SPECIAL ARTICLE

Influence of Some Factors on Development of Experimental Cholesterol Atherosclerosis

By A. I. Myasnikov

This paper is a brief outline of the results of research conducted for many years by my associates at the Institute of Therapy of the Academy of Medical Sciences in Moscow. The purpose of these studies was to observe the influence of different factors on the development of experimental atherosclerosis produced by feeding rabbits with cholesterol according to N. N. Anichkov's method. We have studied factors that both increased and retarded the development of experimental cholesterol atherosclerosis.

Our general program may be represented in the following way. Each study of the effect of a certain agent administered in combination with cholesterol comprised 2 groups of animals: control and experimental. Both control and experimental groups of rabbits received per os an equal amount of cholesterol together with food. The amount ranged from 0.1 to 0.2 Gm. per Kg. of weight daily for 100 days. In addition, the experimental groups received some other factor during the whole period or part of it. Furthermore, additional control studies were made of the possible effect on the vessels of the factor alone without administration of cholesterol. In every series of experiments the animals were of approximately similar weight, age, and sex.

The following factors have been studied: (1) some vitamins; (2) neurotropic drugs acting on the higher parts of the nervous system; (3) anticoagulants; and (4) anoxia and muscular exercise.

The blood cholesterol was systematically determined in all animals at intervals from 10 to 15 days.

At the end of the experimental period the rabbits were killed, and the aorta and the coronary arteries were examined. The arteries were immersed for a certain time in a solution of Sudan III so that the lipoid-infiltrated parts of the blood vessels were colored bright red. The degree of lipoidosis was graded on a scale of 1 to 4 plus.

Histologic examination was made in some cases.

Effect of Vitamins

Among the various vitamins, some, such as vitamin B₁ and riboflavin, exercised no definite influence on the degree of development of experimental atherosclerosis. Other vitamins, such as vitamin A and nicotinic acid, influenced the development of experimental atherosclerosis when administered in doses larger than the usual clinical doses. On the other hand, 2 vitamins, vitamin D₂ and vitamin C (ascorbic acid), had a very marked effect.

Vitamin D₂. The investigations conducted by M. V. Bavina showed that the administration of vitamin D₂ with food drastically increased both the degree and rate of development of alimentary hypercholesterolemia and the intensity of the aortic lipoidosis. These investigations were made on 32 rabbits. The animals received daily 10,000 units of vitamin D₂ (0.25 mg. of crystalline vitamin D₂).

Whereas the cholesterol content in the control group that received cholesterol only rose at the end of the experiment 88 to 300 per cent and averaged 183 per cent, the concentration of cholesterol in the experimental group (vitamin D₂ + cholesterol) rose 272 to 1,821 per cent and averaged 689 per cent (fig. 1). The cholesterol content in the group of animals that
received only vitamin D₂ without cholesterol hardly changed at all at the end of the standard time period.

In the control group of animals that received only cholesterol, the intensity of the aortic lipoidosis was generally 2 plus and, less frequently, 1 or 3 plus; in the experimental group of rabbits (cholesterol + vitamin D₂) the lipoidosis was far more intensive and was appraised 4 plus and less frequently 3 plus (fig. 2). No lipoid deposits were observed macroscopically in the aorta of animals that received vitamin D₂ in the same doses but no cholesterol.

We do not deal here with the problem of the influence of vitamin D₂ on the development of necrosis and calcinosis of the muscular membrane of the blood vessels. In our series of experiments, with the doses of vitamin D₂ used, such changes were observed only occasionally, were slight, and were not related in any way to lipoid infiltrates.

The mechanism whereby vitamin D₂ stimulates the development of vascular lipoidosis has not as yet been sufficiently studied.

Ascorbic Acid. According to the investigations conducted by I. A. Myasnikova, which I reported as far back as 1947 at the Thirteenth Congress of Soviet Therapeutists, and which were subsequently confirmed by a number of clinical institutions, ascorbic acid influences very markedly the development of experimental atherosclerosis of the aorta in rabbits as well as alimentary cholesterolemia, but in a direction opposite to that of vitamin D₂.

**Fig. 1.** The influence of vitamin D₂ on the blood cholesterol level in cholesterol-fed rabbits. Ordinate represents cholesterol in mg. per cent; abscissa, days. Cholesterol only (left), cholesterol plus vitamin D₂ (right).

