Studies in Peripheral Arterial Occlusive Disease

II. Clinical Findings in Patients with Advanced Arterial Obstruction and Gangrene

By Stanford Wessler, M.D., and Norman R. Silberg, M.D.

A controlled clinical-pathologic study of peripheral arteriosclerotic gangrene is reported in which all amputated specimens were examined by a special technic of injection and dissection of the arteries. The type of patient in whom gangrene usually develops is defined. The effect of various clinical and pathologic conditions on the degree of arterial insufficiency is discussed from the viewpoints of pathogenesis and therapy.

The treatment of the patient with peripheral arteriosclerosis is increasingly successful. During the course of the disease, however, the physician is frequently called upon to resolve problems about which there is little unanimity of opinion. These problems include the value of arteriography, the role of anticoagulant and antispasmodic drugs, the indications for sympathectomy, embolectomy and segmental arterial resection, and the selection of the proper site for amputation.

In a previous report1 a method was described for injecting and dissecting the arteries of amputated legs. In that study the extent and location of arterial occlusion, narrowing, calcification and interarterial anastomosis were determined in a large number of extremities removed because of arteriosclerotic gangrene. It is the purpose of the present report to review the clinical data among the patients requiring amputation so that additional information may be realized concerning the mechanisms involved in the precipitation or aggravation of gangrene. A correlation of the pathologic and clinical data has provided the basis for a better understanding of the problems frequently presented in the management of these patients.

The "amputation group" consisted of 38 patients* in whom either the lower leg or thigh had been amputated for arteriosclerotic gangrene at the Beth Israel Hospital in the years 1948 to 1952. A "control" series was included for purposes of comparison. This group consisted of 37 consecutive patients with peripheral arteriosclerosis admitted to the Beth Israel Hospital in the years 1948 to 1950 for ulceration or gangrene of an extremity which healed either with conservative medical management or after local digital or transmetatarsal amputation.

Results

The results of this study are summarized in table 1. For convenience the data have been divided into three groups: group I, factors in which significant† or suggestive differences were found between the amputation and control series; group II, factors which may have played a role in the development or spread of gangrene but in which differences between the two series were not found; group III, factors in which the number of observations was inadequate for conclusions to be reached.

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* Two patients had bilateral leg amputations; one, who had her amputations two years apart, was counted twice.
† Differences were considered to be statistically significant if they were 2.5 times the standard error of the difference.

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Group I. Factors in which significant or suggestive differences were found between the amputation and control series

Congestive Heart Failure. Congestive heart failure appeared before gangrene in 21 per cent of the amputees and in 3 per cent of the control series. This difference was statistically significant.

Debilitating Disease. Debilitating diseases such as uremia and recurrent pancreatitis occurred in 18 per cent of the amputees and in 5 per cent of the control group. Although suggestive, this was not a significant difference.

Mental Aberration. The mental state of each patient was evaluated by one or more staff physicians prior to amputation. In several instances, patients were seen by members of the psychiatric service. Although it is recognized that diabetic patients are frequently subject to minor mental aberrations, almost one-third of the patients in the amputee group were markedly disturbed; they were confused, disoriented and uncooperative; in addition

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**Table 1. Summary of Data**

