Changes in Serum Lipids in Relation to Emotional Stress
during Rigid Control of Diet and Exercise

By Stewart Wolf, M.D., William R. McCabe, M.D., Joe Yamamoto, M.D.,
C. A. Adsett, M.D., and W. W. Schottstaedt, M.D.

In an earlier study of ambulatory human subjects, significant increases in the serum concentration of lipids and cholesterol were observed to correlate with emotionally stressful events in the life situation. Other workers have also observed such changes. The changes seemed to occur independently of diet and exercise, but since it was not possible in ambulatory subjects to rule out such influences, the present study was undertaken while subjects were hospitalized, and with careful attention to maintaining diet and exercise constant.

Methods

Four subjects, three men and one woman, were admitted to the metabolic ward of the Oklahoma Medical Research Foundation and were maintained on balanced regimens for periods varying from 4 weeks to 5 months. Exercise was carefully regulated and maintained as uniform as possible. Three of the subjects had had a well-documented myocardial infarction. Two were hypertensive. The fourth had mild hypertension and hyperlipemia, which was presumed to be familial. As soon as each patient was admitted to the hospital a standard diet approximating his usual eating habits was begun. All four of the diets selected happened to be of the "average American" type, with approximately 40 per cent of calories coming from fat, mainly animal fat. Calories were adjusted to the eating habits and size of the individual. The diet of one of the subjects is illustrated in Table 1. Periodic blood samples were drawn at the same time of day. Cholesterol was determined in some instances by the method of Zak and in others by the technic of Schoenheimer and Sperry, and in others by the auto-analyzer. Frequent checks were carried out with two or more methods. Duplicate determinations were made in each instance. Checks were within 2.3 per cent, and recoveries were within 5 per cent. Triglycerides were estimated by the technic of Zilversmit. Throughout the period of observation psychologic data gathered from interviews and day-to-day observations of the subjects were kept scrupulously separate from the chemical data.

The clinical evaluation included a careful appraisal of emotional growth, life experiences, attitudes, and reactions of the subjects. Then for a period of weeks they remained on the metabolic ward subject to whatever emotionally significant situations arose from day-to-day in relation to their fellows on the ward or in their own private lives. The circumstances were monitored through daily contacts and frequent interviews with the patients. There were no contrived situations or stresses.

Case 1

The first patient was a 60-year-old retired white male truck driver. He was hospitalized in the Oklahoma Medical Research Foundation from January 4 to April 4, 1958, and from April 21 to May 29, 1958. His health had been good until 1950, when he sustained a myocardial infarction from which he recovered uneventfully. He retired from driving because of his physician's recommendation, but was able to tend a small farm without significant symptoms. In June 1957, because of sudden dyspnea and cyanosis, he was hospitalized at the Veterans' Administration Hospital, Oklahoma City, Oklahoma. After 5 days' hospitalization, the patient developed severe anterior chest pain, prostration, and profuse diaphoresis. An electro-

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cardiogram revealed evidence of an old anteroseptal myocardial infarction and recent changes compatible with recent anterolateral and high lateral infarction. Oxygen and anticoagulants were administered. After 2 months he was discharged on a program of progressive activity. In September 1957, upon strenuous exertion he began to experience precordial chest pain that radiated to the left axilla. Mild exertional dyspnea and orthopnea appeared concomitantly and became sufficiently severe by December 1957 to require hospitalization again. He was treated with a 500-mg. sodium diet, digitalis, and diuretics, with a resulting increase in exercise tolerance. On January 4, 1958, the patient was transferred to the Oklahoma Medical Research Foundation for study.

Systemic review and past history failed to elicit additional illnesses or symptoms of significance.

Born in Arkansas in 1898, he spent his early childhood in Arkansas and Indian Territory. His father was a traveling “medicine man” and later a coal mine operator. The patient was the second oldest of five children and the oldest son. The mother was affectionate and enjoyed a warmer relation with the children than did the father. He recalled his father as being undemonstrative. He maintained strict discipline, usually without the need for physical punishment. The family atmosphere was congenial despite the father’s austere disposition. Minimal family tension and parental disagreements were recalled. Their social and economic status was of lower middle class in a rural community. The patient’s education was limited to only about 3 years of formal schooling. He felt bad about not having taken advantage of educational opportunities. Indeed, he attributed his failure to attain economic success in later life to the lack of an adequate formal education. At the age of 11, he began working as a coal miner and continued in the occupation until his induction into military service in 1917. He was extremely proud of his physical abilities and financial independence at this young age.

