Recognizing the considerable excess burden of both cerebrovascular and lower extremity arterial disease suffered by persons with insulin-dependent or non-insulin-dependent diabetes mellitus,12 a workshop was convened to

1. Provide a current review of the knowledge pertaining to the prevalence, incidence, and risk factor associations of cerebral and peripheral vascular disease in diabetes and

2. Review and make recommendations about the methodology for identifying and quantifying lower extremity arterial disease in either the clinical or research setting.

The workshop focused on the specific problems of, and the need for a standard approach to, measurement of peripheral vascular disease in diabetes to ensure appropriate care and facilitate comparability of research findings across studies and over time. Recommendations for the measurement of lower extremity arterial disease (LEAD) in a primary care setting and for epidemiological studies were developed, along with recommendations for more detailed assessment after referral to a vascular clinic. Specific recommendations for the assessment of cerebrovascular disease were not addressed. The detection and appropriate measurement of LEAD was determined to be of great importance, not only in terms of the disease, but also for the strong predictive power that LEAD has for subsequent cardiovascular mortality.3

The workshop started with a series of presentations, which are briefly summarized below, followed by the development of specific recommendations. This report has been written on behalf of all the participants who subsequently reviewed, revised, and approved the final version.

Dr. Curb reviewed the current state of knowledge concerning the epidemiology of stroke in diabetes. Data from Framingham, the National Health and Nutrition Examination Survey, and the Systolic Hypertension in the Elderly Program suggest a twofold increase in relative risk for stroke in subjects with diabetes, although in a further study (the Rancho Bernardo Study) only a small increase was seen for women with diabetes. Data from the Honolulu Heart Study supported a relative risk of around 2 for persons with diabetes for developing stroke, and in common with some earlier reports also suggest that the relative risk is not increased for the subgroup with hemorrhagic stroke. This is particularly true after adjustment for other risk factors. The reasons for this observation remain obscure and should be studied further. One possible explanation suggested was that the hypercoagulable state seen in some patients with diabetes may reduce the risk of bleeding.

Two presentations then focused on the epidemiology of risk factors for lower extremity arterial disease. Dr. Palumbo reported data from the diabetes incidence cohort of Rochester, Minn.24-6 Eight percent of subjects had LEAD at the time of diagnosis of diabetes. The cumulative incidence of LEAD rose with age and duration of diabetes to reach 45% by 20 years of duration of diabetes. In a multivariate analysis of a cohort comprising both nondiabetic and diabetic subjects with and without LEAD at baseline, progression of LEAD was related to the presence of both LEAD and diabetes at baseline, decreased postexercise ankle-brachial index (ABI), increased systolic blood pressure, and smoking. Diabetes control (glycated hemoglobin) and lipoprotein profile did not contribute further to the prediction of progression of LEAD.

In the Schwabing studies reported by Dr. Janka, more than 600 patients with either insulin-dependent or non-insulin-dependent diabetes mellitus were prospectively followed up for LEAD by ultrasonic Doppler measurements.78 At the 5-year, as well as a 9-year follow-up, the incidence of mostly asymptomatic LEAD was consistently and significantly associated with base-
line systolic blood pressure and the dyslipemic complex of high serum triglycerides/low high-density lipoprotein cholesterol level but not with total cholesterol level, weight, or diastolic blood pressure. The association with hemoglobin A1c, plasma C-peptide, and daily insulin dose (in insulin-treated patients with non-insulin-dependent diabetes mellitus) was weaker and at 9-year follow-up only significant in univariate analysis. Sixty-seven percent of diabetic patients dying from cardiovascular causes within the 5-year observation had LEAD (mostly asymptomatic) at baseline compared with 15% in those who survived.

