throughout the maturation that occurs during the life cycle, there is transmission of biological, behavioral, and social processes. This dynamic longitudinal approach has important practical implications for family medicine.

The Systems Model

The general systems model, developed by Von Bertalanffy in 1952, states that "all levels of organization are linked to each other in a hierarchial relationship [with feedback] so that change in one, affects change in the others."[9] To this statement might be added that anything that seriously affects one unit (or individual) of the system will affect the whole system, and anything that affects the system as a whole will affect each individual within the system. Many family therapists such as Minuchin and Satir have adapted this system in their work with families, and the family systems model is frequently used in assessment and management of families in family medicine.

The Epidemiological Model

Epidemiology has many facets, but an accepted definition is that it is the study of the distribution and determinants of diseases, disabilities, injuries, and other health problems in human population groups.[10–12] The epidemiological model states that "health or disease is the resultant of complex interactions between the host, the environment, and the agent or other stressors."[13] Epidemiological techniques have appropriately become some of the basic tools used in family medicine clinical research. Additionally, the flexibility of this model allows it to be adapted to many circumstances, as so well described by Cassel[14,15] and others.[16]

Criteria for Valid Evidence

Before presenting the evidence relating to angina pectoris, it is necessary to ask what type of evidence would be acceptable as criteria of validity for the biopsychosocial model as related to disease. First, it should be stated that although psychosocial values are more difficult to measure than biological variables and are therefore referred to by some as "soft," the criteria for judging psychosocial studies must be as strict as those for any other scientific project. Therefore, a generally agreed statement is, "The most important evidence for establishing a cause and effect relationship is the strength of the research design used to establish the relationship."[13]

The acceptable evidence would fall under the following categories[13,17,18]:

1. Research design
2. Measurable outcomes
3. Analysis: independent and synergistic effect
4. Associations: strength, dose-response gradient, consistency
5. Temporal relationship
6. Biological plausibility

These categories are well known to most of the readers, so only a few comments will be added in respect to *analysis*. This criterion is acceptable if the analyses show either that the predicted psychosocial variables are related to the outcome, independent of other biological or known risk factors, or that these variables in a synergistic form increase the significance or the predictive value of the known variables.

ANGINA PECTORIS AS AN EXAMPLE OF THE BIOPSYCHOSOCIAL MODEL

Although many specific conditions, eg, asthma, duodenal ulcer, or ulcerative colitis, could be discussed, for the purposes of this position paper various aspects of angina pectoris will be reviewed to examine the validity of the biopsychosocial model.

Clinical Vignette

A 72-year-old widower with three children had stable angina for the preceding 2 years. He had typical periodic attacks precipitated by exercise or exertion, lasting approximately 2 minutes and relieved by rest and nitroglycerine. He reported that during the preceding weeks he had noticed his attacks were more frequent, they were precipitated by less exertion, they were longer in duration (up to 10 minutes), and the previous day he had had a severe attack while resting in a chair. His previously stable an-

gina had become unstable, and as the attack at rest could well have been a sign of impending infarction, he was admitted to hospital for further investigation.

Cardiac catheterization showed severe occlusion (90%) of the left anterior descending and moderate occlusion (70%) of the posterior and circumflex arteries. He responded well to medication, but the consultant cardiologist strongly recommended a coronary artery bypass operation. Following discussion with his family, he decided to try medical treatment for a month or two before deciding on the operation.

Ten days following hospitalization, his only daughter, aged 32 years, was killed in a car accident. Approximately 1 hour after hearing the news, he developed severe retrosternal crushing pain, which was not relieved by three nitroglycerine tablets given at short intervals. He was rushed to the hospital but was dead on arrival.

The change from stable to unstable type of angina can be brought about by many factors, but a common one is thought to be a hemorrhage into the atherosclerotic plaque with or without platelet accumulation. The latter also leads to an increase in local concentrations of the vasoconstrictor, thromboxane A_2. Thus, this patient was in a state in which the coronary blood supply was insufficient to meet minimal demands by the heart. Upon hearing the news of his daughter's death, presumably there was overstimulation of the sympathetic nervous system with an increase in catecholamines, causing a further constriction of the artery around the plaques that was sufficient to completely cut off the blood supply.[19,20]

Historical Aspects

Angina, commonly thought to mean pain, is derived from the Greek word *anchein,* meaning to choke, and was first used by Heberden in 1768. In 1772 Heberden first described angina,[21] and his classic description has not been improved upon.[22] John Hunter, himself a sufferer of angina and an astute observer, predicted his manner of demise by saying, "My life is in the hands of any rascal who chooses to annoy or tease me." Indeed, on October 16, 1793, Hunter was involved in an argument with the Board of Governors of St. George's Hospital in London. He stormed out of the meeting in anger and fell down dead.[23]