**Fig. 2.** The effects of cholesterol, vitamin C, and vitamin D on atherosclerosis of the aorta in rabbits.
Ascorbic acid reduces the development of hypercholesterolemia and lessens and retards the development of experimental lipoidosis of the aorta in rabbits.

These experiments were performed on 35 rabbits. Ascorbic acid was administered per os in doses from 0.1 to 0.2 Gm. At the end of the experiment, the level of cholesterol in this series of experiments in the control group that received only cholesterol rose 2 to 4 times and averaged 238 per cent. In the experimental group receiving cholesterol plus ascorbic acid the hypercholesterolemia increased more slowly and reached its maximum later. In some experiments cholesterolemia changed comparatively little during the first 2 months and generally doubled or trebled only toward the end of the experiment. The average increase in this group amounted only to 116 per cent (fig. 3).

At autopsy these rabbits revealed differences in the lipoidosis in the aortas similar to the differences observed in the hypercholesterolemia. Whereas the intensity of lipoidosis of the aorta in the control group could be defined by 2 plus and but rarely by 3 plus, the intensity of lipoidosis in the experimental group could be appraised but by 1 and rarely by 2 plus, while in a number of experiments no lipid deposits were observed macroscopically in the aorta (fig. 2).

The following reservation should be made in this connection. It is well known that rarely lipoidosis may not develop in blood vessels even when cholesterol alone is administered in large doses. Evidently such rabbits are resistant to the development of atherosclerosis. This fact is one of the proofs of the great importance of some internal endogenous mechanisms that participate in the regulation of cholesterol metabolism in the organism and change the nature and degree of the assimilation of food cholesterol.

Absence of marked lipoidosis was encountered far more frequently when ascorbic acid was administered in combination with cholesterol. The mechanism whereby ascorbic acid retards the development of atherosclerosis has been specially studied by us. According to the findings of T. Y. Sidelnikova, the administration of ascorbic acid augments the amount of ketonic bodies in blood and stimulates the metabolism of fats and lipoids. There is reason to believe that, by intensifying the functional capacity of the liver, ascorbic acid stimulates the secretion of cholesterol with the bile. According to the observations by L. A. Typina, the intravenous administration of ascorbic acid to patients with atherosclerosis and hypertonic disease and a high content of cholesterol in the blood leads to a markedly lowered cholesterolemia. Simultaneously a greater concentration of cholesterol in the duodenal contents and the excrements is recorded (fig. 4).

It may be assumed that ascorbic acid reduces hypercholesterolemia and weakens the development of lipoidosis of the blood vessels both by influencing the oxidizing and restorative processes and by intensifying the excretion of cholesterol from the body.

**Effect of Neurotropic Drugs**

A study of the influence of pharmacologic agents changing the functions of the higher parts of the nervous system on the development of experimental atherosclerosis and on cholesterol metabolism was of particular interest for many reasons. First of all, the importance of the nervous factor in the pathogenesis
of atherosclerosis has as yet been very little investigated. Secondly, it has long been assumed in clinical practice that there undoubtedly exists a connection between disturbances in the central nervous system and the appearance of atherosclerosis. Thirdly, insufficient attention has been given to the role of endogenous factors in the development of experimental atherosclerosis. The administration of drugs acting on the nervous system during the production of atherosclerosis is of interest as an effort to influence the endogenous regulating mechanisms.

Pharmacologic agents were utilized that in-
tensify the processes of excitation; others were used that weaken them or intensify inhibitory processes. It was interesting to compare the influence of these neurotropic drugs on the development of experimental atherosclerosis. These investigations were conducted by a number of researchers (Y. T. Pushkar, T. D. Tsybikmakher, I. K. Shkhvatsabaya, and L. A. Myasnikov).

One of the series of experiments was devoted to the study of 2 neurotropic substances acting in opposite directions: phenobarbital (Luminal) and phenamine (Benzedrine). Phenobarbital in doses of 0.2 Gm. and phenamine in doses of 0.04 Gm. were administered periodically throughout the experimental period.