<table>
<thead>
<tr>
<th></th>
<th>Amputation series</th>
<th>Control series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Patients</td>
<td>38</td>
<td>37</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>8/38 (21%)</td>
<td>1/37 (3%)</td>
</tr>
<tr>
<td>Pulsation Present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femoral Artery</td>
<td>34/36 (94%)</td>
<td>34/36 (94%)</td>
</tr>
<tr>
<td>Popliteal Artery</td>
<td>4/32 (13%)</td>
<td>16/30 (53%)</td>
</tr>
<tr>
<td>Dorsalis Pedis Artery</td>
<td>0/38 (0%)</td>
<td>3/37 (8%)</td>
</tr>
<tr>
<td>Posterior Tibial Artery</td>
<td>0/38 (0%)</td>
<td>1/37 (3%)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>22/25 (88%)</td>
<td>13/29 (48%)</td>
</tr>
<tr>
<td>Debilitating Disease</td>
<td>7/38 (18%)</td>
<td>2/37 (5%)</td>
</tr>
<tr>
<td>Mental Aberration</td>
<td>12/38 (32%)</td>
<td>4/37 (11%)</td>
</tr>
<tr>
<td>Cerebral Vascular Accident</td>
<td>6/38 (16%)</td>
<td>0/37 (0%)</td>
</tr>
<tr>
<td>Shock</td>
<td>6/38 (16%)</td>
<td>0/37 (0%)</td>
</tr>
<tr>
<td>Cardiac Arrhythmia</td>
<td>4/38 (11%)</td>
<td>0/37 (0%)</td>
</tr>
<tr>
<td>Local Infection</td>
<td>29/38 (76%)</td>
<td>28/34 (82%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proven Present</td>
<td>28/30 (93%)</td>
<td>28/28 (100%)</td>
</tr>
<tr>
<td>Proven Absent</td>
<td>2/30 (7%)</td>
<td>0/28 (0%)</td>
</tr>
<tr>
<td>Suspected Present</td>
<td>6/8</td>
<td>5/9</td>
</tr>
<tr>
<td>Unknown</td>
<td>2/8</td>
<td>4/9</td>
</tr>
<tr>
<td>Average Age (years)</td>
<td>64.5</td>
<td>63.2</td>
</tr>
<tr>
<td>Sex Ratio (Males/Females)</td>
<td>1.7/1</td>
<td>1.3/1</td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below 11.0 Gm. per cent</td>
<td>6/38 (16%)</td>
<td>5/37 (14%)</td>
</tr>
<tr>
<td>11.1-12.0 Gm. per cent</td>
<td>9/38 (24%)</td>
<td>9/37 (24%)</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>13/38 (34%)</td>
<td>11/31 (35%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30/38 (79%)</td>
<td>25/37 (68%)</td>
</tr>
<tr>
<td>Intermittent Claudication (% of Active Patients)</td>
<td>13/29 (45%)</td>
<td>14/24 (58%)</td>
</tr>
<tr>
<td>Injudicious Therapy</td>
<td>8/34 (24%)</td>
<td>10/33 (30%)</td>
</tr>
<tr>
<td>Local Trauma</td>
<td>12/26 (46%)</td>
<td>9/33 (27%)</td>
</tr>
</tbody>
</table>

**Palpable Peripheral Pulses.** Peripheral arterial pulses in the affected extremity were, in general, not palpable below the femoral artery at the inguinal ligament among the patients with major amputation. Popliteal pulses were present, however, in a significantly greater number of the patients not requiring major amputation.

**Neuropathy.** We have accepted as evidence of peripheral neuropathy alteration in deep tendon reflexes combined with motor or sensory defects. Among 25 patients with major amputations in whom adequate examinations were recorded 88 per cent had abnormal neurological findings. Less than half of the control patients had neuropathy. This difference was also statistically significant.
three exhibited paranoid tendencies, two repeatedly ripped off protective bandages and one assaulted a physician. Similar behavior was observed in only one-tenth of the controls. Although this difference was suggestive, it was not statistically significant.

Cerebral Vascular Accident. Hemiplegia involving a lower extremity had occurred from 6 months to 18 years prior to the onset of gangrene in six of the patients with major amputations. In five of these patients residual evidence of upper motor neurone damage was present. In each of these six patients gangrene necessitating amputation developed in the hemiplegic limb. No cerebral vascular accidents occurred in the control group.

Shock. Shock occurred in six amputee patients and in none of the control group. In each patient the vascular collapse developed after the onset of gangrene and prior to the amputation. In no instance did the clinical status of the leg appear to be aggravated by the development of hypotension; yet, multiple fresh occlusions were demonstrated in four of these six patients. Of the two remaining patients with shock, in whose extremities fresh occlusions were not found, one had experienced hypotension in association with a myocardial infarct six weeks prior to amputation (case 23) and had been treated with bishydroxycoumarin (Dicumarol) for 28 days. In the remaining patient (case 36) shock occurred three days before amputation from acute pancreatitis. Since in this latter instance the leg had been amputated below the knee, it is possible that fresh occlusions were present in the arteries proximal to the site of amputation of the lower leg.1

Cardiac Arrhythmia. Four patients in the amputee group had paroxysmal arrhythmias after the onset of gangrene. Fresh occlusions were demonstrated in three as the most proximal arterial occlusion in the amputated extremity. This finding suggests the possibility that these lesions may have been embolic from the heart. There were no instances of arrhythmia in the control group.

