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Evaluation of amputations of the lower extremity

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AN EVALUATION OF AMPUTATIONS OF THE LOWER EXTREMITY

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INTRODUCTION

The purpose of this thesis is to investigate and evaluate some aspects of arteriosclerotic disease of the lower extremity. This study consists of findings in patients from private and charity hospitals in this area. These findings are compared with those of others investigating this subject. Only patients having had amputation of the lower extremity as a result of arteriosclerosis are considered in this paper.

TERMINOLOGY

Before beginning a discussion of this subject the problem of terminology must be considered. Atheromatosis and/or atherosclerosis are terms in which the lesion is manifested by patchy areas of endothelial proliferation. These are associated with lipid deposits and fibrous strands and occur mainly within the intima of the large and medium sized arteries. Arteriosclerosis is generally thought of as a

more inclusive term, ie. a lesion capable of involving the entire arterial tree. It is characterized by hypertrophic changes and an increase in fibrous elements of the arterial wall. More specifically arteriosclerosis should be confined to a group of conditions manifested by medio-necrosis and calcium deposits which appear primarily in the media of large and medium sized arteries, particularly of the muscular type. Probably the best example of this type of change is the Monckeberg type of arteriosclerosis (12, 16). Either of these processes may occur independently, but a combination of the two is most common, in which case the term atherosclerosis is best applied. However, by general usage arteriosclerosis also applies here (6, 8). Also as a result of general usage, atherosclerosis and atheromatosis may be used to mean the same thing. On occasion the arteriosclerotic process may extend to the intima thereby occluding the lumen of the vessel. This condition is known as arteriosclerosis obliterans (16).

THE ARTERIOSCLEROTIC LESION

Its Nature. More commonly it is the intimal plaques of atheromatosis which result in occlusion

of the vessel lumen. Pathologically this process may vary from small yellowish streaks, which have been described as early lesions seen in the abdominal aorta and may be found even in young individuals, to the extensive plaques of lipid and fibrous material which may almost completely cover the inner surface of the vessel. The earliest lesions are usually found under the endothelium and are apparently deposits of lipid material. There appears to be swelling and loosening of the inner cellular substance of the intima and the deposits of lipid material consist mainly of cholesterol esters (30). Fatty infiltration may be even more apparent in the intercellular substance than in the cell, especially in the deeper layers of the intima, and then as the process continues the endothelium is reached (16).

Its Location. As has already been mentioned, this degenerative process is largely confined to the main vessels of the body and of these the aorta is the first to be attacked (12). However, within these main arteries there are certain sites of predilection, or areas where the changes tend to be most severe. With respect to the lower extremities the sites are: the lower end of the aorta and the upper common iliac

arteries; the femoral artery at the level of the adductor opening; and the popliteal artery at the bend of the knee, opposite the upper border of the femoral condyles (5). Generally speaking the collateral vessels are not involved, nor are the smaller main vessels such as the dorsalis pedis artery or the digital arteries. However, though the collateral vessels are not primarily affected, their origins may be secondarily involved as they pass through the diseased walls of the larger artery from which they arise. This is more often true in long standing cases, especially where gangrene is threatening. This factor is often important in the final failure of the circulation of the extremity (19).

This localization phenomenon has several important results. With proximal obstruction the distal arterial system maintains blood supply through the collateral circulation and the digits of the extremity, whose arteries are patent, receive a blood supply that under usual conditions is adequate for the part at rest. Under these circumstances gangrene does not occur unless injury or sepsis is superimposed in which case the demand for increased blood flow cannot be met. It must also be remembered that gangrene may result

from embolism of distal vessels by a thrombus dislodged from a proximal plaque or by extension of a thrombus from above.

The commonest site of intimal thickening and subsequent obstruction is the superficial femoral artery at or about the adductor hiatus. Next in line, and not far behind in its susceptibility to obstruction, is the common iliac artery. It is frequently involved bilaterally and may involve the terminal aorta as well.

In the lower leg the posterior tibial and, to a lesser extent, the anterior tibial arteries are often obstructed. Obstruction may occur in patches or sometimes in their entire course, although there is a distinct tendency for their terminal parts to maintain patency. The vessels of the forefoot are rarely affected by atherosclerosis. The same applies to the peroneal artery and for this reason both tibial arteries can be obstructed and the patent distal arteries of the foot will still have a blood supply through the peroneal artery, provided flow through the popliteal artery is adequate (19).

SECONDARY THROMBOSIS

The process of secondary thrombosis may be responsi-

ble for the actual occlusion of the vessel lumen, rather than intimal changes alone. Secondary thrombosis holds an important place in vascular disease and should be looked at more closely. Usually by the time secondary thrombosis occurs the collateral circulation is well enough developed that the process is without pain or detrimental affect. This is not always the case, however, for in some instances the collateral circulation may not be adequately developed. In still other instances the thrombosis may be so located as to obstruct both the primary and the collateral circulation. In this instance acute ischemic changes do take place.

Boyd, in following 1440 patients who originally presented with claudication, but without gangrene, has been able to give us the locations and the relative incidence of secondary thrombosis. It will be noted that these locations correspond with those found to be most frequently and severely involved by arteriosclerotic disease. First there is what he calls the "high block" which involves the lower end of the aorta and/or the common iliac arteries. In his study their relative incidence was 0.7% and 5.2% respectively. The thrombosis of the common iliac artery often extends into the internal iliac artery. Next, secondary

femoral thrombosis was found to occur in 34.2% of his patients. Thrombosis begins at the level of the adductor opening and ends about a centimeter below the origin of the profunda femoris. We have already pointed out that with occlusion at this site the profunda vessels usually provide enough collateral circulation to the lower half of the extremity to prevent ischemic changes. Secondary popliteal thrombosis was noted in 33.6%. It occurs where the artery is anchored firmly to the posterior oblique ligament of the knee joint. With obstruction at this level collateral circulation usually is not as good as it is with femoral obstruction. As a result such changes as wasting of the pads of the toes, interference with nail growth, dry skin, and wasting of the calf muscles, do occur (5).

PATHOGENETIC FACTORS

Probably the greatest intivestigation and contraversy concerning arteriosclerosis has centered around the etiology and pathogenesis of the lesion. The factors under consideration are numerous and in many instances highly speculative.

Age. Age is a factor we like to discuss in almost

all disease processes. With regard to arteriosclerosis it has been noted that the most prominent quantitative increase in aortic atherosclerosis occurred between the ages of eight and eighteen years. This suggests a possible relationship between atherosclerosis and hormonal changes at puberty. The same observer (12) noted that early lesions (fatty streaks) appeared in all subjects over three years of age and that the lesion persisted in a potentially reversible form for a period of many years. He therefore proposed that the atherosclerotic problem is basically a pediatric one. In this light, age becomes a very important factor. Another observer (11), in a comparative autopsy study, showed that in the coronary arteries men showed higher grades of severity early in life and tend to reach a plateau in the fifth decade whereas women begin at the lowest level of severity and then show nearly a straight line increase in severity, finally reaching the highest grades in late life. This comparison may not hold for other areas of the vascular tree however. Boyd (5), in his series of 1440 patients with symptoms of arterial insufficiency of the lower extremity, found the greatest incidence between fifty-five and sixty-four years of age. Berry (4), in his

review of the pathogenesis of atherosclerosis, claims women are generally affected ten years later than men.

Sex. In discussing the age factors above, sex was noted several times to be involved. It is important to note that in Boyd's 1440 patients only 10% were women. This, no doubt, is of significance in evaluating the age incidence. It would be interesting to know the age incidences in men and women separately. An almost identical sex ratio has been reported by another group of investigators (14). In 201 patients with occlusion of the aorta or one of its immediate branches due to atherosclerosis, 179 (89%) were men and 22 (11%) were women.

Cholesterol and Related Compounds. The greatest interest and investigation in the past few years has been devoted to the relationship of lipids to arteriosclerosis. In fact, one can hardly think of one without thinking of the other. The role of lipids and related substances has been widely investigated by many competent men and still there remains considerable dispute over the pathogenetic relationship. As will be pointed out later, there are several aspects of arteriosclerosis which cannot be correlated with plasma lipids. We know

that lipids and related compounds must be considered as only one of many important factors in the pathogenesis of arteriosclerosis.