The blood cholesterol and lecithin and the blood pressure were measured at definite intervals throughout the period of the experiment. For blood pressure measurements the carotid artery was brought out into a skin strip.

Phenobarbital little changed the cholesterol and lecithin content in the blood, tending rather to reduce the concentration of either lipid. Under the influence of phenobarbital the behavior of the rabbits changed; they lost some of their agility and remained most of the time in a semi-drowsy state. As phenobarbital was administered, the arterial systolic and diastolic pressures regularly dropped 20 to 40 mm. Hg (fig. 5). The fluctuations of blood pressure, which were quite marked in the rabbits of the control group, considerably diminished in this case.

The development of atherosclerotic changes in the aorta in the rabbits receiving phenobarbital was quite markedly reduced: only 1 of 10 rabbits in the group showed 3 plus; in 7 the atheromata were manifest to a medium degree (2 plus), and in 2 to a slight degree (1 plus) (fig. 6).

The administration of phenamine (Benzedrine) led to an abrupt rise in the excitability of the central nervous system, to greatly increased instability of arterial pressure, and, in a number of experiments, to rises in arterial pressure.

The cholesterolemia increased considerably. Whereas in the control group of animals (only cholesterol) the maximum cholesterol content in the blood was 800 mg. per cent at the end of the experimental period, the maximum concentration of cholesterol in the blood of most rabbits that received phenamine increased to 2,100 mg. per cent (fig. 7). Accordingly, a more extensive development of aortic lipoidosis was re-
corded in the experimental group (cholesterol plus phenamine) than in the controls (fig. 6). Of the 10 rabbits that received cholesterol with phenamine, lipoidosis in 6 of them was appraised as 4 plus and in 4 as 3 plus.

The administration of phenamine led to a more pronounced degree of lipoid infiltration at some points and also to a more diffuse lipoidosis of the aorta.

A series of experiments was performed in which, besides cholesterol, not only phenobarbital and phenamine were applied, but simultaneously choline as well. It is known that choline reduces to some extent the development of experimental cholesterol atherosclerosis in rabbits. It was ascertained from this series of experiments on 20 animals that this effect becomes more marked when choline is combined with phenobarbital, and, quite the contrary, it is blocked when phenamine is administered simultaneously. In these experiments the influence of the neurotropic factors and choline on atherosclerosis was studied not only in the aorta, but also in the large coronary arteries, which exhibited the same changes as the aorta, though to a lesser degree.

The next series of investigations was devoted to studying 3 other drugs: amobarbital (Amytal) sodium, caffeine, and chloral hydrate.

When cholesterol was administered with food, the level of cholesterol in the blood of the control group reached 450 to 550 mg. per cent at the end of the experimental period, and in some cases 800 to 900 mg. per cent. In most instances atherosclerosis was quite pronounced. In the experimental group receiving cholesterol and caffeine the level of cholesterol in the blood differed but little from that in the control group. Atherosclerotic changes in the former group likewise approximated those in the control group.

Cholesterolemia of a slighter degree was recorded in the experimental group when amobarbital sodium was administered in addition to cholesterol. In some experiments no increase was observed (fig. 8). Similar results were obtained in the group receiving chloral hydrate in addition to cholesterol. The level of cholesterol in the blood rose rather slightly, despite systematic administration of cholesterol with food. In all the rabbits the aorta lipoidosis

**Fig. 7.** Influence of neurotropic drugs on the blood cholesterol level (ordinate) in experimental atherosclerosis. Left, cholesterol plus phenamine; right, cholesterol only.
Blood pressure was systematically measured in these groups of rabbits. The caffeine rabbits exhibited greater fluctuations of blood pressure than the controls. The Amobarbital sodium and chloral hydrate groups of rabbits showed a pronounced lowering of blood pressure and reduced fluctuations.

Under the influence of soporifics, the behavior of the rabbits changed: they became less agile, indifferent to the surroundings, and inert. In the amobarbital sodium series after the administration of the drug sleep set in daily, and lasted from 2 to 5 hours.

These findings lead us to the conclusion that when the excitability of the central nervous system is reduced, respiratory inhibition is intensified, an abrupt decrease of alimentary hypercholesterolemia is observed, and of particular importance, a decreased lipoidosis of the blood vessels occurs. It is difficult to state whether this reduction is related to lowered alimentary hypercholesterolemia or to the reduced level of blood pressure and to a decrease in its fluctuations or to both.