Local Infection. Gross infection was present in the extremities of 29 patients in the amputee group and 28 patients in the control group. Appropriate antibiotics were given locally and systemically. The incidence of infection and the type of bacterial flora were similar in both groups. In the control group, of course, subsidence of the infection, as evidenced by healing of gangrene or ulceration, was accomplished in all patients.

Group II. Factors which may have played a role in the development or spread of gangrene but in which differences between the two series were not found

Diabetes Mellitus. A diagnosis of diabetes mellitus was accepted if either a fasting venous blood sugar6 exceeded 130 mg. per 100 ml. or an abnormal glucose tolerance was obtained.6 Among 30 patients with major amputations in whom the presence or absence of diabetes could be established, all but two were diabetic; intermittent glycosuria existed prior to amputation in six of the remaining eight patients in whom blood sugar determinations were not made.

Diabetes was considered to be mild if less than 10 units of insulin daily were required and severe if in excess of 40 units were needed. By these criteria there were no severe diabetics in the entire amputation group. Moreover, in no instance was diabetic coma or acidosis associated with the onset of gangrene. On the other hand, only two patients in the amputation group satisfied the criteria of good diabetic control as manifested by fasting and one hour postprandial blood sugars of less than 120 and 160 mg. per 100 ml. respectively.7

The actual duration of the diabetic state was not known; the disease was first recognized in seven patients after hospitalization for gangrene. The average known duration of diabetes, including the patients discovered on admission, was seven years. The duration in patients who had established diabetes prior to hospitalization for gangrene was approximately 10 years; the longest known duration was 30 years.

The incidence of diabetes as well as its severity, duration and adequacy of regulation did not differ significantly between the amputees and the control patients.

Age and Sex. The age distribution curve as
well as the average age and sex ratio did not differ significantly between the two groups. Most of the patients were in the seventh decade and the sex ratio showed only a slight male preponderance.

Anemia. Hemoglobin levels (Cenco photometer) below 11 Gm. per 100 ml. in males and females were considered to represent anemia. Only hemoglobin determinations performed prior to amputation were utilized in this analysis. When multiple determinations were made, they were averaged. Sixteen percent of the patients in the amputee and 14 percent in the control groups had anemia. One-fourth of the patients in each group, moreover, had hemoglobin levels between 11 and 12 Gm. per 100 ml.

Coronary Artery Disease. A diagnosis of coronary artery disease was accepted if a patient had angina pectoris, coronary failure or myocardial infarction. In approximately one-third of the patients in both the amputation and control groups such a diagnosis could be established.

Hypertension. Arterial hypertension was considered to be present if the systolic or diastolic pressure reached or exceeded 150 or 90 mm. Hg respectively. More than three-fourths of the patients in the amputee series had elevated blood pressures. These figures did not differ significantly from those in the control group.

Intermittent Claudication. A diagnosis of intermittent claudication was accepted when physical exertion produced in the foot, calf, or thigh, pain or cramps promptly relieved by cessation of the activity. In no patient did unusual activity precipitate or aggravate gangrene. Marked restriction of physical activity was necessitated by advanced congestive failure, cerebral vascular accidents, chronic nephritis or leg fracture in one-fourth of the patients who required major amputations: claudication was not present prior to restriction of activity in any of them. Among the remaining 29 active patients in this group, claudication was present in less than half. The duration of the claudication prior to the onset of gangrene varied from 3 months to 29 years with an average of approximately six years. Intermittent claudication occurred in a similar number of the control group.

Injudicious Therapy and Local Trauma. Injudicious therapy was defined as the application of any procedure or treatment that increased the disparity between the local blood supply and the metabolic requirement of the involved extremity. Eight of 34 amputees in whom this factor could be assessed had applied hot soaks or received diathermy to the extremity. Twelve episodes of local trauma were recorded in 26 patients subsequently undergoing major amputation. These consisted of laceration of the skin from cutting of the toe nails in four patients, a scratching or stubbing of a toe in five patients, a brick falling on a toe in one patient and ankle injuries in two other patients. Three patients had had recent fractures of the same leg that subsequently became gangrenous. The incidence of injudicious therapy and trauma in the control group was, however, similar to that among patients requiring major amputations.

Digital and Transmetatarsal Amputation. Toes were amputated in nine patients from the amputation group without success and in 14 from the control group with healing. Healing time was prolonged up to a year in two patients in the latter group.