The clinical aspects of lower extremity arterial disease in diabetes were reviewed by Dr. Graor. An increase in hospital mortality and higher amputation rates amongst those with diabetes was stressed, as well as the higher proportion of diabetic subjects with stenoses in the medium-sized arteries below the knee. The importance of determining the neuropathic as well as the ischemic status of any diabetic subject with foot ulcers was also stressed, as was the need for protective care for any subject with neuropathic lesions.

Attention then turned to methodological issues, Dr. Lassen provided an overview of atraumatic methods for measuring cerebral blood flow. The xenon 133 inhalation method showed normal cerebral blood flow in long-term diabetes. This was the case even in patients with extracranial atherosclerotic occlusive disease. However, a defect in cerebral blood flow autoregulation may be present, as manifested by the variation in cerebral blood flow that is observed with blood pressure variations. This defect, that also has been shown by other techniques, probably reflects increased stiffness of the hyalinized arterioles. The ill-defined syndrome of diabetic encephalopathy, a form of vascular dementia in very-long-duration insulin-dependent diabetes, may be related to these arteriolar changes, that set the stage for subcortical lesions, particularly lacunar infarcts.

The role of the clinical exam for LEAD was reviewed by Dr. Criqui.20 Using data from an elderly, population-based cohort of more than 500 subjects (5% of whom had diabetes), clinical signs and symptoms were correlated with LEAD defined by segmental blood pressure ratio and flow velocity assessed by Doppler ultrasound. The recording of a pulse deficit had a low predictive value for LEAD. The sensitivity of the Rose Questionnaire for detecting LEAD was 9% while only 20% of those with LEAD had exercise calf pain not present at rest. These low values were partly explained by a high proportion of LEAD being due to isolated disease in the posterior tibial artery which would not lead to exercise-induced calf pain. A decreased or absent posterior tibial pulse had a relatively high sensitivity (71%) for LEAD and a fair (50%) positive predictive value. Dr. Criqui stressed that even isolated posterior tibial disease carried a threefold risk of all-cause mortality and a fourfold risk of coronary heart disease mortality.

The usefulness of the ankle:arm blood pressure index (ABI) was discussed in a presentation by Dr. McMillan, who described studies in nearly 400 diabetic patients, a quarter of whom had Type I diabetes. Patients with either low (<0.90) or high (>1.30) ABIs, the latter suggestive of medial wall calcification, were studied. A high prevalence of proteinuria was noted in those persons with diabetes aged less than 40 years old who had high ABIs. Little influence of gender was noted. In persons with diabetes more than 40 years old, the association of a high ABI with proteinuria was lost. A high ABI was observed more often in men, with little relation to either age or duration of diabetes, as was a trend to higher serum calcium levels. The milk intake of the affected (high ABI) patients was not unusual. The frequency of high and low ABIs together in the same patient was low (about 2% overall or 5% of patients with one or more abnormal ratios) and predominantly in middle-aged men. While concern exists about missing the diagnosis of occlusive disease because of arterial calcification, the problem is less than had originally been expected. The prevalence of low ABI suggestive of occlusive disease increases with both patient age and diabetes duration, and low ABIs are almost as common in women as in men.

Non-ABI methods of assessing LEAD were discussed by Dr. Strandness, who stressed the value of measuring the toe systolic blood pressure (TSBP)10 in patients referred to a vascular clinic. This measurement overcomes the false elevation of ankle pressures from calcification and has a similar repeatability to the ABI. In the vascular clinic, evaluation of velocity patterns (loss of normal triphasic or biphasic waveform, spectral broadening, and increasing peak systolic velocity >100%) between segments are further findings of significance. Recent improvements in duplex scanning techniques allow such assessments from the aorta to the ankle and permit localization of lesions with good accuracy and precision.

The value of TSBP recording in the management of diabetic foot lesions was further demonstrated by Dr. Holstein,11,12 based on his 20 years of experience with this technique. The spontaneous healing of ulcers was shown to be predicted by this measurement, such that a TSBP of <20 mm Hg was associated with only a 29% healing rate, compared with a healing rate of 92% for a TSBP of ≥30 mm Hg. Two thirds of limbs with a TSBP of <30 mm Hg eventually went on to amputation, as opposed to none in those with a TSBP of ≥30 mm Hg. TSBP also enables pressure to be assessed in patients with leg ulcers where the use of an ankle cuff is not possible.