During his adolescence and early adult life the patient considered himself to be quite a “hell-raiser.” He gambled, drank frequently, and often became involved in fights. He was very sensitive to any insult and was quick to fight in defense of his dignity. This type of aggressive response was characteristic of his reaction to threatening situations throughout his life.

Enuresis, nail biting, night terrors, and other childhood neurotic traits were denied.

While the patient was still a child, his family joined an extremely austere religious group that forbade medical care for its members and the use of cosmetics, and indulged in unusual practices such as handling reptiles and prophesying. His father stopped drinking, gambling, and dispensing “home remedies.” Although the patient attended his parent’s church, he was never able fully to accept their religious tenets.

The patient lived with his parents until his military service, from 1917 to 1919. This period was spent entirely in the United States, guarding German prisoners of war. Just before his discharge he married a girl of French ancestry in New Orleans. They were very happy until she died in the 1919 influenza pandemic. Following his wife’s death, the patient returned to his parent’s home, but remarried a year after, in 1920.

His second wife was a devout and important member of his parents’ church. She was believed to have the “gift of prophecy,” and
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handled the reptiles during religious ceremonies. Five children, three boys and two girls, were born. All except the eldest were born without medical attendance because of the wife's religious beliefs. She objected to and ridiculed several of the patient's friends and induced him to discontinue many of the activities he had previously enjoyed. Over a period of years the patient discontinued gambling and drinking, but was never completely able to accept his wife's religious faith. Because of his wife's religious convictions, however, he did feel considerable emotional conflict when he sought medical attention for his heart disease. Despite his inability to accept her faith, he felt a deep desire for her wholehearted acceptance of him.

Soon after his second marriage the patient leased a coal mine and managed it for several years. Later, he farmed unsuccessfully for a short while, and then returned to coal-mining as a work foreman. When he failed an examination to become a mine superintendent, he accepted employment as a truck driver for a construction company. While employed in this capacity, he became closely attached to the company's president, who gave him considerable responsibility. He distributed the company payroll and served as the president's chauffeur. This relationship, which gave the patient a feeling of considerable importance and success, was terminated by the death of the president from a myocardial infarction in 1949. Thereupon, during the ensuing change in management, the patient's position deteriorated to that of an ordinary truck driver. His own myocardial infarction followed within a few weeks. After his recovery he became embroiled in a legal contest with his employers over industrial compensation. The suit was settled in his favor, but almost the entire settlement was spent in legal and medical fees. Thereafter he was never steadily employed except for a brief period as a service station manager. Although his service station was a financial success, he gave it up because of his dislike of catering to the demands of others. In his own words, "I was never one to be a porter.' Thereafter his only income came from government disability compensation and what he earned from odd jobs.

Physical examination revealed a well nourished plethoric white man. The blood pressure was 160/110 in both arms. No cardiomegaly was detectable by percussion. A faint short systolic murmur was audible over both the mitral and aortic areas. The abdomen was soft and a rounded liver edge was felt 4 cm. below the right costal margin. There was no edema. The remainder of the physical examination was not remarkable.

The hemoglobin was 13.5 Gm. per 100 ml. and the hematocrit level was 45. The leukocyte count was 8,600 mm.\(^3\) with 59 per cent polymorphonuclear leukocytes. Urinalysis and urine culture were negative. Blood urea nitrogen was 17 mg. per cent and serum glutamic oxaloacetic transaminase was 8 units per 100 ml. Radioactive iodine uptake by the thyroid gland was 13 per cent of the orally administered dose 24 hours after ingestion. A protein-bound iodine was 6.5 \(\mu\)gm. per 100 ml. Total cholesterol was 256 mg. per cent and lipid phosphorus was 11.6 mg. per cent. Beta lipoprotein determination revealed 236 mg. per cent in the 0-12 fraction, 8 mg. per cent in the 12-20 fraction, and 2 mg. per cent in the 20-100 fraction. Triglycerides were 97 mg. per cent. An electrocardiogram revealed a QRS interval of 0.11 second with a broad Q wave in leads I, aV\(_L\) and V\(_5\) and a Q8 pattern in leads V\(_1\)-V\(_4\). These findings were thought to be consistent with anteroseptal, anterolateral, and high lateral myocardial infarction and peri-infarction block.

The patient was given a constant diet of 2,170.7 calories containing 931 mg. of sodium. Forty per cent of the caloric intake was supplied by fat. The other constituents of the diet are enumerated in table 1. No dietary variation occurred during the entire period of hospitalization; spot dietary analyses revealed no significant variation in the content of the previously enumerated constituents. While on the metabolic balance study the patient received 0.1 Gm. of digi-
The only variation in dietary intake consisted of infrequent ingestion of nitroglycerin (0.4 mg.) for chest pain, carmine 0.5 Gm., and cascara 3 cc. for stool collections. All stool and urine specimens were collected for measurement of nitrogen, creatinine, sodium, potassium, and chloride.