Through the years angina was related to many coronary factors.[23] Among these were coronary calcification (Jenner, 1799), inadequate blood supply (Burns, 1809), and relief by amyl nitrite (Brunton, 1867).[24] Angina was distinguished from myocardial infarction (Hammer, 1878, and Dock, 1896), diagnosed as a myocardial infarction during life (Herrick, 1912), and was determined to be related to myocardial ischemia (Resnick and Keeler, 1928).[23,25] In 1933, Evans and Hoyle demonstrated that
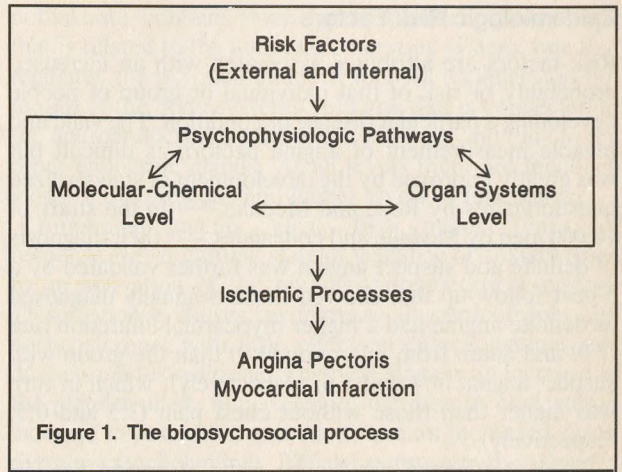

Figure 1. The biopsychosocial process

lactose used as a placebo was in certain cases effective as treatment of angina. The decades of the 1970s and 1980s saw the development of the β-blockers, calcium blockers, and thrombolytics; the identification of the major epidemiological risk factors; the performance of coronary bypass operations and angioplasty; and the role of coronary spasm and dynamic coronary obstruction. Mention must be made also of the remarkable autopsy, performed by Long in 1931,[26] of an Egyptian mummy reputedly 3,000 years old. He found evidence of fibrous thickening and calcification of the coronary arteries and scar-like areas in the myocardium, presumably as a result of ischemia. Interestingly, Katon[27] found that patients with chest pain and normal coronary arteriograms had a higher level of anxiety, depression, and panic disorder than those whose arteriographic studies showed coronary stenosis. The significance of this needs further elucidation.

The Biopsychosocial Process

The biopsychosocial process leading up to the end result of angina pectoris can be viewed in a number of systemic steps (Figure 1). First, the external and internal risk factors, as defined by clinical and epidemiologic studies, act on the individual. In the latter the risk factors are transmitted and interpreted by numerous psychophysiologic pathways to affect and be affected by the various organ systems (cardiovascular, endocrine, nervous) through numerous molecular physical processes. The interrelated systems lead to a state of myocardial ischemia that produces angina pectoris, silent ischemia, or myocardial infarction.

In the following sections a closer examination will be made of each of these biopsychosocial processes.

Epidemiologic Risk Factors

Risk factors are attributes associated with an increased probability or risk of that individual or group of people developing a particular disease or condition. The valid and reliable measurement of angina pectoris is difficult but was greatly improved by the development of standardized questionnaires by Rose and Medalie.[28,29] In the study of 10,000 men by Medalie and colleagues,[29,30] their diagnosis of definite and suspect angina was further validated by a 5-year follow-up that showed those originally diagnosed as definite angina had a higher myocardial infarction rate (7.0) and death from infarction (3.9) than the group with suspect angina (4.7 and 1.6, respectively), which in turn was higher than those without chest pain (3.5 and 0.5, respectively).

The age-adjusted prevalence rates of angina for US men were found to be 3.9% for whites, 6.2% for blacks, and 2.8% for Mexican-Americans; the corresponding rates for women were 6.3%, 6.8%, and 5.4%, respectively.[31] The Framingham Study reported an incidence rate of 2.7 per 1000 men in the 45- to 54-year age group, which rose to 7.5 per 1000 in the 55- to 64-year age group and 5.6 per 1000 in the 65- to 75-year age group.[32]