Transmetatarsal amputation was performed in five patients in the amputee group: healing occurred in one. In this patient (case 18) one and a half years after a transmetatarsal amputation gangrene developed proximal to the amputation site. Four control patients had transmetatarsal amputations with healing.

Group III. Factors in which the number of observations were inadequate to justify conclusions

Anticoagulant Therapy. Although anticoagulant therapy was given to eight patients in the amputee group after the onset of gangrene, in only two instances (cases 18 and 23) was the hemostatic mechanism significantly altered for a prolonged period. These two patients, hospitalized because of gangrene, developed acute myocardial infarction while in the hospital and receivedbishydroxycoumarin (Dicumarol) for 21 and 28 days respectively. Low thigh am-
putations were carried out 61 and 50 days respectively after the onset of the infarction and 40 and 22 days after the discontinuance of Dicumarol. In one of these patients (case 18) multiple recent occlusions were demonstrated in the amputated extremity, but it could not be conclusively established by pathologic examination whether or not their deposition antedated the cessation of the anticoagulant therapy. No patients in the control group received adequate anticoagulant therapy.

Drugs. Vasodilating agents such as benzyl-imidazole (Priscoline), papaverine and ether were given orally or intravenously to 10 patients who subsequently underwent major amputation. In no instance was there evidence of beneficial or harmful effect on necrosis or pain. The drugs were used, however, only for brief periods in varying dosages so that their efficacy could not be fairly evaluated. Five patients in the control series also received vasodilators without definite effect.

Lumbar Sympathectomy. Lumbar sympathectomy was carried out in seven patients from the amputee group. In no instance was the clinical course altered favorably. In fact, one of these patients (case 20), in whom sympathectomy was performed because of a cold painful extremity, developed an ulceration of a toe on the sixth postoperative day. In 5 of the 11 control patients who underwent sympathectomy, healing of the ulcerations or gangrene occurred promptly. Among the remaining six healing was so delayed that the role of the sympathectomy in the final result was not clear.

Leg and Thigh Amputation. There were 17 lower leg and 22 thigh amputations. Four of the lower leg amputations had to be revised. Only one patient (case 28) required revision of a low thigh amputation and this was necessitated because of massive extension of a fresh occlusion proximally to the iliac artery.

Clinical Implications

Absent popliteal pulsation, congestive failure and neuropathy were significantly more common among patients requiring major amputations than among those with ulceration and gangrene who did not need such extensive surgery. There was also a suggestively higher incidence of debilitating diseases and serious mental disturbances among the amputee group.

The consistent development of gangrene in the hemilegic leg was of considerable interest since it has been suggested that blood flow to such extremities is increased.11 The impaired control of these extremities by the patient may, however, have been responsible for the development of gangrene in these limbs. This is supported by the finding that in three patients with arterial insufficiency who had sustained recent hip or thigh fractures, gangrene developed in the injured extremity.

When other factors such as shock, local injury, infection or anemia are superimposed on the ischemic limb the disproportion between blood supply and demand may be exaggerated and gangrene result. The role of anemia in this regard deserves special mention. The possibility was considered that many of the observed low hemoglobin levels may have been a reflection of age unrelated to specific disease processes. Shapleigh, Mayes and Moore, however, have found that the peripheral blood and bone marrow do not change strikingly as people grow older.8 In anemia the tissues are given enough oxygen for their basal requirements, but the low tissue oxygen tensions which exist result in a diminution of the margin of safety.12 In the presence of advanced obliterative disease, even a mild anemia may decrease this margin of safety sufficiently to tip unfavorably the delicate balance between viability and necrosis.

It has been demonstrated that anemia may stimulate interarterial anastomoses.13 Once clinical manifestations of ischemia have developed in an extremity, however, viability will be enhanced by correction rather than maintenance of the anemia. In these elderly patients this can be achieved by multiple small transfusions.