For the entire period of metabolic study the patient remained in borderline to good cardiac compensation; his only symptoms consisted of brief episodes of angina pectoris. During the relatively long period of study he adjusted well to the rigors of dietary monotony. The relationship of the small community of patients undergoing metabolic study was on the whole harmonious. Several personality differences and evident emotional disturbances did arise, however, during the study periods. The first occurred during the early days of hospitalization when he resented the psychologic probing necessary for the study. Later, as indicated in figure 1, he came into conflict with the patient who was sharing his room. He felt that he was being "pushed around," although his roommate was a frail little man suffering from muscular dystrophy. After the roommate was assigned other quarters serenity was restored until a new patient was admitted—an alcoholic who was to be studied from the standpoint of the effects of heavy drinking on magnesium metabolism. This man was given the privilege of coming and going as he wished at night. Frequently he came in noisy and drunk. One morning at breakfast he picked up the patient’s napkin and blew his nose on it. The patient interpreted this as an unfriendly gesture and was barely able to resist striking the man. A few days later the two had a quarrel over the setting of the television dial. When the alcoholic man called our patient a derogatory name, a fight was prevented only by the intervention of the nursing personnel. A blood cholesterol drawn soon after this encounter proved to be the highest observed during the patient’s hospitalization (fig. 1).

Case 2

The second patient was a 39-year-old woman who had mild hypertension with blood pressure in the neighborhood of 160/100, and

Figure 1

Changes in serum concentration of cholesterol in case 1 during several months of constant diet and exercise. Twenty-five days independently judged as stressful are marked with circle. (Mean cholesterol concentration: 283, with S.D.=12.5. Mean concentration on 10 non-stressful days: 212, with S.D.=10.3).
a persistently high serum cholesterol in the neighborhood of 300 mg. per cent. She had been in conflict with her husband for 10 years, mainly because of his infidelity. She had dealt with this difficulty by attempting to ignore her husband’s behavior and suppressing her feelings about it. After entering the hospital, serum cholesterol and triglycerides rose. Like the first patient she resented the psychologic probing. In fact, she had so much difficulty in adjusting to her physician that it became necessary to assign her another. Thereafter she became much more relaxed and 2 days later the serum concentration of cholesterol had fallen from 404 to 326 mg. per cent. During the next 3 weeks the patient became increasingly well adapted to the metabolic ward. She liked her new doctor and enjoyed making friends with the other patients. She was given, as a placebo, the vehicle in which androsterone was later to be administered. Despite the constant diet (protein 68 Gm., fat 89 Gm., cholesterol 206 Gm., calories 1855) and no weight change, her serum cholesterol concentration fell progressively to the neighborhood of 275 mg. per cent as shown in figure 2. During the 10-day period of androsterone therapy that followed, cholesterol remained low. It was still low 4 months after androsterone had been discontinued and after she had been discharged from the hospital. In fact, when measured on follow-up visits, it was below 300 mg. per cent except for two occasions when there was conflict at home because of her husband’s infidelity.

Case 3

The third patient, a 49-year-old white man, had suffered a myocardial infarction 3 years prior to his admission to the metabolic ward. Thereafter he had been recurrently hospitalized with manifestations of congestive failure and one additional episode of myocardial infarction.

There were no serious illnesses in childhood until the age of 14 when he had mumps with orchitis. At that time he recalls his doctor having said, “You might as well estra- tate him.” To this his father replied, “Then he might as well be dead.” Later the patient suffered two accidental injuries to the testes; the first at age 26, and the second while in the Navy at age 36. Ultimately, he developed a hydrocele. The remainder of the medical history was unremarkable except for accidental fractures of the clavicle in 1914 and 1927, and for hemorrhoids.