Apart from the above experimental investigations, clinical observations also were made on the influence of neurotropic drugs on serum cholesterol level of patients with hypertonic disease and atherosclerosis. Patients with a pronounced rise in the blood cholesterol were observed. Various drugs were administered, some calming the nervous system by reducing the excitability of the higher parts of the nervous system or increasing inhibition, such as phenobarbital, chloral hydrate, and amobarbital sodium, and others exciting the nervous system, such as phenamine and caffeine. The drugs were administered in comparatively large doses: Phenobarbital, 0.3 to 0.2 Gm.; chloral hydrate, 1 Gm.; Amobarbital sodium, 0.3 Gm.; caffeine, 0.3 Gm.; and phenamine, 20 mg. Observations were made in 128 patients. In some individuals different drugs were employed, thus facilitating the comparison of their effect.

The observations were of 2 kinds: short ex-
Experiments with blood cholesterol levels measured 1, 2, or 3 hours after single doses and prolonged observations of the blood cholesterol levels for a week or 2, when, after daily doses, the results of these observations proved to be similar to those of experimental observations. The drugs reducing the excitability of the central nervous system and inhibiting its function (amobarbital sodium, chloral hydrate, and phenobarbital), reduced the blood cholesterol level; the drugs exciting the activity of the central nervous system (phenamine and caffeine), exerted an influence in the opposite direction, raising the choles terolemia (fig. 9). These changes were revealed most clearly after single doses; when administration was prolonged, changes in cholest erolemia appeared less pronounced, though in the same direction.

Our findings confirm the conclusion that the cholesterol content in the blood is controlled by the central nervous system. The opposite nature of the effects on the central nervous system of the neurotropic pharmacologic drugs caused opposite effects on the cholest erolemia and experimental lipoidosis of the vessels. It is difficult to believe that the consistent pharmacologic effects could be unrelated to their central influence, but due to some other collateral influence on the internal organs, i.e., the liver and the endocrine glands, although such influences can hardly be left out of account altogether.

**Effect of Anticoagulants**

It is common knowledge that anticoagulants play a significant role in treating of patients with myocardial infarction, one of the most important manifestations of atherosclerosis. Attention has been centered on the effect of anticoagulants in retarding or preventing thromboembolic phenomena. However, the problem has recently been raised as to the possible influence of anticoagulants on the development of the atherosclerotic process itself. In a series of experiments we administered daily 30 to 60 mg. of heparin intravenously in prolonged courses of treatment, in addition to the regular doses of cholesterol introduced with food. In other experiments, another anticoagulant, neodicoumarin (Pelentan) was administered instead of heparin in doses of 20 to 40 mg. per Kg. of weight, simultaneously with the cholesterol.

Control experiments were carried out with the administration of cholesterol only; the results obtained were quite similar to those produced in the other control series, both in respect to the degree of alimentary hypercholesterolemia and the pronounced lipoidosis of the aorta and other arteries.

Finally, control experiments were conducted with the administration of heparin or neodicoumarin alone, without simultaneously administered cholesterol. No markedly pronounced lipoid deposits were discovered in the aorta walls in this group.

The findings of the investigations are shown in diagrams. Figure 10, for example, demonstrates the fluctuations of the blood cholesterol content in various groups of rabbits. No sharp difference was apparent between the development of alimentary cholesterolemia in the control series (cholesterol only) and the series where neodicoumarin was administered in addition to cholesterol. In the cholesterol plus heparin group of experiments, a somewhat less pronounced alimentary hypercholesterolemia was observed.

The degree of atherosclerosis in the group of
experiments with neodcoumarin plus cholesterol was quite similar to the experiments in the control group (i.e., cholesterol only), but sometimes the degree of lipoidosis was more pronounced.

Different results were obtained when heparin was administered in addition to cholesterol. In the "heparin" group the degree of lipoidosis of the aorta and other arteries was reduced compared with the group where cholesterol only was administered, or in the group of cholesterol plus dicoumarin, as shown in figure 11 (borrowed from the material collected by A. P. Efimova, who conducted this part of the investigations).