The issue of medial wall calcification was further addressed by two studies that included x-ray data. Dr. Cavanagh reviewed 94 patients with diabetic sensory neuropathy who had undergone standardized weight-bearing radiographs and compared the findings with those in 43 diabetic patients without neuropathy and 50 age-matched nondiabetic controls. The results showed a strong and statistically significant association between the presence of medial arterial wall calcification and peripheral sensory neuropathy. Arteries at the level of the ankle were more frequently calcified than those at the toe level. A history of foot ulceration was also associated with presence of calcification, which itself was more frequently seen in the arteries in the dorsum of the foot than in the planter arteries. Marked calcification was also associated with elevated serum creatinine.

There were 147 participants in the Pittsburgh Epidemiology of Diabetes Complication Study (based on an incident cohort of patients with childhood-onset insulin-dependent diabetes mellitus). Dr. Orchard reported a
high prevalence of calcification in these subjects (mean age, 34 years; mean duration of diabetes, 26 years): 32% had calcification in the posterior tibial artery on ankle view x-rays and 28% had calcification in the anterior tibial artery. Calcification was detected even more frequently in the foot; 47% had calcification in arteries at the metatarsal level. However, the prevalence of calcification was low in toe arteries, consistent with the data reported by Dr. Cavanagh. Arterial calcification was twice as prevalent in men as in women and was unrelated to the ABI in that it was present at all levels of ABI. A difference of 75 mm Hg between ankle and arm systolic blood pressure gave a 100% positive predictive value for the presence of arterial calcification by x-ray, although the sensitivity was low, between 6 and 9% (depending on which arteries were studied).

Data on the relation between resting and postexercise ABI were also presented. Data from 657 subjects with insulin-dependent diabetes mellitus from the first cycle of the Pittsburgh EDC study showed that 4% had an ABI of <0.8 and 15% had an ABI of <0.9 at 1 minute postexercise compared with only 1% and 5%, respectively, at rest.\(^\text{13}\) Though the postexercise test would appear to be more sensitive, it was noted that a resting ABI of \(\geq 0.80\) and \(\leq 0.89\) had only a 26% sensitivity of predicting a postexercise ABI of <0.80. An analysis of risk factors and complications suggested that subjects with an ABI of <0.80 at rest or with an ABI of <0.90 at rest and <0.80 postexercise had a greatly disturbed lipoprotein profile, were more likely than other subjects to have hypertension, and have been smokers. This subgroup also had a high prevalence of neuropathy (75%), overt nephropathy (42%), and proliferative retinopathy (75%). They also had a high 2-year incidence of overt nephropathy and retinopathy of 40% and 33%, respectively. Such associations were not seen for those with an ABI of <0.90 by either exercise or resting ABI alone. The 25 subjects with an ankle systolic blood pressure 75 mm Hg higher than the arm (who were presumed, therefore, to have medial arterial wall calcification) showed strikingly disturbed lipoprotein profiles and an extremely high prevalence of hypertension (60%), neuropathy (88%), overt nephropathy (88%), and proliferative retinopathy (92%).

In the final presentation of data, Dr. Hiatt confirmed that there was a weak relation between the resting and postexercise ABIs in a population-based study of both diabetic and nondiabetic subjects from the San Luis Valley Diabetes Study.\(^\text{14}\) Subjects diagnosed as having peripheral arterial disease by the resting ABI did not necessarily have an abnormal postexercise ABI (the converse was also true). Additional findings from this study concerned the development of criteria for an abnormal ABI. Normal ranges for resting ABI were determined from a healthy, nondiabetic control subset of the study population. This analysis revealed that women had lower ABIs than men and that the ABI derived from the dorsalis pedis artery was lower than the ABI from the posterior tibial artery. These findings raise the need for further investigation as to whether definitions of an abnormal ABI should be both gender- and vessel-specific.