The patient was the second of 10 children born to a farm family. Until age 6 or 7 he felt that he was treated like a girl. “They tried to make a girl out of me, fiddling around the house, so I could pluck a chicken and do things like that.” Until the age of 12 he was enuretic despite vigorous training “under the guidance of a physician.” The patient rejected his mother and consciously identified much more strongly with his father. He described his mother as a “roly-poly, five by five woman, who wasn’t very saving and wasted a great deal.” He blames his failure to complete his high school education on his mother’s eagerness for the sisters to continue their education beyond high school. At 19 he eloped with a 15-year-old girl. This first wife was the daughter of the man for whom he worked, a man who had for several years been “like a second father to me.” He described the wife as sexually unfaithful but otherwise the “perfect wife, very saving and economical.” There were
three children born of this marriage, a daughter, a son, and another daughter. Finally, after 8 years of marriage, his wife deserted him and he divorced her. When she returned to him, however, at a time when he was recovering from an accidental injury to his back, they were reconciled and remarried. In 1944, his wife's continued infidelity prompted him to enlist in the Navy, although he had a defense job that would have deferred him. While the patient was in the Navy his father died, apparently of myocardial infarction. He divorced his wife a second time, 10 years after the first divorce. "One of her boy friends just wouldn't leave her alone," he said. The daughters went to live with his wife. His son, whom he described as his "pride and joy," stayed with him. At this time the patient worked as a butcher. He and his son had an unusually close relationship. They actually slept together in the same bed. When the patient was 41, his mother, at the age of 58, died of a "heart murmur." The following year his son married, and 5 months later the patient himself remarried a woman, then 46, whose first husband had committed suicide 20 years before. His second wife was cold sexually, meticulous, and excessively preoccupied with cleanliness. She made constant demands on him to keep the house orderly. The patient described this period as a "living hell." He threw himself into his work, very anxious to succeed vocationally, since he was having such problems at home. In this setting he had his first myocardial infarction. Three years later, while hospitalized for congestive heart failure, he met another woman who was very friendly, motherly, and kind to him. When he was transferred to the metabolic ward for study she visited him daily, while his wife rarely came to see him. During his first few days on the metabolic ward, he and his woman friend were pleasantly engaged in making plans to divorce their separate spouses and marry each other. The patient described her with considerable warmth. "This little old girl, she talked to me, babied me and petted me. She's had the same life I've had for twenty some years. I can be at my lowest and she'll come and talk to me thirty minutes and I'll feel better. I guess it's understanding."

Physical examination: At the time the patient was admitted on September 10, 1957, he was neither in acute distress, nor did he appear chronically ill. Blood pressure was 120/80, pulse 84, and respiration 24. The optic fundi revealed slight segmental constriction of the arterioles. He was edentulous, and there was an increase of the anteroposterior diameter of the thorax. The heart was slightly enlarged with a blowing systolic murmur over the base. The liver was palpable three finger-breadths below the costal margin at the right midclavicular line. The remainder of the general physical and neurologic examinations was within normal limits.

Laboratory findings: Urinalysis and blood cell counts were unremarkable. Chest x-rays revealed an enlarged heart and findings consistent with passive congestion of the lungs. An electrocardiogram was interpreted as indicating (1) old inferoseptal, anterolateral, and anteroseptal infarction; (2) complete right bundle-branch block; (3) primary T-wave changes characteristic of digitalis effect; (4) occasional atrial extrasystoles.

Hospital course: The patient seemed happy and reasonably relaxed, although very eager to please during the first few days of the study while receiving daily visits from his new woman friend. When she left town for a few days without telling him, however, he became anxious. Serum cholesterol concentration rose somewhat until she returned, re-visited, and reassured him. During this visit, however, she had met another man whom she preferred. Her daily visits to the patient fell off and on November 13, 1957, she told him that she had abandoned the plan to marry him and would not see him again. He became intensely depressed. Again the serum cholesterol rose and the following day he had a recurrent myocardial infarction. Four days later he died. See figure 3.

Necropsy: Evidences of myocardial infarc-
tion, both recent and old, were found. Other findings were marked bilateral pulmonary edema, bilateral pleural effusion, pulmonary emphysema, marked atherosclerosis of the coronary arteries, aorta and splenic artery with infarcts in the kidneys and the spleen.

Case 4

The fourth patient was a 49-year-old rancher and cafe operator. In 1943 he developed throbbing bilateral headaches. In 1945 it was discovered that his blood pressure was elevated in the neighborhood of 150/100. Between 1945 and 1958 he was seen regularly by physicians for treatment of his headaches and hypertension. Mainly he received reserpine and phenobarbital.

There was no family history of hypertension. His father died of a "heart attack" at the age of 64. One brother had died of a "heart attack" about a year before the patient's illness at the age of 42, and another brother, age 37, had angina pectoris. A sister, age 46, apparently was also said to have some type of heart disease.