With this clarification the apparent relationship will now be discussed. Pathologists have shown that atheroma are basically composed of intimal infiltrates of cholesterol. However, it should be noted that with regard to cholesterol itself, its importance in the problem of atherosclerosis may be exaggerated by the fact that it is the only serum lipid which can be easily determined in the laboratory by a color reaction. Also, it is not known whether hypercholesterolemia is the cause of atheroma or if it merely accompanies the lesion. However, it has been noted that plasma cholesterol content is a useful index in determining susceptibility of individuals to circulatory accidents (13).

It is also fairly well recognized by authorities that cholesterol level itself is not the important factor, but rather the size of the molecule and the type of lipoprotein involved (16). The role of phospholipids, fatty acids, glycerides, lipoproteins, and the phospholipid cholesterol ratio are all now under investigation. It is still too early to make further

conclusions as to the ultimate relationship between atherosclerosis and lipid substances.

Probably the single most important factor which will confound the proponents of serum lipids and arteriosclerosis, especially when one tries to consider it as a sole or even major factor, is the fact that atherosclerosis is a patchy disease, forming rather isolated plaques. Even though all blood vessels are exposed to the same plasma constituents and concentrations, only certain vessels and areas are affected. This is most strongly borne out in comparing the aorta, where atherosclerosis is predominant, with the pulmonary artery, where it rarely occurs.

Nutrition. Closely associated with the lipid factor is the factor of nutrition. The placing of patients with arteriosclerotic disease on low fat diets is one weapon used by some clinicians to fight this disease. Keys (15) is noted for his observations that in national groups where fat intake is low (less than 30% of total calories) the incidence of atherosclerosis is lower. In turn, there are lower incidences of cerebral and coronary thrombi, perivascular disease, and vascular nephropathy. However, the affect of lesser tensions, other dietary differences, and

racial group difference also must be considered in evaluating such national variation (9). Other observers have emphasized the importance of nutrition. Wilens (34) noted a much lower incidence of pathologic changes in the vessels of individuals in poorly nourished states and a proportionately higher incidence of pathologic change in the vessels of well nourished and overweight individuals.

Hypertension. Recently there are those who feel that atherosclerosis can be attributed, to a large extent, to hypertension and they present reasonable findings to support their belief (4, 6). For instance, when there is hypertension atherosclerotic lesions appear at an earlier age and are more severe. Atheroma are common in the aorta, but infrequent in the pulmonary artery where blood pressure is much lower. Too, atherosclerosis is less common and less severe in hypotensive individuals. Atherosclerotic lesions are intensified at points of resistence in the arteries. In coarctation of the aorta the atherosclerosis is proximal to the obstruction where the tension is highest. The fact that vascular lesions are much more common in the lower extremity than in the upper extremity suggests a relationship to forces of greater pressure acting on

the vessels of the lower extremities under the addition of gravitational influence. It also seems significant that the low pressure venous system is usually spared from atherosclerosis even though after fatty meals lacteals and mesenteric veins contain the highest recorded levels of fat and cholesterol.

The most convincing argument the proponents of this theory have is the frequent finding of severe arteriosclerotic lesions in the systemic arteries of an individual who has no arteriosclerotic lesions in the low pressure pulmonary artery circuit nor the entire venous system. This is in spite of the fact that the two arterial systems are exposed to the same lipids, the same stress, and other factors except for blood pressure. But, when pressure does increase, as in the pulmonary artery in mitral stenosis, atheroma do appear.

Just how hypertension brings about such pathologic change is not clear and the issue is still unsettled. One cannot say that the hypertension per se is the cause of atheroma. Some feel it is more likely that the various factors which are responsible for the development of hypertension are also the same factors which play an important role in the development of

atheromatosis (16).

Mechanical and Structural Factors. Closely associated with the speculated affect of hypertension are the mechanical, structural, and hemodynamic differences in the circulatory system. Some feel these differences are important. Atheroma are more common and seen earlier in the aorta, which is a more or less passive elastic tube, than in the coronary arteries which are known to actively constrict in response to certain stimuli. The fact that atherosclerotic plaques are distributed irregularly, even somewhat segmentally, suggests that local conditions in the blood vessel, as well as the blood flowing through it may be important in pathogenesis (11). Atheroma are more prominent over the outer circumferance of the distal arch of the aorta and the fixed posterior wall where the greatest kinetic energy from flowing blood is exerted. That atheroma are commonly found at sites of bifurcations is well known (6). In the development of atheroma, medial fibrosis has been found to be most marked in areas of longitudinal hypertrophy thought to be subject to hemodynamic stress. Subsequently the elastic hyperplastic layers over these areas tend to become nodular in later decades,

atheromatous. In this way many fetal cushions may determine the site of future atherosclerotic plaques (27).

Hemodynamic Concept. One group of investigators (29) have launched a hemodynamic concept which they present as the primary factor in the development of atherosclerosis. They feel that the laws of fluid mechanics are responsible for the predilection of atheroma to appear at areas in the vascular bed characterized by converging boundaries, curvature, bifurcation, branching, or external attachment. Such sites are subject to a relative decrease in the local lateral pressure in accordance with the laws of fluid mechanics. In these areas the blood stream shows greater velocity and the decreased lateral pressure creates, in effect, a suction phenomenon. This gives rise to the early intimal changes which subsequently form typical atheroma. The concept applies to the aorta, the coronary arteries, and the arteries of the viscera and the extremities. It also applies to the pulmonary artery and the venous circulation in general where velocity of flow is lower and lateral pressure greater. It considers the given hydraulic specifications and the nature of the biological response of the tissue as

important in determining the variations in degree of atherosclerosis among different individuals. However, additional secondary factors may modify the hemodynamic mechanism.

They claim that statistical data, specimens from 100 consecutive autopsies, and the demonstration of the applicable laws of fluid dynamics in models support the scientific validity of their hemodynamic concept of atherosclerosis.

Diabetes. It is generally agreed that diabetes not only predisposes an individual to atherosclerosis, but also accelerates its development. This relationship will be discussed in greater detail subsequently.

Miscellaneous. Numerous other factors have been mentioned at one time or another by various investigators. At their present stage of investigation, these factors warrant mention only. Body build or obesity may play a role as atherosclerosis is seen earlier in stocky individuals (mesomorphs) (4). Stress is rather commonly associated with atherosclerosis (11, 14). Stress may increase the vulnerability of blood vessels, increase blood pressure, increase lipid materials and accelerate blood clotting (4). Tobacco is thought to be important in coronary artery disease

and certain infectious diseases (typhoid fever, rheumatic fever, and pyogenic infections) may initiate atherosclerosis and vasculitis (4). Denaturation or disturbance of collagen with deposition of mucopolysaccharides has been suggested (4, 16). Hormones or endocrine glands are recently receiving attention. Included are the adrenal glands, the thyroid gland, the gonads, and the pituitary gland (16). Economic status has its role (11). This will be discussed as a separate entity later. Still other factors which have been mentioned include trauma and fever (9), heredity and constitution (9, 16), race (14), and high serum levels of uric acid (16).

THE EFFECT OF ARTERIOSCLEROSIS

With regard to the lower extremities then, what results do the pathologic changes give rise to and what are the signs and symptoms they incur? It is obvious that as a result of the pathologic changes, the vascular supply to the extremity is compromised. This is of varying degrees of severity and gives rise to signs and symptoms of proportional severity.

First of all it should be pointed out that the palpable pipe-stem artery and extensive arterial

calcification of extremities, as occasionally seen radiologically, represent the Monckeberg type of medial sclerosis and this has no direct relationship to the problem of vascular occlusion. Rather, it is the intimal lesions which favor occlusion (21).

The most common symptom associated with peripheral vascular insufficiency is intermittent claudication. Although it is most often seen in the calf muscles, it may also occur in the foot, thigh or buttocks, depending on the site of vascular occlusion. In general, trophic changes in the extremity are less pronounced the more proximal the obstruction occurs. However, wasting of calf muscles may be prominent. Dependent rubor is a manifestation of severe ischemia of long duration, but if pallor replaces the rubor on elevation, patency of the arterial tree remains. When rubor or cyanosis persist in spite of posture, there is obstruction of the distal vessels by embolism or secondary thrombosis. This is often initiated by trauma or sepsis, and in such a case gangrene is imminent. Rest pain is an important symptom to observe as its presence demands immediate treatment. The severity of the pain varies with the degree of ischemia, increasing with greater ischemia and decreasing with

lesser ischemia. When rest pain is severe and unrelieved one can expect gangrenous changes in less than six months (19).