**Recommendations**

Based on the data presented at the workshop, previous published data, and extensive discussion, the workshop participants developed the following recommendations for the detection and follow-up of LEAD in the primary care setting and for more detailed assessment after referral to a specialized vascular clinic. In addition, further comments are provided to help extend the recommendations made for use in the detection of LEAD in the primary care setting to use in epidemiological studies.

**Recommendations for the Detection and Follow-up of LEAD in Diabetic Subjects Being Followed in a Primary Care Setting**

(Items 1 through 4 can be addressed as part of the generally recommended annual physical examination for patients with diabetes).

1. **Claudication**

On an annual basis, diabetic patients should be asked about the presence of exercise-induced calf leg pain not present at rest. Patients with lifestyle-limiting exercise-induced calf pain should be referred for specialist vascular assessment. The assessment may be at a vascular laboratory or clinic or by a specialist, depending on local facilities and physician preference. Specialist vascular assessment will allow confirmation of LEAD, disease localization, and possible determination of the toe systolic blood pressure (TSBP). The TSBP will permit a more accurate assessment of vascular status independent of medial wall calcification. Measurement of an ABI or referral for specialist vascular assessment should also be considered for patients with any leg pain not clearly ascribed to a nonvascular cause. The ABI, which should be assessed according to the protocol described later in this article, will help determine whether this pain may be due to ischemia. Because ischemic leg pain has a negligible prevalence in diabetic children, this recommendation is limited to patients with insulin-dependent or non-insulin-dependent diabetes 18 years old or older.

2. **Signs of Critical Ischemia**

The presence of any potential signs of critical ischemia, ie, foot or limb ulceration, the presence of skin changes (nail or skin atrophy, or dependent rubor), or the detection of gangrene, should lead to a referral for specialist vascular assessment. Because of the potential for medial wall calcification to raise systolic ankle pressure above the normal range even in the presence of occlusive disease, the ABI alone may not be sufficient to detect vascular insufficiency. Further testing, eg, TSBP, may be indicated (see below).

3. **Palpation of Peripheral (Tibialis Posterior and Dorsalis Pedis) Pulses**

Palpation of leg pulses should be performed on an annual basis for all adult patients (18 years old and older) with diabetes. An absent or decreased tibialis posterior pulse is an indication for performing an ABI (see “Ankle Brachial Index” below) or referral to a vascular laboratory for evaluation if the ABI cannot be determined by the primary physician. It is further recommended that, whenever possible, the presence of decreased or absent pulses be confirmed by a second observer or repeat examination before referral.
Palpation of peripheral pulses has a limited but useful place in the detection of LEAD. Although repeatability and interobserver agreement are low, sensitivity and positive predictive value are moderate for the detection of LEAD; therefore a significant number of cases will be identified by detection of a reduction or absence of these pulses. Furthermore, the presence of these pulses in low-risk diabetic subjects helps to confirm the absence of significant disease. It should be noted that the dorsalis pedis pulse is sometimes congenitally absent.

4. Femoral Bruits

Auscultation for femoral bruises on an annual basis is recommended for all adult patients with diabetes. The detection of femoral bruises is an indication for performing an ABI (see "Ankle Brachial Index" below) or, if that is not possible, referral to a vascular laboratory. Although it is recognized that auscultation for femoral bruises has similar difficulties to those described for pulse palpation, it nonetheless has sufficient sensitivity to merit its performance on an annual basis.