Hence the data testify that heparin possesses the valuable supplementary property of reducing the development of experimental cholesterol atherosclerosis. Dicoumarin, the other widely used anticoagulant, is devoid of this property.

The influence of heparin on the development of experimental atherosclerosis was of approximately the same degree when smaller (30 mg.) and larger (60 mg.) doses were used. We have not as yet sufficient material at our disposal to discuss the mechanism by which heparin achieves this effect. It is noteworthy that in the heparin series, the blood concentration of cholesterol was slightly less than in the control series. Consequently, heparin reduces the development of experimental lipoidosis not only through reducing the degree of alimentary hypercholesterolemia, but by means of some other mechanisms as well.

Additional measurements in similar experiments of the phospholipid content have not given any clue to the solution of the problem. The administration of heparin produces substantial changes in the lipoprotein fractions. The injection of heparin causes a marked reduction of the $\beta$-lipoprotein fraction both in the experiments on the rabbits and in patients with hypercholesterolemia. The evaluation was made by means of paper electrophoresis. The reduction persists for several hours after the injection and can also be recorded after repeated injections.

The administration of other anticoagulants, preparations of the decoumarin group, does not lead to such a drop in the content of both cholesterol in the blood and $\beta$-lipoprotein in patients suffering from atherosclerosis and hypertonic disease.

**Effect of Anoxia and Physical Exercise**

This series of experiments was performed not only to ascertain the influence of these factors on the development of the atherosclerosis, but also to study the dystrophic and sclerotic changes in the myocardium. This research was carried out by N. N. Kipshidze, Assistant Professor of the Institute of Therapy.
Fig. 11. The influence of anticoagulants on the development of experimental atherosclerosis. *Top series*, cholesterol; *middle series*, cholesterol plus Dicumarol; *bottom series*, cholesterol plus heparin.
Experiments with hypoxia were performed on 27 rabbits that were divided into 3 groups. The first group, consisting of 10 rabbits, received cholesterol daily as long as 6 months in comparison with the preceding series of experiments. The second group, comprising 12 rabbits, received cholesterol daily during the same period, and during the last 4 months was kept for 3 to 6 hours daily in chambers with a reduced amount of oxygen (up to 12 per cent). The third group, consisting of 5 rabbits, did not receive any cholesterol; during 4 months they were kept daily for 3 to 4 hours in chambers with a reduced amount of oxygen. The cholesterol level of the blood was analyzed in each rabbit twice a month. At the end of 6 months the rabbits were killed, and their aortas, coronary arteries, and myocardium were studied morphologically.

Under the influence of oxygen starvation, the cholesterol content in the blood of the rabbits that received cholesterol rose much more than in the control group receiving the same doses of cholesterol, but not subjected to oxygen starvation. The factor of anoxia appears to have a drastic effect on the endogenous mechanisms of metabolism, which results in insufficient assimilation of cholesterol administered with food, and accumulation in the blood in greater quantities.

In conformity with the changes in blood cholesterol, oxygen starvation resulted in a pronounced lipoidosis of the aorta and the coronary arteries of the heart (figs. 12 and 13). The aortas of this group of rabbits were covered with atherosclerotic atheromas confluent one with another and prominent above the surface of the intima. In most experiments atherosclerosis of the coronary arteries was also markedly reduced in those rabbits kept in low oxygen chambers.

In the rabbits receiving cholesterol and kept in low oxygen chambers the myocardium showed disseminated necrosis that was confluent in several areas. In most cases these necroses were subendocardial and greatest in the left ventricle, notably in the papillary muscles. Atherosclerosis of the aorta and coronary arteries was much less pronounced in the rabbits that received only cholesterol—
only moderate focal cardiosclerosis was recorded.

The rabbits that received no cholesterol but were kept in chambers with a reduced amount of oxygen exhibited no signs of atherosclerosis of the aorta or coronary arteries; small proliferations of histiocytes occurred, however, in the myocardium.

The experiment with physical exercise was performed on 43 rabbits of the same breed. They were divided into 3 groups. The first group of 10 rabbits, the controls, received cholesterol only for 6 months; the second group, numbering 25, received daily for the same period cholesterol and physical exercise in an electric treadmill until signs of marked fatigue appeared; the third group of 8 rabbits received no cholesterol but was subjected daily to the same physical exercise for 6 months. Examination of the experimental animals was conducted in the same way as in the group of rabbits subjected to anoxia.