Clinically and pathologically, angina pectoris is closely related to myocardial infarction, but epidemiologic studies have pointed up some important differences. In myocardial infarction the male-to-female ratio is four to five men to one female, whereas the ratio in angina pectoris is almost equal and in some studies even higher among women.[31] Psychosocial factors, eg, type A personality, anger, hostility, physiological reactivity to a stressor, anxiety, family problems, have shown significant associations with angina pectoris but, with the exception of type A personality, have not been significantly correlated with myocardial infarction.[30,33] Cigarette smoking is another variable with differing associations. As is well known, all major epidemiologic studies have demonstrated significant associations of smoking to myocardial infarctions, but the association with angina varies. Some studies have shown no significant association, whereas in others it varies by different age and sex groups.[30,33] In nearly all cases smoking has a much weaker association with angina than with infarcts.[31,32,34]

A multivariate analysis of a 5-year angina incidence study of 10,000 men showed the associated factors displayed in Table 1.[30] As indicated, the top four factors are anxiety, family problems, serum cholesterol, and blood pressure. The synergistic effect of these four variables is further shown in Table 2, where the incidence of angina rises from 12 per 1000 when all four variables are low, to 97 per 1000 when all are high. Other studies using different psychosocial variables have found significant associations with depression, chronic conflict, and type A

TABLE 1. ANGINA PECTORIS RISK FACTORS: MULTIVARIATE ANALYSIS OF 10,000 MALES, OVER 5 YEARS

Variable	Standard β Coefficient	
Anxiety	0.29	
Psychosocial (family) problems	0.25	
Total cholesterol level	0.24	$P < .01$
Blood pressure	0.20	
Age	0.18	
Electrocardiogram abnormalities	0.14	
Diabetes	0.10	$P < .05$
Overweight (ht/wt^2)	0.10	

*Modified from Medalie et al[29].

personality[14,15,35–37]. Subjects with the latter personality were shown after 8.5 years of follow-up to develop angina pectoris at an average incidence rate of 6.9 per 1000 as opposed to a similar-sized type B group, whose rate was 3.2 per 1000.[33]

A family history of angina and early coronary heart disease (under age 55 years) is another important independent risk factor.[38,39] In addition to family history, which has a genetic and environmental component, there are other clues in respect to genetic aspects such as increased rates with blood group A_1 BJK^{a-} (A_1B Kidd negative) and exciting new discoveries regarding genetic markers.[29,40]

Finally, inadequate social support systems within or external to the family have been found to be an important associated factor both for myocardial infarction and angina pectoris.[35] Social support can be defined as the emotional, instrumental, or financial aid that is obtained from the social environment. Certain major studies have found low levels of social support systems or social networks to be related to increased mortality, nonfatal infarcts, and coronary heart disease in women.[41,42] In respect to angina, the effects of support, or lack of, at work (bosses, co-workers) and at home (wife, family) as perceived by the male subjects were examined.[30] The strongest relationship found was with the subject's perception of his wife's love and support (Table 3). From this table it can be

TABLE 2. SYNERGISTIC EFFECT OF ANXIETY, FAMILY PROBLEMS, CHOLESTEROL LEVEL, AND BLOOD PRESSURE ON INCIDENCE OF ANGINA PECTORIS PER 1000 MEN

		Cholesterol and Blood Pressure	
		Low	High
Anxiety and Family Problems	Low	12	39
	High	51	97

*Modified from Medalie et al[29]

TABLE 3. INTERACTION OF WIFE'S LOVE, SUPPORT, AND ANXIETY ON THE INCIDENCE OF ANGINA PECTORIS PER 1000 MEN

		Wife's Love and Support			
		Highest...Lowest			
Anxiety	Low	21	28	24	25
	High	52	45	73	93

seen that when the level of anxiety is low, the amount of support received is immaterial. When anxiety is high and support is low, the incidence of angina rises to 93 per 1000. With high support this group of high anxiety drops to almost one-half that rate, ie, 52 per 1000.