5. Ankle Brachial Index

It is recommended that all physician offices providing routine care to adult diabetic patients should be able to measure ankle and brachial blood pressure to detect LEAD. The additional equipment needed is minimal: a hand-held ultrasound Doppler device at 5 to 10 MHz, costing $300 to $600. The same blood pressure cuffs used for the arm can, in most cases, be used for the ankle pressure (see Appendix A). The justification for this recommendation is the low sensitivity of clinical history and examination to detect LEAD and the high morbidity and mortality of patients with this condition. The objective is not only to optimize care for the developing ischemic limb, but also to identify a high-risk group of diabetic subjects for general cardiovascular disease in whom risk factor modification should be maximized.

ABI measurement is recommended for the following situations:
- Any diabetic patient newly detected to have decreased pulses, femoral bruises, or a foot ulcer.
- Any diabetic patient with leg pain of unknown etiology.
- All patients with insulin-dependent diabetes mellitus aged 35 years or older, or with 20 or more years' duration of diabetes, undergoing baseline examination.
- All patients with non-insulin-dependent diabetes mellitus aged 40 years or older undergoing baseline examination.

A detailed protocol for performing the ABI is in Appendix A. Some major points are that:
- The patient should be strictly supine for at least 5 minutes before testing.
- Arm as well as ankle pressures should be taken with the Doppler device.
- Ideally, both right and left arm pressures should be measured and the higher one used.
- Ideally, both dorsalis pedis and tibialis posterior pulses should be measured in each leg.
- The same sequence of recordings between patients and over time should be used.

The ABI should be calculated based on the brachial pressure closest in time to the specific ankle pressure being evaluated.
- The suggested sequence of measurement is as follows.
  Pressure 1: Right arm, left arm; take highest reading
  Pressure 2: Right dorsalis pedis
  Pressure 3: Right tibialis posterior
  Pressure 4: Arm with higher reading as determined for Pressure 1
  Pressure 5: Left dorsalis pedis
  Pressure 6: Left tibialis posterior
  Pressure 7: Arm with higher reading as determined for Pressure 1
- Calculate ABI ratios:
  1. Right dorsalis pedis: pressure 2
  2. Right tibialis posterior: pressure 3
  3. Left dorsalis pedis: pressure 4
  4. Left tibialis posterior: pressure 6

The ratios calculated this way relate the ankle and arm pressures taken closest together in time and are therefore more meaningful.

Recommended action to take after ABI testing:
- ABI < 0.50 in any vessel. Prompt referral for specialist vascular assessment is recommended because these patients almost certainly have severe peripheral vascular disease.
- ABI > 0.50 and < 0.90 in any vessel tested. The ABI should be repeated within 3 months as these patients are likely to have mild to moderate peripheral vascular disease. If repeat ABI is < 0.90, start intensive risk factor modification and annual ABI follow-up. If repeat ABI is ≥ 0.90, repeat ABI every 2 or 3 years.
- ABI ≥ 0.90. Repeat testing every 2 to 3 years as these patients are unlikely to have peripheral vascular disease.

Any incompressible ankle artery (systolic ankle pressure > 300 mm Hg) or ankle pressure ≥ 75 mm Hg above arm pressure. The measurement should be repeated within 3 months; if confirmed, refer these patients for specialist vascular assessment because they almost certainly have significant medial wall calcification, and measurement of ankle pressure to determine LEAD is therefore compromised. These patients are also at high risk for both macrovascular and microvascular complications and should be entered into an intensive risk-factor modification program.

It should be noted that repeatability of the ABI measure is moderately low (coefficients of variation between 10% to 15% have been reported). Thus, like arm blood pressure readings for hypertension or cholesterol measurements, it is important to confirm abnormal values before referral or intensive risk-factor intervention. Variability can be reduced by performing all blood pressures in duplicate and calculating their mean.

6. Postexercise Ankle Brachial Index

This measure is not recommended for use in the primary care setting.