Some of the important signs an examiner may look for are: the character of the skin, ie its color, temperature, moisture, etc.; the presence or absence of pulses; the result of the pallor-flush test; and the claudication time. All of these will aid the examiner in determining the nature of the disease and the severity of it (21).

Finally, the occurrence of sepsis and ulcers in the diseased limb as a manifestation of vascular insufficiency should be discussed. With regard to these entities one can determine rather quickly the severity of the insufficiency and the chance of healing in a particular case simply by noting the nature of the discharge. If the process is frankly purulent, with significant amounts of pus, then the blood supply has to be adequate because production of such pus is part of the process of repair. On the other hand, if the discharge is watery, healing is unlikely (19).

PROGNOSIS

In considering the prognosis for a given individual

with arteriosclerosis of the lower extremity one must take into account the extent of progression already present, the rate of progression, the age of the individual, the care exercised by the individual, environment and physical factors, and many other variable factors. For this reason one cannot very well predict how rapidly or to what extent the pathological changes will develop and, in turn, what type of treatment will be required. However, we can look as some figures and then make predictions on a group basis.

Again looking at Boyd's series of 1440 patients who presented with complaints of claudication and subsequently were followed up to fifteen years. In his series the chance of 5 year survival was 73.5%, for 10 years 38.8%, and for 15 years a 22% chance. This includes the group as a whole regardless of age at onset of claudication. It was noted that the chance of survival is inversely proportional to the age and we must therefore consider age itself as a factor in evaluating these figures. In his patients the chance of major amputation, again calculated from onset of symptoms, was 7.2% for 5 years and 12.2% for 10 years. The chance of further thrombosis in the leg, as

calculated from the first episode in each patient, was 10.3% in 5 years and 17.8% for 10 years in the affected leg and in the opposite leg it was 10.6% in 5 years and 18.6% for 10 years. From his studies he concluded that three fourths of the sufferers from intermittent claudication die of their disease (5).

In another series (140 patients) with symptomatic peripheral vascular disease, ulceration or early gangrene was present in 55. The amputation rate in these was 71% and 42% died of associated disease within three years. In patients with claudication as the only complaint 15% required amputation and 18% died within three years (26).

In still another series (89 patients) with vascular insufficiency due to arteriosclerosis, followed by major amputation, 15.5% died within one year from the time of operation and 22.5% within two years. An operative mortality of 6.1% for major amputation was reported. The authors state that most authors report a mortality of 10% or higher (7).

All of these figures verify the fact that peripheral vascular insufficiency due to arteriosclerosis is a severe and progressive disease process and one that soon terminates fatally in a number of individuals.

DIABETES AND ARTERIOSCLEROSIS

A discussion of arteriosclerotic and diabetic vascular disease is most appropriate for the simple reason that atherosclerotic gangrene is fifty-three times more frequent in diabetic men than in nondiabetic men over forty years of age and seventy-one times more frequent in diabetic women than in nondiabetic women over forty years of age. About two-thirds of atherosclerotic gangrene in men under eighty years of age and about one-fourth in men over eighty years of age is a result of diabetes. Approximately 80% of atherosclerotic gangrene in women results from diabetes (3). Further, vascular disease is by far the most serious complication of diabetes mellitus (20). Finally, according to Warren and LeCompte (32), atherosclerosis of the medium sized arteries is the largest single cause of death among diabetic patients.

THE LESION IN DIABETES

Its Nature. Some observers (30) feel that the vascular lesion in the diabetic patient morphologically and chemically resembles the atheroma in the nondiabetic patient. They feel that it is similarly associated

with increased serum levels of lipoprotein and cholesterol, but that it tends to affect smaller and more distal vessels and is distributed differently about the body.

However, Goldber and his associates, in a study of vessels taken from amputated limbs of diabetic patients, discovered that in the digital arteries the most prominent factor was an endothelial proliferation of such magnitude as to almost occlude the lumen and that the internal elastic lamella consisted of a single intact wavy membrane. This membrane differed from the ordinary arteriosclerotic lesion in which there is usually a duplication and fraying of the elastica. They also found that the cellularity of the mass impinging on the lumen consisted of a deposition of an acellular hyaline material covered on its inner surface by only a single layer of flattened endothelium. Another difference noted is that the media in the artery of a diabetic patient is essentially uninvolved, whereas in arteriosclerotic lesions of the digital artery muscular hypertrophy or hyalinization is sometimes found. The adventitia of vessels in diabetic and simple arteriosclerotic patients shows little difference (10).

Its Location. It has already been stated that diabetes tends to cause changes in smaller and more distal vessels. It is common to find the toes affected by arterial insufficiency before any other area of the body. One may even be able to palpate good dorsalis pedis and posterior tibial pulses in the foot of a diabetic patient and at the same time see gangrene of one or more toes. This is one of the reasons why most observers feel that vascular disease in the diabetic patient has a predilection for the "end-arteries" and that these arteries are occluded or thrombosed at an earlier stage than in the nondiabetic. Gangrene of the heel or sole is another common site in a diabetic patient. Next to gangrenous disease of the toe or foot, one sees symptoms of generalized ischemia of the lower extremity. Most frequently in the diabetic patient one sees a generalized arteriolar and small arterial obstruction, including the retina and kidney (25).

PATHOGENETIC FACTORS

When it comes to discussing the pathogenesis of diabetic peripheral vascular disease the reader may merely refer back to the same discussion regarding

atherosclerosis. Many investigators feel that the underlying pathogenesis is nearly the same. Diabetes merely modifies the basic disease process as to onset and rapidity and ultimate degree of development. On the other hand, there are several important differences and some factors have received greater investigation than others. These factors are emphasized below.

Age. It is generally agreed that peripheral vascular disease appears considerably earlier (the bulk of the literature seems to suggest about ten years earlier) in the diabetic than in the nondiabetic patient.

Sex. More women are affected by diabetic peripheral vascular disease than men. This parallels the greater incidence of diabetes in women, the ratio being about three to two (23).

Duration. Some observers have felt that duration of diabetes appears to be a most important factor in the etio-pathogenesis of vascular degeneration. They (20) state that complications seldom occur before the tenth year of the disease, but are almost always present after the twentieth year. Others (3, 17) have made an entirely opposite observation stating that the process is not related to the duration of the diabetes. Still

another observer (16) feels that such a relationship may exist, but that there are many issues still remaining to be explained before such a conclusion can be accepted entirely. So we see this area of investigation is still unsettled.

Severity of Disease and Degree of Control. A similar air of uncertainty surrounds the relationship of diabetic peripheral vascular disease to the severity and degree of control of the diabetes. It has been said that most clinicians who treat diabetes extensively feel that such a relationship does exist, but that complete unanamity is lacking (20). This latter remark is borne out by those (3, 17) who feel there is no definite relationship between these factors and again there are those (16) who say it may be so, but it is still too early to be sure. No doubt the difference in opinion with regard to these factors can be, at least in part, attributed to trying to accurately define the severity and the degree of control of diabetes in a given patient.

Cholesterol and Lipoproteins. An area which has received considerable investigation is that of whether or not there is a relationship between vascular disease in the diabetic patient and the blood levels of cholesterol

and lipoprotein. In a study of 273 diabetic patients, Pomeranze and Kunkel found total blood lipid contents elevated in half of the patients and below the normal average in the other half (22). Similarly Barach and Lowy in studying 614 diabetic patients, found elevated blood cholesterol concentrations in 58% and normal concentrations in 42%. They found blood lipoprotein values to be elevated in less than half of their diabetic patients (1). However, Barr and his associates feel that there is a definite disturbance of lipoproteins in diabetic patients (2). Again we are left with an area of uncertainty. It has been stated, however, that in general the lipoprotein and cholesterol values tend to be increased more frequently in the poorly controlled diabetic patients than in the well controlled (20). Perhaps here is where the answer to the confusion lies.

Infection. One area of importance with regard to diabetic peripheral vascular disease is that infection plays a much greater role in its development and effect than it does in the nondiabetic patient (3).