The prominence of diabetes among the patients with peripheral arteriosclerosis and gangrene in this study is striking. This metabolic disorder may contribute in several ways to peripheral arterial insufficiency. Diabetes probably accelerates the atherosclerotic process itself14; it is, thus, associated with cerebral atherosclerosis which often interferes with the
exercise of good judgment by the patient and with coronary atherosclerosis with resultant congestive failure. It is also associated with retinal and peripheral neuropathy which alters the patient’s awareness of local trauma. Finally, resistance to infection may be impaired in diabetic patients. The incidence of diabetes in the present series is higher than that reported by other investigators. Yet, in 7 of the 30 diabetic patients requiring major amputation in this study, the disease was first recognized after the onset of gangrene. Among 33 patients from the Boston City Hospital in whom low thigh amputations were performed because of arteriosclerotic gangrene only two were clearly nondiabetic. The discrepancy between our findings and those in the literature may have resulted, in part, from different criteria used to establish the presence or absence of diabetes. Since the severity of the diabetic state is not related to the development of gangrene and since in several patients the metabolic defect was recognized only after examination of the blood sugar, diabetes should be suspected in every patient with peripheral arteriosclerosis. It is only in this way that any possible benefits from good management can be realized.

The pathologic substrate for gangrene in the arteriosclerotic limb is extensive occlusive disease. The subsequent development of fresh occlusions may obstruct the main leg arteries and block previously effective collateral channels. Arrhythmias and hypotension were found frequently in this study to be associated with multiple and extensive fresh occlusions. From the standpoint of tissue viability it is immaterial whether these fresh occlusions are embolic from the heart or local thromboses of arterial segments in the leg. Our previous pathologic studies have shown the important factors to be the location and the length of the occlusions. Usually a small fresh occlusion can be tolerated by an arteriosclerotic limb because of a previously formed and rich collateral circulation. An extensive occlusion, however, is dangerous because it blocks the large arteries which are acting as communications between many sets of collateral vessels. Sudden spread of gangrene developed in two patients (cases 10 and 28) while they were under observation in the hospital. This rapid progression of necrosis was shown subsequently to be related to the deposition in the popliteal arteries of fresh thrombi, 11 and 13 cm. in length, respectively. If such catastrophes could have been prevented in these patients, it is conceivable that conservative management might have salvaged these extremities. A major therapeutic attempt should thus be made, in patients with incipient or limited gangrene, to prevent the deposition or extension of fresh occlusions in the main arterial channels. There are a number of experimental studies indicating that the development and growth of thrombi may be aborted by anticoagulant therapy. Such therapy, although not without dangers, may be effective in diminishing the necessity for major amputations.

From our own studies, the role of embolectomy has yet to be clearly defined. Frequently it is difficult to determine clinically whether one is dealing with an embolus or a thrombus. Emboli in the popliteal artery and below are not easily accessible for removal and the surgical procedure itself may sever crucial collateral arterial channels. In addition, operative incision of atherosclerotic vessels carries some risk of subsequent thrombosis. The prime consideration is not the presence of an arterial obstruction, per se, but rather its length and its potential for propagation. Ideally, therefore, the management of choice in most patients with fresh peripheral arterial occlusion would appear to be adequate anticoagulant therapy in order to prevent the propagation of clot which has already formed.

The theoretic value of vasodilatation by surgical or medical means in combating gangrene is not so firmly grounded as is anticoagulant therapy. In the first place a very rich collateral circulation is already present in the legs of patients with advanced obliterative arterial disease: this collateral circulation is, moreover, remarkably free of intrinsic occlusions and narrowings. In the second place, there is little clinical or experimental evidence to support the concept of “spasm” in this collateral circulation which need be overcome by inactivating all or part of the sympathetic
nervous system. Whether it is helpful even to remove normal vascular tone in these patients remains unsettled. The fact that interruption of sympathetic activity may increase skin temperature does not necessarily imply a similar vasodilation in deeper structures.29, 30 The reverse has, in fact, been claimed.31 Finally, some observers32, 33, 34 believe that lumbar sympathectomy may occasionally even precipitate gangrene.

Drugs capable of blocking vasoconstrictor tone in an extremity may also cause hypotension and tachycardia. In patients with coronary artery disease such disturbances in hemodynamics may precipitate myocardial ischemia and even necrosis.35 It is, therefore, important to recall the high incidence of coronary artery disease among elderly diabetic patients36 as well as the fact that many patients may have coronary artery obstruction without clinical manifestations.37 In the five patients in the amputee group who came to necropsy, examination of the hearts by the method of Schlesinger38 revealed in each instance the presence of coronary artery occlusions. In one of these five patients (case 4) a diagnosis of coronary artery disease had not been made ante mortem.