Both parents were extremely strict, requiring the children to conform in order to be able to obtain their affection and acceptance. They constantly emphasized to the patient that he must like every one and be friendly. Anger and fighting were frowned upon and he frequently was spanked or reprimanded by his parents for fighting with his brothers and sisters. On one occasion he was badly frightened when in a fight with another boy he hit him across the face with a bridle rein. He was severely reprimanded by his parents and the principal of the school and was told that the next time such a thing happened he would be handed over to the sheriff. Since this episode the patient states he has never had a fight or a serious argument.

The patient was admitted to the Oklahoma Medical Research Hospital on February 2, 1959, for study. Physical examination showed a well-developed, stocky man about 50 years of age, who kept his gaze averted, and who moved his hands about restlessly. There were upper and lower dentures. The fundi showed slight narrowing and sclerosis of the arterioles without arteriovenous nicking, hemorrhage, or exudates. The chest was clear. The heart appeared normal in size. The rate was regular at 78 a minute, and no murmurs were heard. Blood pressure was 180/114 in the right arm supine. The remainder of the physical examination was unremarkable.

Chest x-ray showed the heart to be within normal limits in size and shape. Both lung fields were clear. An electrocardiogram indicated slight left ventricular hypertrophy with an intrinsicoid deflection of 0.05 at V₄ and T was low in V₅ and V₆. Urinalysis and blood cell counts were normal. Blood urea nitrogen was 10 mg. per cent; total serum protein 6.4, albumin 4.3, and globulin 2.2 mg. per cent.

On the ward the patient made a great effort to please everyone. During the first 2 weeks serum cholesterol hovered in the neighborhood of 280 mg. per cent. He was particularly happy because his friends at home had had a television set installed in his room. Cholesterol rose to 321 after the patient came into conflict with another man on the ward over the rules of a card game. He felt that the man had taken advantage of his good nature, but was unable to express his resentment about the episode. Disagreements continued. The patient became taciturn and troubled because

![Figure 3
Changes in serum cholesterol during stressful and nonstressful days in case 3.](http://circ.ahajournals.org/lookup/doi/10.1161/01.CIR.26.3.385)
"the nurses seem to have sided with the other man." His serum cholesterol rose to the neighborhood of 315 mg. per cent. A week later it was 318. His wife had refused to come for him because she was busy "looking after his affairs." Finally, his situation become more satisfactory. His wife was more solicitous, and within 2 weeks his serum cholesterol concentration had fallen to 261 mg. per cent, a decrease of 47 mg. per cent without change in diet or exercise.

Stress Interviews

In order to ascertain the length of time required for the changes in serum concentration of cholesterol observed under stressful circumstances, short-term experiments were undertaken with two of the patients (cases 1 and 2), in which blood was drawn before and after an interview lasting from 1 to 2½ hours. In "control" interviews the subject was engaged in pleasant conversation about reassuring topics. Stress interviews covered topics of known troublesome emotional significance to the patient. The data are recorded in figures 4 and 5. During the "neutral" interviews there was no increase in cholesterol concentration. In fact, in the first patient cholesterol decreased in each of them. This subject had always been apprehensive about the interviews. When they failed to touch on sensitive points, he appeared to be considerably relieved. During stressful interviews, however, increases of 70 mg. or more in the concentration of serum cholesterol were achieved within an hour. In patient no. 2 in whom triglycerides were measured, they, too, rose significantly during emotional stress.

Conclusions

Without change in diet or exercise it has been shown that striking alterations in the serum concentration of cholesterol and triglycerides correlate with the occurrence of emotionally stressful situations. Such changes may be brought about during stressful interviews within 60 minutes.

No inferences are drawn with respect to the significance of emotional stress in the pathogenesis of coronary atherosclerosis or myocardial infarction, but it is clear that the mechanisms that govern the serum concentration of certain lipids are connected with and capable of responding to impulses from the higher centers of the brain.

References


Religio Medici

Where we desire to be informed, 'tis good to contest with men above our selves; but to confirm and establish our opinions, 'tis best to argue with judgments below our own, that the frequent spoils and Victories over their reasons may settle in ourselves an esteem and confirmed Opinion of our own. Every man is not a proper Champion for Truth, nor fit to take up the Gauntlet in the cause of Verity: many, from the ignorance of these Maximes, and an inconsiderate Zeal unto Truth, have too rashly charged the Troops of Error, and remain as Trophies unto the enemies of Truth. A man may be in as just possession of Truth as of a City, and yet be forced to surrender; 'tis therefore far better to enjoy her with peace, than to hazard her on a battle. —Sir Thomas Browne. Religio Medici. Edited by W. A. Greenhill, M.D. London, MacMillan and Co., Ltd., 1950, p. 13.
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