Hyperglycemia. Warren (16) has speculated on the possible affect of hyperglycemia, suggesting that perhaps "fluctuations in blood sugar concentration

might aid in producing swelling of the intimal ground substance through changes in osmotic pressure". He also noted that in his studies of skin biopsies in diabetic patients with hyperglycemia, there was slight edema with basophilic infiltration of the connective tissue of the corium. These changes resemble those seen in the intimal substance in early arteriosclerosis.

Heredity. There is little factual information at present to implicate heredity as a cause of vascular degeneration, but this possibility is gaining favor. Certainly when diabetes is mild and the vascular disease is severe or, on the other hand, when the diabetes is severe and the vascular disease is absent other factors must be involved. Such factors may be constitutional and perhaps hereditary (20).

INCIDENCE

While it is impractical, if not impossible, to talk about the incidence of arteriosclerosis, we can look at the incidence of diabetes in general and with respect to peripheral vascular disease. A recent estimate of the prevalence of diabetes in the United States was 2.9 million cases. Of this number about

1.5 million were estimated to be known cases and about 1.4 million unsuspected cases. The rate per 1000 population would be 8.1 unsuspected and 8.8 known cases. These figures were determined by the Chronic Disease Program of the Public Health Service for 1958 (24).

With regard to the incidence of peripheral vascular complications in the diabetic patient the most important factor is that it is increasing (16, 17). In a series of diabetic patients dating from 1921 the following increases were observed: in 1000 cases between 1921 and 1930 the incidence of vascular disorders was 17.3%; in 1000 patients between 1931 and 1941 it was 21.6%; in 1000 patients between 1942 and 1951 the incidence was 50.7%; and in 800 patients between 1952 and 1959 the incidence was 53.5% (16). One may say that the incidence of diagnosis may be increasing too. This may be true, but these figures would appear to reflect a greater change than could be accounted for on the basis of improved diagnosis alone.

PROGNOSIS

The outlook for the diabetic patient in general is much poorer than for the average individual.

Diabetes is the eighth leading cause of death. Longevity of the diabetic ranges from seventeen fewer years of life among those ten years of age to almost four years less among those seventy years of age than for the general population (24).

In a comparative study of diabetic and nondiabetic patients the diabetics as a group did less well than nondiabetics. However, the average age of the diabetic patient was eleven years greater than the nondiabetic patient. The complication of skin ulceration was more than twice as common in the diabetic patient. This seemed to be quite important in the response to treatment and resultant prognosis. Diabetic and nondiabetic patients with complaints of claudication alone showed little difference in response to treatment in spite of the older age of the diabetic patients. The age difference was accounted for on the basis that probably 75% of diabetics are not recognized until after fifty years of age (26). Bell (3) in his study reported that the average age of survival after amputation is longer in the diabetic than in the nondiabetic patient.

It is difficult to know just how much can be concluded from these reports. In general it would

appear that the overall outlook for life is poorer in the diabetic, that with relatively early peripheral vascular manifestations the prognosis is as good in the diabetic as in the nondiabetic, but that with more advanced peripheral vascular manifestations the diabetic reponds less well to treatment and hence the prognosis is not as favorable. It has been emphasized that arteriosclerotic disease is seen earlier and probably progresses more rapidly in the diabetic patient and this also is important in considering the prognosis in diabetes.

THE FINDINGS IN A LOCAL STUDY OF AMPUTATIONS

In order to study some aspects of arteriosclerosis in this area, 208 selected hospital charts were reviewed. Patients included in this review were those who had undergone an amputation of the lower extremity, or a part thereof, as a result of arteriosclerotic disease of the extremity. The study was limited to the period from January 1, 1955 through June 30, 1960. Patients were divided into diabetic and nondiabetic groups. The following tables and figures illustrate the result of this investigation.

Age. Table I shows the average age and age ranges

of the patients in the study. The average age of all nondiabetic patients was 72.5 years and of diabetic patients was 67.2 years. This difference is about one half that generally reported in the literature which, as mentioned earlier, is about ten years.

It also is important to observe the significantly younger age at which diabetic patients require amputation as opposed to nondiabetics. Several factors probably account for this. It was pointed out in the discussion of the relationship of arteriosclerosis and diabetes that peripheral vascular disease is seen earlier and advances more rapidly in the diabetic than in the nondiabetic patient. Secondly, the diabetic patient is less likely to respond to conservative measures and thus amputation will be resorted to earlier. See graphs I and II (pages 33a and 33b).

Sex. Table II reports the sex ratio in the diabetic and nondiabetic groups. Most significant here is the observation that in nondiabetic patients men far exceed women, but in diabetic patients women predominate. This is in keeping with other studies mentioned above. However, one generally thinks of the incidence of diabetes as being considerably higher in women than in men (23), but in this study of amputations

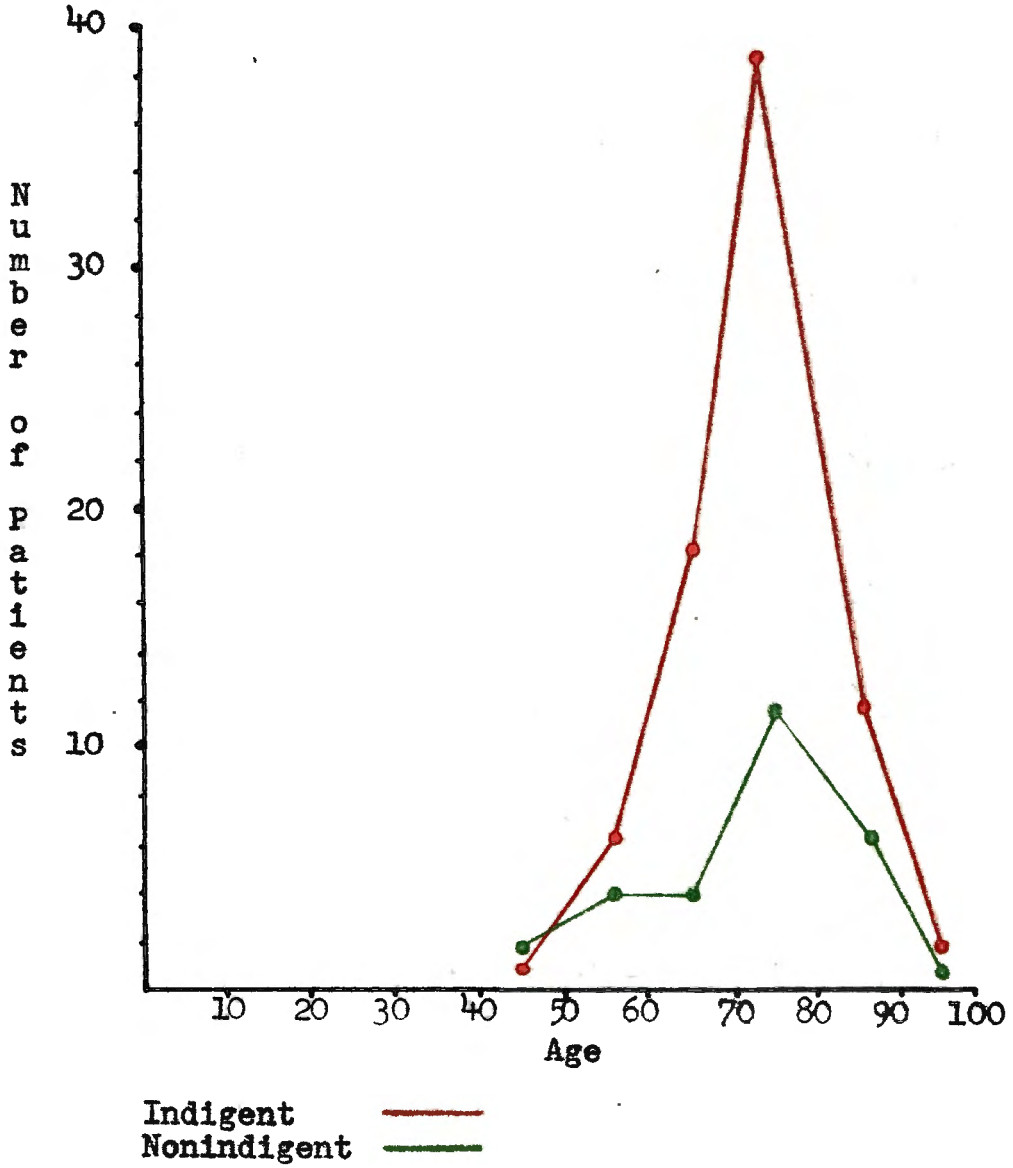
TABLE I

Hospital	Age Range Non-Diab.	Age Range Diab.	Average Age Non-Diab.	Average Age Diab.	Mean Age Non-Diab.	Mean Age Diab.	Total No. Non-Diab.	Total No. Diab.
Charity No. 1	47-90	34-88	72.3	69.1	73	72	50	25
Charity No. 2	50-86	26-80	72.9	62.9	75	66	27	28
Private No. 1	49-94	35-90	73.3	66.9	76	70	15	23
Private No. 2	43-79	52-87	69.0	67.4	74	70	6	10
Private No. 3	59-71	67-75	65.0	71.0	--	--	2	2
Private No. 4	64-94	55-79	81.0	72.0	--	73	3	10
Private No. 5	51-82	64-85	71.0	71.7	--	--	3	4
Totals	43-94	26-88	72.5	67.2	74	70	106	102