There have been several reports of the value of intra-arterial vasodilators in the management of advanced peripheral arteriosclerosis.39, 40 This route of administration, it has been claimed, will minimize the systemic effects of the drug. Recently, however, intra-arterial Priscoline has also been found to produce myocardial infarction.39 Intra-arterial therapy, requiring as it does repeated arterial puncture, invites, of course, the risk of thrombosis in sclerotic arteries. The value of such therapy in patients with advanced obliterative disease remains to be established.

It is curious that, in the heart where occlusions are small, comparatively few in number and preformed anastomoses rare, current therapeutic trends have emphasized the value of anticoagulants rather than measures designed to stimulate the collateral circulation. On the other hand, in the leg where occlusions are extensive and a relatively adequate anatomic circulation is already present most of the effort has been designed toward stimulating collateral circulation and little toward preventing the major channels from becoming extensively occluded.

From the clinical viewpoint, gangrene usually develops in the elderly, mentally disturbed mild diabetic with peripheral neuropathy and absent pulsations distal to the femoral arteries. Almost invariably two or more conditions such as extensive fresh occlusions, congestive failure, anemia, shock, local injury or infection aggravate the circulatory imbalance. These criteria may be of little prognostic help in individual cases because our ability to assess the extent of the occlusive disease and of the local injury is very crude. Occasionally patients who appear inevitably headed for a major amputation will escape such an outcome with prolonged and diligent conservative management. Conversely even in the presence of proven minimal occlusive disease a severe neglected insult to the leg may result in extensive gangrene and amputation. Thus, occlusions were found in only one of the three tibial arteries in a special group of patients from the Boston City Hospital. In these patients neglect of small lesions because of psychosis, diabetic acidosis, or application of excessive heat resulted in spreading sepsis and made amputation necessary even occasionally in the presence of pedal pulsations.

The value of arteriography is limited since most occlusions lie between the knee and the ankle where it is relatively difficult to visualize them roentgenographically. Moreover, the procedure itself carries a small but definite risk.42 Unless surgical intervention in the form of embolectomy or arterial resection is contemplated, arteriography should not be performed in patients with arterial insufficiency.

Recently, the more extensive use of lower leg amputation for peripheral gangrene has been advocated.17, 19 In our own series more difficulties were encountered with the lower leg than with the low thigh stumps. One of the principal explanations for the difference in healing of the two procedures may be that the lower leg amputation does not eliminate sites of major arterial obstruction which are diffusely scattered over the area from the knee to the ankle.1 Obstructions in the femoral artery are rarely as extensive as in the tibial vessels.1, 43
One of the most encouraging conclusions from this study is that the leg can tolerate a tremendous amount of occlusive disease because of a well-developed collateral circulation. The major threats to viability of the arteriosclerotic limb come from the sudden extension of fresh occlusions and the placing of excessive demands upon a compromised circulation. At the present time the former may be treated by anticoagulant therapy and the latter by prophylaxis and vigorous treatment of infection, anemia and other factors which increase local metabolic demands. Antibiotics have already played a large role in reducing the necessity for major amputations. Today, short of a cure for atherosclerosis, prophylaxis remains the real key to therapy. By insuring proper care of his feet, the patient and his physician, rather than the extent of the occlusive disease, per se, will largely determine the incidence of gangrene and amputation.

Summary

1. A clinical-pathologic study of peripheral arteriosclerotic gangrene was carried out in a group of 38 patients who underwent major amputation. These surgically removed specimens were all examined by a special technic of injection and dissection of the arteries. The clinical records of a control group of 37 patients with arteriosclerotic gangrene but not requiring major amputation were also reviewed.

2. Gangrene usually develops in the elderly, mild diabetic with peripheral neuropathy and absent pulses distal to the femoral arteries.

3. Extensive fresh occlusion, congestive failure, marked mental disturbances, debilitating diseases, anemia, shock, local injury and infection may precipitate gangrene in the ischemic limb by aggravating the disproportion between local blood supply and demand. If this disparity between supply and demand is sufficiently great, gangrene may supervene in extremities with relatively little occlusive disease.

4. Therapy to prevent the development and propagation of fresh occlusions in the main arterial channels is probably more important for survival of the ischemic limb than efforts to stimulate the collateral circulation.

5. One of the most encouraging conclusions of this study is that the leg can tolerate a tremendous amount of occlusive disease because of a well-developed anastomotic circulation. By insuring proper care of his feet, the patient and his physician, rather than the extent of the occlusive disease, per se, will largely determine the incidence of gangrene and amputation.

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