The rabbits subjected to physical exercise as well as cholesterol feeding showed a marked decrease of the blood cholesterol as compared with the group of rabbits that only received cholesterol. It appears that the physical exercise by intensifying metabolism in the body, results in a more intensive assimilation of alimentary cholesterol and thereby lowering of its level in the blood. Morphologic examination of the aorta and coronary arteries proved that the physical exercise reduced to some extent the development of atherosclerotic changes. These findings might serve as a proof of the beneficial effect of physical exercises and sports in preventing atherosclerosis and conform to the conclusions derived from general medical practice.

Quite substantial changes were, however, recorded in the myocardium in the series of rabbits given physical exercise in addition to the administration of cholesterol. Focal necrosis both small and extensive, as well as sclerotic changes, were observed mainly in the muscle of the left ventricle, but sometimes in the right ventricle as well. In some cases the necroses were so extensive that myocardial infarction might be supposed (fig. 14).

In some cases the myocardium exhibited quite extensive cicatricial areas apart from fresh necrotic changes (fig. 15). In one experi-

Fig. 13. Atherosclerotic plaques in the left coronary artery. Left, in a rabbit fed cholesterol. Right, in a cholesterol-fed rabbit kept in a chamber with reduced oxygen content.
EXPERIMENTAL CHOLESTEROL ATHEROSCLEROSIS

Fig. 14. Large region of necrosis in the myocardium with a mild cell infiltration in a rabbit that received cholesterol in combination with physical strain for a 6-month period.

Fig. 15. Sclerotic areas after myocardial necrosis in a rabbit that received cholesterol and physical strain for a 3-month period.

Fig. 16. Aneurysm of the left ventricle in a rabbit with experimental atherosclerosis of the coronary arteries.

In all instances in which extensive necroses were found, pronounced atherosclerosis and stenosis of the coronary arteries were seen. No pathologic changes except hypertrophy of the myocardium were recorded in the rabbits given physical exercise alone without administration of cholesterol. Cardiosclerosis was slightly manifest in the rabbits receiving cholesterol only, but no physical exercise. Hence, in spite of the fact that physical exercise itself reduces the degree of alimentary cholesterolemia; in spite of the fact that lipoidosis of the aorta and coronary arteries does not attain a high degree but proves to be less pronounced than in the control group which received cholesterol only, the changes in the myocardium appear to be drastic in this series of experiments. These myocardial changes are disproportionately greater than the degree of coronary atherosclerosis. These changes appear to depend to some extent on the functional overstrain of the myocardium under conditions of physical...
exercise, but are observed only with organic changes of the coronary arteries, and are in this case of an atherosclerotic nature. It may be admitted, therefore, that both the factor of atherosclerosis of the coronary arteries and that of the functional overstrain of the myocardium are equally indispensable for the development of these necrotic and cicatrical changes. Atherosclerosis itself, even when pronounced, or similar physical exercise alone in rabbits without atherosclerosis, does not produce this type of myocardial infarction.

It appears to us that these investigations set up a new model of experimental myocardial infarction, which, by the conditions of its pathogenesis, are in principle quite close to the pathologic process underlying myocardial infarction in man.

Conclusions

This research has supplied us with convincing proof that it is quite possible to change the course of development of cholesterol atherosclerosis under experimental conditions. We have become convinced that a number of chemical substances, including food (vitamins) and medicinal (neurotropic drugs and anticoagulants) drugs may either lessen or increase the development of atherosclerosis.

Apart from this, we have become convinced that such general physiologic factors as anoxemia and physical exercise may also affect the course of the atherosclerotic process in experiments. These factors are of importance for prophylaxis and therapy in that they decrease and retard the development of atherosclerosis. These effects may be considered useful to some degree in preventing atherosclerosis in man as well—we attach particular importance to ascorbic acid in this respect.

There is no doubt, however, that negatively acting factors, i.e., influences that intensify atherosclerosis, also appear to play a significant role. From the viewpoint of preventive medicine, certain measures should be avoided in order to eliminate these influences.