The table compares the age range, average and mean age between diabetic and nondiabetic patients in each hospital in the series. Mean age was not listed for some hospitals because of the small number of patients.

GRAPH I

Nondiabetic Amputations



GRAPH II

Diabetic Amputations

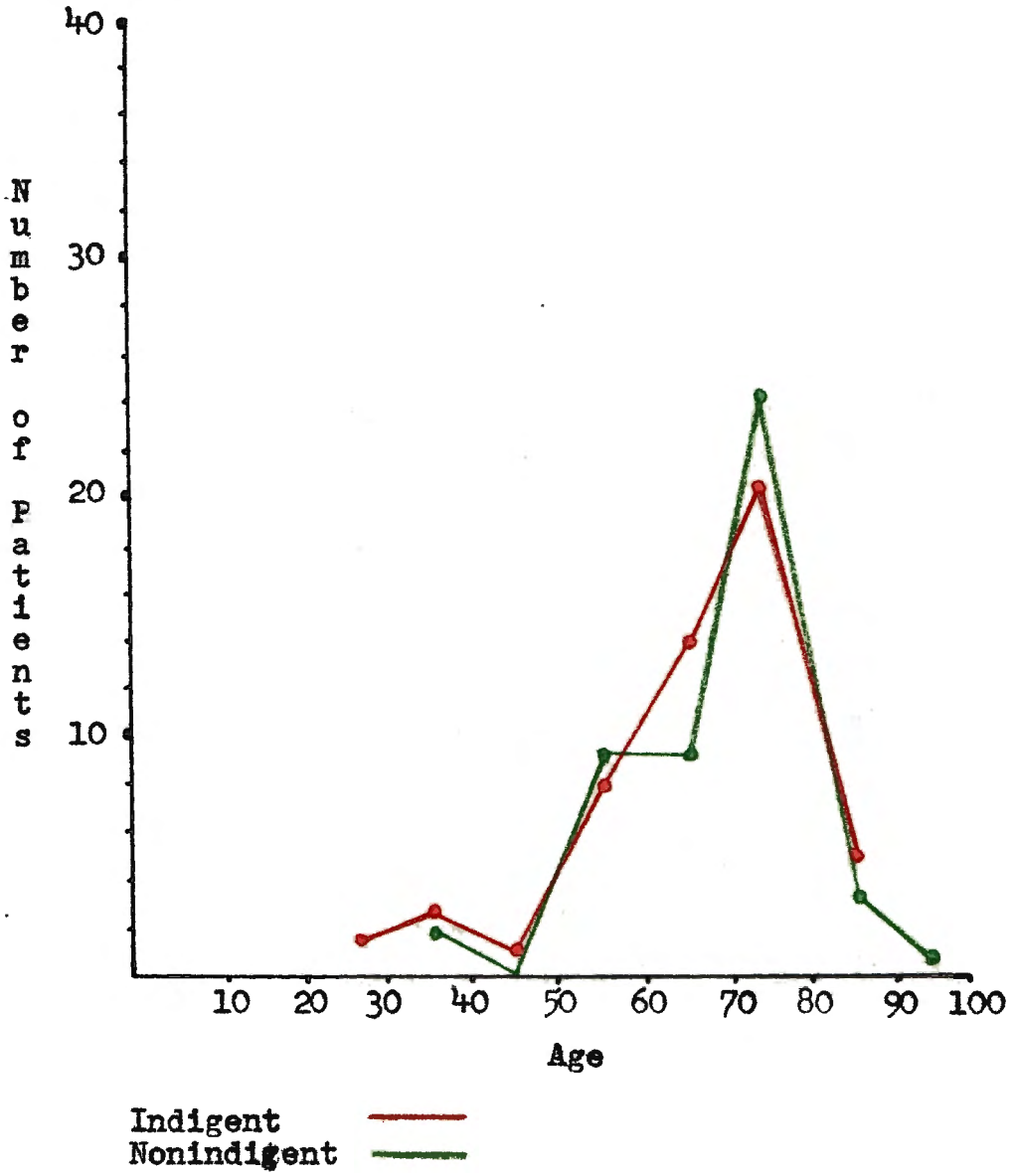


TABLE II

Hospital	Nondiabetic Men	Nondiabetic Women	Diabetic Men	Diabetic Women
Charity 1	40	10	11	14
Charity 2	24	3	15	13
Private 1	10	5	8	15
Private 2	2	4	6	4
Private 3	2	0	2	0
Private 4	2	1	3	7
Private 5	2	1	2	2
Totals	82	24	47	55

The table shows the number of men and and women in the diabetic and the nondiabetic groups.

the difference is not great. This would suggest that other factors are imposed in men making them more susceptible to the need for amputation. If this were not the case, we would expect the ratio of amputations to parallel the incidence ratio of diabetes in men and women.

Type of Amputation. The comparative results of the types of amputations are given in table III. It is important to point out that these represent the ultimate type of amputation in which healing was obtained for a reasonable period of time or, in some instances, the type the patient had at the time of his death. This point is made because in innumerable instances one or more amputations at a lower level were done in which healing was not satisfactory and reamputation at a higher level was required. A significant number of patients (10) had bilateral amputations. In several instances these were carried out during the same hospital stay, but in most instances were over a year apart.

It is interesting to note the comparative incidence of above knee and toe amputations in the diabetic and nondiabetic patients. There were 106 nondiabetic patients and 102 diabetic patients. In the nondiabetic

patients the above knee to toe amputation ratio is eight to one while in the diabetic patients the ratio is nealy three to one. There also were more trans-metatarsal, Syme, and below knee amputations in the diabetic than in the nondiabetic patients. This, I feel, only verifies what was stated earlier, that peripheral vascular disease in the diabetic patient has a greater tendency to involve the more distal arterial tree whereas arteriosclerosis in the non-diabetic patient involves the larger and more proximal vessels. Thus higher levels of amputation are required in the nondiabetic if healing is to occur.

In nearly all instances where a good history had been obtained, the ultimate lesion requiring amputation had been preceded for some time by lesions or complaints of lesser degree. See table IV. Claudication was a complaint in 19 (18%) of the nondiabetic patients. A good history probably would have elicited the complaint in an even greater number of patients. The lower incidence of claudication in the diabetic patient (4%) again shows the difference in the sites of predilection. Claudication may occur in the calf areas, ankles, or proximal foot regions. These sites all represent areas where the vessel caliber is of moderate

TABLE III

Nondiabetic Patients

Hospital	Above Knee	Bilat-eral	Below Knee	Symes	Transmeta-tarsal	Toe(s)
Charity 1	45	4	0	0	1	4
Charity 2	22	0	1	0	0	4
Private 1	12	0	2	0	0	1
Private 2	5	2	1	0	0	0
Private 3	1	0	0	0	0	1
Private 4	3	0	0	0	0	0
Private 5	1	0	1	0	0	1
Totals	89	6	5	0	1	11

Diabetic Patients

Hospital	Above Knee	Bilat-eral	Below Knee	Symes	Transmeta-tarsal	Toe(s)
Charity 1	20	1	0	0	0	5
Charity 2	14	1	4	2	2	6
Private 1	14	1	1	0	2	6
Private 2	7	0	0	0	1	2
Private 3	2	0	0	0	0	0
Private 4	7	0	0	0	0	3
Private 5	2	0	1	0	0	2
Totals	66	3	6	2	5	24

The table shows the number of patients having had the specific type of amputation indicated. All bilateral amputations were above knee amputations.

size. With diabetic vascular changes tending to occur at a more distal site, the smaller terminal arteries, claudication is less common.