Psychophysiologic Pathways

The stressful impact of an event depends upon the meaning that event has for the individual.[43] This meaning is dependent on two factors: the potential symbolic referents of the stressor (relative to certain unresolved conflicts), and the effectiveness of the ego defenses and coping ability of the individual. The question is how to explain the mechanism when an event leads to clinical sequelae. Recent advances in knowledge of the brain's functioning and the pathways from the brain to the peripheral organs are beginning to clarify the mechanisms. A simplified version of the psychophysiologic pathways is displayed in Figure 2. The meaning of events or stimuli from the environment is processed in the cortex, which then activates neurotransmitters to the brain stem, limbic system, and directly and indirectly to the hypothalamus. The hypothalamus seems to be the center where psychological 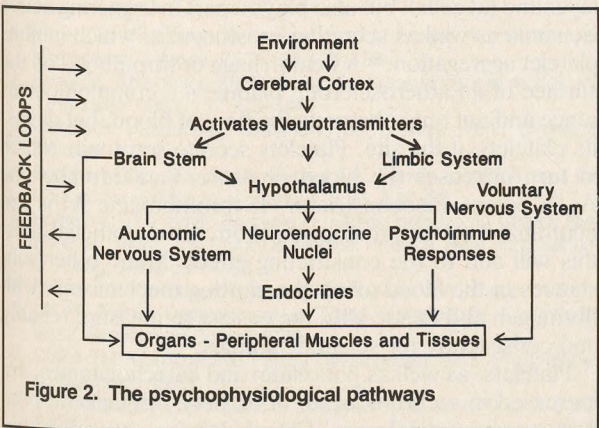stress is transduced into physiologic function.[43] The hypothalamus contains three types of nuclear groups: one that is related to the autonomic nervous system, one that regulates the psychoimmune responses (cellular and humoral) of the body systems, and one that is connected to the neuroendocrine nuclei of the pituitary and thus to the other endocrine glands. At all levels there are feedback loops to the previous and higher levels of functioning.

Emotional events elicit two major types of response.[44,45] A chronic state of vigilance or anxiety leads to an activation of the pituitary-adrenocortical system. This response causes an increase in corticotropin and corticosterone, with little effect on catecholamines and decrease in testosterone. The next stage is an increase of the platelet mass, hypertension, increase in cholesterol, increase in potassium excretion, and an increased sensitivity to catecholamines. This response sets the stage for the body's reaction to an acute crisis superimposed on this chronic anxiety state.

The acute response (fright-flight-fight reaction) is characterized by activation of the sympathetic-adrenal medullary system, with increased levels of catecholamines and testosterone, leading to tachycardia, enhanced cardiac contractility, increased cardiac output, and increased peripheral vascular resistance. This response sets the stage for acute cardiovascular dysfunction.

Pathophysiology of Myocardial Ischemia

For practical purposes the total energy expenditure of the normal heart can be equated with its oxygen consumption.[46] In normal people the oxygen supply by way of the coronary blood flow is maintained and responds to the myocardial oxygen demand throughout the 24 hours for all activities. An imbalance will occur if the supply cannot be increased to meet extra demands or if the supply is decreased and cannot meet normal everyday demands. These instances usually result in what is known as myocardial ischemia, with or without chest pain. The following factors are involved in myocardial ischemia.[46–48]

1. Increased myocardial oxygen demand (MVo_2) is dependent on an increase in intramyocardial systolic tension, an increase in heart rate, and an increase in the contractile state of the myocardium. A simplified index of MVo_2 is heart rate × blood pressure.

2. Diminished oxygen supply (coronary obstruction) is usually due to atherosclerotic plaques but can occur from, or be aggravated by, increased coronary tone (generalized or segmental), external compression of the coronary vessels, or hypotension.

3. There can be a combination of increased demand and diminished supply.

Figure 2. The psychophysiological pathways

Vasotonic Angina and Emotional Factors

Vasotonic angina is the term used by Robertson et al[49] for patients with transient coronary occlusions causing ischemia with no exertional angina. These attacks are not preceded by changes in heart rate or blood pressure.

Coronary vasospasm as a cause of angina was postulated by Latham in 1876 and stressed by Osler in 1910. It was not generally accepted until the 1970s, however, when Oliva et al[50] and then Maseri et al[51] documented coronary spasm of the major arteries in patients undergoing angiography. This spasm can occur in arteries with no evidence of atherosclerosis, or it can be superimposed on an atherosclerotic plaque, as might occur in unstable or variant angina, and thus be a precipitant of a myocardial infarction.[52]

Dynamic coronary obstruction is the term given to the dynamic changes that occur in and to coronary arteries impeding the flow of blood. In addition to spasm of the epicardial coronary arteries, Steudel[52] has shown that constriction can also affect the intramyocardial arterioles and the subendocardial capillaries, all of which can be affected simultaneously, ie, along the whole length of the artery, or each segment may be affected alone, by spasm, increased tone, or external compression.[52] This knowledge has important implications for understanding various types of angina, the possible production of arrhythmias, and more specific treatment (surgery, vasodilation, type of medications) to be used in different circumstances.[53] It would seem that increased vasomotor tone probably plays a significant role in all types of angina and in precipitation of infarcts.