In addition to influencing atherosclerosis of the vessels actively, one should bear in mind that it is possible to affect the state of tissues that suffer the most during the development of atherosclerosis, notably the myocardium. Our research has shown that the cholesterol factor itself, or, to be more precise, the degree of development of atherosclerosis, does not determine to the full the deranged function and structure of the myocardium, although it is a major factor in this derangement. Of particular importance in the development of the pathology of myocardium in the presence of atherosclerosis are supplementary unfavorable factors, such as physical overstrain or anoxia.

The material presents some illustrations pointing to the possibility of influencing the development of experimental atherosclerosis in a purely nervous way, through pharmacologic effects on the higher parts of the central nervous system. If it were possible, even though approximately, to correlate these findings with clinical experience, it would then follow that excessive excitation or stimulation exerts an unfavorable effect in the sense of increasing or hastening the development of atherosclerosis, while reduced excitability of the higher components of the nervous system associated with a state of inhibition acts favorably, tending to retard or decrease the development of atherosclerosis.

Summario in interlingua

Le hic-reportate recerces provide provas definitive pro le possibilitate de alterar sub conditiones experimental le curso del disveloppamento de atherosclerosis a cholesterol. Nos ha convincite nos que un numero de substantias chimic—incule alimentos (i.e. vitaminas) e medicamentos (i.e. drogas neurotropic e anticoagulante)—es capace a reducir o a augmentar le disveloppamento de atherosclerosis.

In plus, nostre recerces ha convincite nos que factores physiologic general como per exemplo anoxemia e exercitios physic pote equalmente alterar le curso del processo atherosclerotic experimental. Iste factores es de importantia in le prophylaxe e le terapia in tanto que illos reduce e retardar le disveloppamento de atherosclerosis. Le effectos in question pote esser considerate como utile in varie grados in le prevention de atherosclerosis etiam in humanos.
Ab iste puncto de vista nos ascribe importancia special a acido ascorbic.

Tamen, il ha nulle dubita que factores de action negative—i.e. influentias capace a intensificar le proceso atherosclerotic—es etiam presente e capace a exercer un rolo significative. Ab le puncto de vista del medicina preventive, certe mesuras deberea esser evitate pro eliminar tal influentias adverse. A parte le question del influentia active super le processo atherosclerotic in le vasos, on debe rememorar se que il es possibile afficer le stato del histos que suffre le plus durante le disveloppamento de atherosclerosis, i.e. notabilemente le myocardio. Nostre recercas ha demonstrate que factor representate per le concentration de cholesterol—o, plus specificamente, le grado de disveloppamento de atherosclerosis—non es le sol determinante del disordine functional e structural del myocardio, ben que illo es certo un factor principal in iste disordine. Alte importancia—in le disveloppamento de pathologia myocardial in le presentia de atherosclerosis—es a attribuer a adverse factores supplementari como per exemplo excesso de exercitio physic e anoxia.

Es presentate un numero de illustrationes que signala le possibilitate de influentiar le disveloppamento de atherosclerosis experimental per un via purmente nervale, i.e. per le application de agentes pharmacologic que affice le partes superior del systema nervose central. Si il eseva possibile—ben que solmente de maniera approximative—correlasionar le presente constatationes con observazione clinic, il sequera que excessos de excitacion e de stimulation resulta in effectos adverse, i.e. in le intensification e acceleration del disveloppamento de atherosclerosis, durante que un reduction del excitabilitate del componentes superior del systema nervose central, i.e. un stato de inhibition, produce effectos favorabile in le senso que illo retarda o reduce le disveloppamento de atherosclerosis.


A report is presented by the authors of a patient who had 2 commissurotomies for the treatment of mitral stenosis. Subsequently the patient died, and an autopsy was performed. It was found that the process of recurrence of the stenosis of the mitral valve following commissurotomy was not a closure of the operative fracture but rather a progression of the rheumatic disease. Microscopic examination of the heart demonstrated evidence of a smoldering rheumatic myocarditis and valvulitis.

Abramson
Influence of Some Factors on Development of Experimental Cholesterol Atherosclerosis
A. L. MYASNIKOV

_Circulation._ 1958;17:99-113
doi: 10.1161/01.CIR.17.1.99
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1958 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/17/1/99.citation