Pregangrenous Lesions. Chronic or recent ulcers were the most common lesion preceding gangrene and were more common in the diabetic (45%) than in the nondiabetic (25%) patients. This finding agrees with those of another observer (26) whose study was mentioned in the discussion of the prognosis in diabetes. This observer also noted that ulceration was quite important in determining the response to treatment, that is to say, those with ulceration responded less well and were more likely to require amputation than those who did not have ulceration. The findings in this study tend to support his observation. At least it can be said that ulcerations were a rather significant pregangrenous lesion in the diabetic patient.

Table IV also emphasizes that infection and sites of irritation are extremely important in the diabetic patient with vascular disease. Infections, blisters, "sores", etc. were five times more common in the diabetic patient than in the nondiabetic patient. This finding is in agreement with those of Bell (3).

Trauma, of mild to moderate degree, was a predis-

TABLE IV

Nondiabetic Patients

Hospital	Claudication	Ulceration	Trauma	Other*
Charity 1	6	10	4	5
Charity 2	9	13	5	0
Private 1	2	4	0	0
Private 2	2	0	0	1
Private 3	0	0	0	0
Private 4	0	0	0	0
Private 5	0	0	0	0
Totals	19	27	9	6

Diabetic Patients

Hospital	Claudication	Ulceration	Trauma	Other*
Charity 1	0	5	4	5
Charity 2	3	13	0	7
Private 1	1	6	0	8
Private 2	0	5	1	4
Private 3	0	0	1	1
Private 4	0	5	0	1
Private 5	0	0	0	1
Totals	4	36	6	30

The table shows the number of patients giving a history of the complaint indicated prior to the onset of gangrene.

* Includes infection, blisters, "sores", etc.

posing factor to gangrene in a relatively small number of patients in each group.

Sites of Arterial Occlusion. Table V indicates the vessels where complete occlusion of the lumen occurred either by atheroma itself or by secondary thrombosis. The most common site in both diabetic and nondiabetic patients was the popliteal artery, the next most common being the posterior tibial. Once again the lesser tendency for vessels of larger caliber to be attacked in the diabetic patient is noted. Occlusions of the femoral and popliteal arteries occurred nearly twice as often in the nondiabetic patients. Occlusion as a whole in these vessels showed an incidence ratio of approximately three to two, between the nondiabetic and diabetic patients. In all but a few instances, dissection of the most distal arteries was not done and therefore the occurrence of occlusion at this level could not be evaluated. I certainly would expect the incidence to be significantly higher in the diabetic patients in view of the other findings already mentioned.

Amputation of the Opposite Extremity. In this study roughly 10% of the patients had amputations involving the opposite lower extremity prior to the

TABLE V

Nondiabetic Patients

Hospital	Unspecified*	Femoral	Popliteal	Ant. Tibial	Post. Tibial	Peroneal
Charity 1	5	3	16	1	6	0
Charity 2	2	2	6	0	2	0
Private 1	0	3	5	0	2	1
Private 2	0	0	0	0	0	0
Private 3	0	2	4	1	1	2
Totals	7	10	31	2	11	3

Diabetic Patients

Hospital	Unspecified*	Femoral	Popliteal	Ant. Tibial	Post. Tibial	Peroneal
Charity 1	0	3	7	1	2	0
Charity 2	0	0	4	4	2	1
Private 1	3	0	6	1	2	1
Private 2	0	0	0	0	1	0
Private 3	0	1	1	0	3	1
Totals	3	4	18	6	9	3

The table shows the site of arterial occlusion in patients in which the pathologist reported an occlusion.

*Unspecified refers to instances in which the specific artery was not identified by name, but rather as "the artery", the "main artery of the lower leg", etc.

TABLE VI

Previous Amputation Involving The Opposite Leg

Nondiabetic Patients	Diabetic Patients	Hospital No.
6	4	Charity 1
4	3	Charity 2
0	2	Private 1
0	0	Private 2
0	1	Private 3
0	1	Private 4
0	1	Private 5
Totals 10	12	

The table shows the number of patients giving a history of amputation involving the opposite lower extremity.

present amputation. Ten were nondiabetic and twelve were diabetic patients.

Duration and Severity of the Diabetes. No definite or significant relationships could be established between the duration of the diabetes or the insulin requirement and severity of the vascular disease in the diabetic patient. As mentioned earlier, there are some (20) who feel that such a relationship does exist and some (3, 17) who feel it does not. On the basis of the findings in this study, I must agree with the latter.

Indigent versus Nonindigent Patients. Table VII compares indigent patients with nonindigent patients. This was a primary interest in this thesis and the difference proved to be of much greater magnitude than was anticipated. The table speaks for itself, but some key points should be emphasized.

The most striking observation is that indigent patients accounted for about 65% of the amputations. This is in spite of the fact that indigent patients made up only about 23% of the hospital admissions and only about 17% of the operations performed.

It is recognized that many more minor surgical procedures are conducted in the private hospitals.

TABLE VII

Hospital	Total No. of Adm.	Total No. of Oper.	Number of Amputations: Nonindigent Non-diab.	Nonindigent Diab.	Indigent Non-Diab.	Indigent Diab.	Total Non-Ind.	Total Ind.
Charity No. 1	22,045	4,967	0	0	50	25	0	75
Charity No. 2	23,235	11,893	0	0	27	28	0	55
Private No. 1	56,377	41,790	15	21	0	2	36	2
Private No. 2	50,485	26,332	6	9	0	1	15	1
Private No. 3	22,199	4,530*	2	2	0	0	4	0
Private No. 4	11,476	2,848	3	8	0	2	11	2
Private No. 5	7,993	2,477	3	4	0	0	7	0
Totals			29	44	77	58	73	135

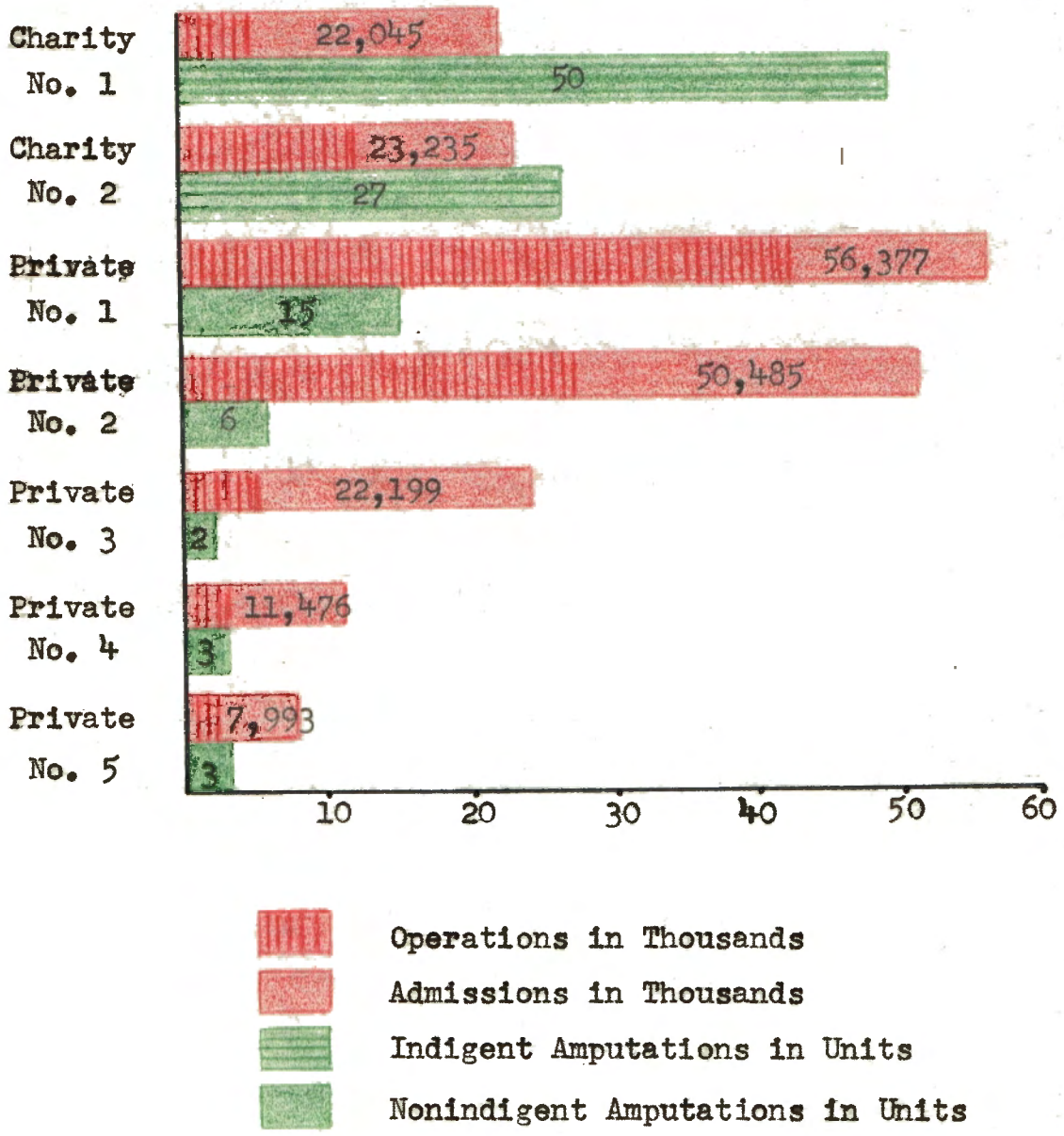
The table compares the total hospital admissions (excluding newborns), total operations, number of indigent and number of nonindigent patients of each hospital in the study for the period January 1, 1955 through June 30, 1960.