Mental Demands and Myocardial Ischemia

Patients with angina and coronary disease have many episodes of symptomless transient myocardial ischemia, and when monitored on an ambulatory basis, these episodes seem to be triggered by ordinary daily activities not necessarily related to increased physical exertion.[19,20,54,55] To test this hypothesis, Deanfield and his colleagues[54] chose 16 patients with chronic stable angina and 13 normal controls with no symptoms or signs of coronary disease. They visualized regional myocardial perfusion and ischemia by the uptake of rubidium 82 with positron tomography after simple mental arithmetic and physical exercise. They then simultaneously recorded their electrocardiogram and noted the presence or absence of clinical symptoms. None of the controls showed any abnormalities either with exercise or mental arithmetic. Conversely, the 16 patients all showed perfusion abnormalities and ST depression with physical exercise, and 15 developed clinical angina. With mental arithmetic, 12 of the 16 showed regional perfusion abnormalities, 6 exhibited ST depression on their electrocardiogram, but only 4 had clinical angina. In other words, 6 of the 12 with perfusion abnormalities showed no electrocardiographic or clinical changes. These episodes were silent ischemia. Deanfield concluded that "the association between mental activity and myocardial ischemia may operate frequently during everyday life and may explain many of the transient and symptomless electrocardiographic changes in patients with coronary disease."[54]

Rozanski et al[19] recently validated Deanfield's work and extended it by comparing the effects of a series of mental tasks with those induced by exercise. They found that an emotionally arousing mental task induced as much cardiac dysfunction as that of exercise in patients with coronary heart disease. They concluded that mental stress may be an important precipitant of myocardial ischemia (often silent) in patients with coronary heart disease. Epstein et al[55] estimated that perhaps as much as 70% of ischemic episodes are silent, and Selwyn and Granz[20] feel that this ischemia might be more important in prognosis than the clinical symptoms of angina.

The Molecular-Chemical Level

The last link in the chain of evidence is at the molecular-chemical level. These interactions are complex and not totally understood. Under experimental conditions in animals or humans, each of the substances and mechanisms mentioned below have been reliably shown to reduce or obstruct coronary flow or to substantially increase the demand of the myocardium for oxygen.[20,48,49]

The coronary artery walls play an active role through various mechanisms. The α and β adrenoceptors in the wall are usually balanced in favor of slight vasodilatation, but if there is an imbalance, then the added effect of catecholamines will produce vasoconstriction.[56] The endothelial layer of the coronary wall is not only an integral part of atherogenesis (together with cells of the muscular layer and fat cells), but also plays a part in triggering active ischemia as well as secreting prostocyclin, which inhibits platelet aggregation.[20] A hemorrhage or thrombosis on the surface of an atherosclerotic plaque is a common occurrence and not only obstructs the flow of blood, but deposits platelets at the site. Platelets secrete serotonin, which in turn increases the blood pressure, and thromboxane A_2, a potent vasoconstrictor. If thromboxane A_2 is not neutralized by the prostocyclin from the endothelial cells, this will add to the constricting effect. Many other substances in the blood affect the clotting mechanisms, with fibrinogen and factor VIIc the easiest to measure reliably and consistently for scientific studies.

Platelets, as well as potassium and catecholamines, are increased in a chronic state of anxiety through the pituitary-adrenocortical axis. Catecholamines are also sub-

stantially increased during periods of reactions to acute stress by way of the sympathetic-adrenomedullary axis.[44,45]

Myocardial cellular requirements for oxygen control the demand for coronary blood flow, so these requirements can be a factor in causing ischemia when demand exceeds supply. The myocardium also reacts to a severely diminished oxygen supply with a wide range of changes in cell metabolism, function, and structure. When oxygenated, the normal myocardium metabolizes fatty acids and glucose to carbon dioxide and water. With severe oxygen deprivation, fatty acids cannot be oxidized, and glucose is broken down to lactate. Concurrently, intracellular pH becomes reduced as do the myocardial stores of high-energy phosphates, adenosine triphosphate (ATP), and creatine phosphate. Impairment of cell membrane function leads to leakage of potassium and uptake of sodium by myocytes.[57]

Ischemia also alters the electrical properties of the heart, as evidenced by the electrocardiographic changes. T-wave inversions and ST segment depression or elevation reflect subendocardial or transmural ischemia.

SUMMARY

The dynamics of angina pectoris have been used to examine the validity of the biopsychosocial model by seeing how the risk factors lead to myocardial ischemia through the interrelated systems of psychophysiologic pathways, the relevant organ systems, and molecular chemical processes. From this attempt at an integrated review, it seems clear that angina pectoris is a validation of the biopsychosocial model.

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