*These figures refer only to the period from March 1, 1957 through June 30, 1960. Prior statistics were not available from this hospital.

GRAPH III

Nondiabetic Amputations

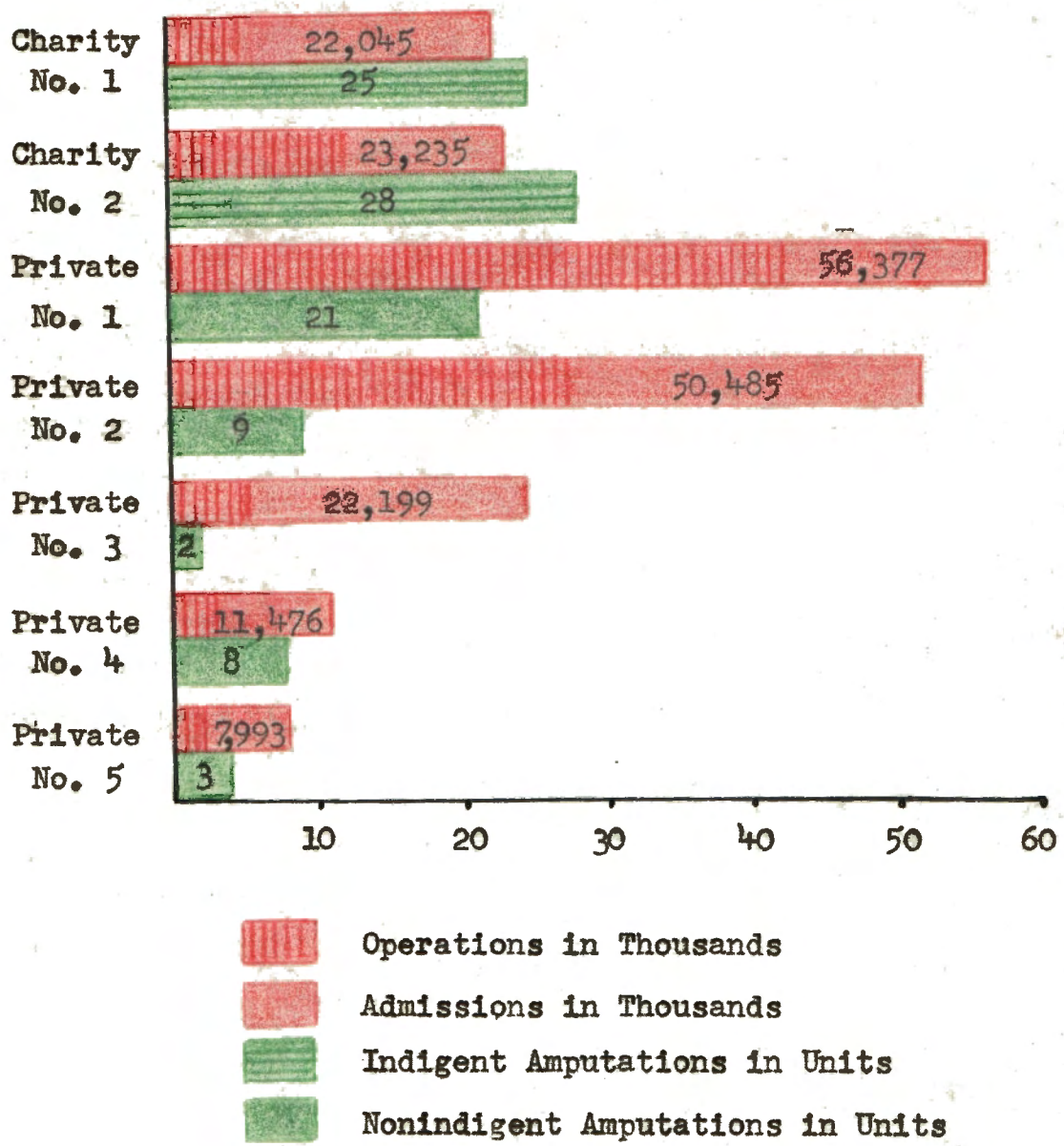
Amputations versus Admissions and Operations



GRAPH IV

Diabetic Amputations

Amputations versus Admissions and Operations



However, the difference in proportion of minor procedures to total procedures between the private and charity hospitals is not felt to be great. This is true because many more major procedures are also performed in the private hospitals.

It is interesting to note that there is not as wide a margin between diabetic indigent and nonindigent patients as there is in nondiabetic patients. It is also interesting to note that in the private hospitals more amputations were performed on diabetic patients than on nondiabetic. In the charity hospitals the reverse was true.

It would be easy to simply say that the facts speak for themself, that is, lower class (indigent) patients are more inclined to require amputation of the lower extremity than higher class (nonindigent) patients by a sizeable margin. However, there are numerous factors which might contribute to this difference. Perhaps conservative care may be of poorer quality in the charity hospital ad therefore the patient is more apt to develop gangrene and require amputation. Granted, there may be a difference in quality of care in different hospitals, but I do not feel it is nearly important enough to account for such a large difference

as has been demonstrated here. Secondly, the vast majority of the patients in this study had gangrene of such severe ischemia at the time of admission that the process was already irreversible and conservative treatment had no chance to play a role.

It is also likely that the indigent patient by his nature, his type of work, etc. is more apt to neglect himself medically and put off seeking medical attention until it is too late. This might be especially true of the indigent diabetic patient who might take his illness less seriously and fail to maintain proper control of it. In this series of patients this was true in a few instances, but was not an important factor for the group a a whole.

There are several important implications that this indigent to nonindigent ratio brings out. First of all it would tend to weaken the cholesterol and arteriosclerosis relationship as it is the higher class individuals who seem to have the higher fat diets. The aspect of stress is similarly weakened as we usually think of the higher classed (executive type) individual as being subjected to the greater stress.

One is left with the question of just why more indigents have amputations than nonindigents. This

is a question for which the answer can only be speculative. It has already been stated that the inherent nature of the individual, his environment, his type of work, etc. may contribute a small part, but this certainly is not the whole answer.

One is left, then, with the mere difference in economic status to account for the question at hand. Certainly this is not a new concept or one confined to arteriosclerosis alone. Several studies conducted in recent years have shown that individuals of low economic status, as a group, have a higher morbidity and mortality for many diseases.

A study of the mortality in the socio-economic districts of New Haven was made about fifteen years ago by the Public Health Service and Yale University School of Medicine. After dividing the city into socio-economic districts and determining mortality from various diseases in each district during the period from 1930 to 1934 they concluded that an adverse relationship existed between socio-economic status and mortality from all causes, from degenerative disease, from accident and violence, from diabetes, and from respiratory disease. This relationship was present at all ages, but was most striking below the age of

five and between the ages of forty-five and sixty-four. This adverse relationship did not exist for the mortality from tumors, infections and parasitic disease, diseases of infancy, and congenital malformations (28).

Though very few such studies have been conducted, these findings are in general agreement with those of similar studies. The following tables of figures (tables VIII and IX) represent two such studies, one in England and Wales and one in the United States. They, too, show a signigicant adverse relationship between socio-economic status and mortality.

Mortality. The mortality in my series also demonstrates an adverse relationship between mortality and economic status. (See table X). The mortality for indigent patients was 28 deaths in 133 patients (21.0%) and for nonindigent patients 7 deaths in 55 patients (12.7%). All deaths included were during the post operative period prior to dismissal from the hospital.

TABLE VIII

Cause of death and year	Social Class: Men I	II	III	IV	V	Married Women I	II	III	IV	V
All causes										
1921-23	82	94	95	101	125	-	-	-	-	-
1930-32	90	94	97	102	111	81	89	99	103	113
1950	97	86	102	94	118	99	84	101	104	117
Coronary dis.										
1930-32	77	92	94	105	122	54	75	99	110	129
1950	67	82	97	98	137	66	67	98	120	134
Diabetes										
1921-23	125	145	92	75	66	-	-	-	-	-
1930-32	122	155	95	82	69	56	89	104	108	106
1950	167	97	97	91	108	86	88	98	109	117

I- Professional
II- Intermediate
III- Skilled
IV- Semi-skilled
V- Unskilled

Social Classes of England and Wales

From "Social Class Variations in Mortality", Logan, W.P.D. Public Health Reports 69:12 Dec. 54, 1217-23.

This table shows the number of deaths among men and married women in each social class for the period specified.

TABLE IX

Social-Economic Class and Component Occupations	Standardized Death Rates	Comparative Ratio
All gainfully occupied men in selected occupations	9.1	100
I. Professional men	6.7	74
Technical engineers	5.5	60
Lawyers and judges	7.0	77
Physicians and surgeons	7.9	87
II. Proprietors and officials	7.8	87
Managers and officials	6.1	67
Bankers and brokers	6.7	74
Retail dealers	8.4	92
Restaurant keepers	10.8	119
III. Clerks and kindred workers	7.8	87
Bookkeepers and cashiers	6.9	76
Salesmen	7.1	79
Real estate agents	7.4	81
"Clerks" in stores	7.7	85
Other clerks	9.1	100
IV. Agricultural workers	6.2	68
V. Skilled workers and foremen	8.3	91
Foremen and overseers	6.1	67
Carpenters	7.2	79
Electricians	7.3	80
Machinists	7.7	86
Masons and tile layers	8.9	98
Plumbers and gas fitters	9.0	99
Policemen	9.3	102
Blacksmiths	9.6	105
Compositors and linotypers	9.7	107
Molders and casters	10.2	113
Tailors	10.8	119
VI. Semiskilled workers	10.1	111
In manufacturing	10.4	115
Others	9.4	103
VII. Unskilled workers	14.5	159

Standardized Death Rates per 1,000 gainfully occupied men 15 to 64 years of age in selected occupations, according to social-economic class and component occupations. Represents 10 states in the U.S. in 1930. The comparative ratio is based on a unit number of 100 as the average with each occupation then compared to it proportional to the standardized death rate for that occupation. From Whitney (33).

TABLE X

Hospital	Indigent	Non-Indigent	Indigent Deaths Non-diab.	Diab.	Total	Nonindigent Deaths Non-diab.	Diab.	Total
Charity No. 1	75	0	10	10	20	0	0	0
Charity No. 2	55	0	4	4	8	0	0	0
Private No. 1	2	36	0	0	0	3	3	6
Private No. 2	1	15	0	0	0	0	0	0
Private No. 3	0	4	0	0	0	1	0	1
Private No. 4	Not determined							
Private No. 5	Not determined							
Totals	133	55	14	14	28	4	3	7

The table demonstrates the number of deaths among indigent and nonindigent patients in the series.

SUMMARY

This thesis is concerned with (1) a discussion of arteriosclerotic disease in the lower extremity, (2) a discussion of the same problem in the diabetic patient and, (3) information obtained from a local survey of seven hospitals concerning arteriosclerosis in the diabetic and nondiabetic patient.

Arteriosclerotic disease is discussed as to the nature and location of the lesion, its pathogenetic factors, its affect, and its prognosis. It is of interest to note that there are numerous factors involved in the development of the arteriosclerotic lesion, each of which seems to play an important role, but none of which is adequate in itself to account for the process. This is particularly true of serum cholesterol and related lipids. Mechanical, structural and hemodynamic factors seem to be equally, if not, more important than cholesterol. The relationship of diabetes to arteriosclerotic disease is presented. It is noted that the two are closely allied. The pathogenetic factors are probably identical. However, the lesion appears earlier and the progress is more rapid in the diabetic patient. It also has

a different location. As in the nondiabetic, the arteriosclerosis is progressive and the prognosis is not good, particularly in the diabetic patient.

Finally, a study of hospital charts of 208 patients with amputation of the lower extremity for gangrene, revealed some interesting findings. The age difference between diabetic and nondiabetic patients was noted, but more interesting was the factor of sex. In the nondiabetic patients the disease was far more prominent in men while in diabetic patients the incidence was nearly equal. The most common type of amputation was an above knee amputation and a significant number were bilateral. Amputations at a lower level were more common in the nondiabetic patient, emphasizing the difference in the location of the lesion. The same is true of the site of arterial occlusion and also, the type of lesions and symptoms preceding the gangrene.

Most significant was the fact that the incidence of amputation in indigent patients far exceeded that of nonindigent patients. It appears that socio-economic status, itself, is the main reason for this difference. This factor has been blamed for the same finding in other studies considering many diseased

states.

Finally, the mortality in this area following amputation is presented. This only further emphasized the importance and the progressive nature of arteriosclerosis.

CONCLUSIONS

From the figures and findings presented above the following conclusions have been made:

1. Diabetic patients are likely to require amputation of the lower extremity at a younger age than nondiabetic patients.
2. More diabetic women require amputation than nondiabetic women. More nondiabetic men require amputation than nondiabetic women, but in diabetic patients the difference between sexes is small.
3. Nondiabetic patients have a significantly higher incidence of above knee amputations while diabetic patients have a higher incidence of more distal amputations. This is interpreted as verifying the fact that vascular disease in diabetic patients attacks smaller and more distal arteries, while arteriosclerosis in nondiabetics is more prominent in larger and more proximal arteries.

4. Most patients with gangrene give a history of signs and symptoms of peripheral vascular disease. The most common lesion preceding gangrene was ulceration and this was more common in the diabetic than in the nondiabetic patient. Infection and irritation of the skin is also more important in the diabetic patient. Claudication was more prominent in nondiabetic patients and this probably is related to the difference in sites of predilection of the arteriosclerotic process.
5. The commonest site of vessel occlusion is the popliteal artery, followed by the posterior tibial artery. Larger and more proximal vessels (femoral and popliteal arteries) are occluded more frequently in nondiabetic than in diabetic patients. This too, emphasizes the difference in predilection sites.
6. A significant number of patients (10%) have a history of previous amputation of the opposite extremity demonstrating the generalized and progressive nature of arteriosclerosis.
7. No relationship can be demonstrated between the duration and severity of diabetes and the severity of diabetic vascular disease.
8. Amputations in indigent patients greatly exceed

amputations in nonindigent patients. The only seemingly significant factor that can be advanced to account for this, is the difference in socio-economic status itself. This finding agrees with other studies comparing morbidity and mortality and socio-economic status.

9. The mortality in indigent patients following amputation is quite high (21.0%). In nonindigent patients it is significantly lower (12.7%), but still quite high. This again demonstrates the adverse relationship between mortality and socio-economic status. It also demonstrates the seriousness of arteriosclerotic gangrene.

ACKNOWLEDGEMENT

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