7. Intensive Risk-Factor Modification

All patients with a confirmed ABI of < 0.90, and/or ankle systolic pressure > 300 mm Hg, and/or ankle blood pressure ≥ 75 mm Hg above arm pressure and/or exercise-induced calf pain not present at rest, should be
Summary of Recommendations for Detection, Management, and Follow-up of Lower Extremity Arterial Disease in Diabetic Patients

<table>
<thead>
<tr>
<th>Test</th>
<th>Who</th>
<th>Frequency</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claudication</td>
<td>All adults with diabetes</td>
<td>Annually</td>
<td>If present, do ABI annually. If ABI is &lt;0.90, start IRFM. If present and life-style-limiting, refer for SVA.</td>
</tr>
<tr>
<td>Signs of critical ischemia</td>
<td>All adults with diabetes</td>
<td>Annually</td>
<td>If present (ie, there are gangrene, ulcer, skin changes, or ischemic rest pain), refer for SVA and start IRFM.</td>
</tr>
<tr>
<td>Peripheral pulses/femoral bruits</td>
<td>All adults with diabetes</td>
<td>Annually</td>
<td>If abnormal, do ABI annually. If ABI is &lt;0.90, start IRFM.</td>
</tr>
<tr>
<td>ABI</td>
<td>IDDM:</td>
<td>Depends on baseline result</td>
<td></td>
</tr>
<tr>
<td></td>
<td>All patients 35 years old or older or for whom duration of diabetes is 20 or more years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NIDDM:</td>
<td></td>
<td>If ABI is &lt;0.50, refer for SVA and start IRFM.</td>
</tr>
<tr>
<td></td>
<td>All patients 40 years old or older</td>
<td></td>
<td>If ABI is &gt;0.50 and &lt;0.89, repeat within 3 months. If it is confirmed to be:</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;0.90, start IRFM and determine ABI annually.</td>
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<td></td>
<td></td>
<td></td>
<td>≥0.90, repeat every 2 to 3 years.</td>
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<td></td>
<td></td>
<td></td>
<td>If ABI is ≥0.90, repeat every 2 to 3 years.</td>
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<td></td>
<td>If ankle pressure is ≥75 mm Hg above arm pressure, repeat within 3 months.</td>
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<td></td>
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<td></td>
<td>If confirmed, refer for SVA and start IRFM.</td>
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<td></td>
<td></td>
<td></td>
<td>If not confirmed, repeat every 2 to 3 years.</td>
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<td></td>
<td></td>
<td></td>
<td>If ankle pressure is &gt;300 mm Hg, refer for SVA and start IRFM.</td>
</tr>
</tbody>
</table>

Adults are here defined as persons 18 years old and older. 
ABI, ankle brachial index; IRFM, intensive risk-factor modification; SVA, specialist vascular assessment (may be a vascular specialist or clinic or laboratory, depending on local facilities and physician preference); IDDM, insulin-dependent diabetes mellitus; NIDDM, non–insulin-dependent diabetes mellitus.

carefully screened for cardiovascular risk factors, including, if not already available, two fasting lipoprotein profiles (total cholesterol, high-density lipoprotein cholesterol, triglycerides, and calculated low-density lipoprotein cholesterol). In patients with diabetes, triglyceride concentration appears to have greater cardiovascular predictive power than in the general population and is also particularly related to LEAD.1,15-17 Therefore, careful attention should be paid to correction of an elevated triglyceride concentration (by means of good glyemic and weight control) in addition to that of a low high-density lipoprotein cholesterol level and a raised low-density lipoprotein cholesterol level. The National Cholesterol Education Program guidelines for the management of cholesterol in adults18 and the recommendations in the consensus statements of the American Diabetes Association “Role of Cardiovascular Risk Factors in Prevention and Treatment of Macrovascular Disease in Diabetes”19 and “The Detection and Management of Lipid Disorders in Diabetes”20 should be followed. It is recommended that patients with diabetes who have LEAD be treated as if they had coronary heart disease for these purposes. Recent reviews concerning lipid management in diabetes are also available.21,22 Blood pressure should also be carefully monitored and managed according to recommendations for people with diabetes.23 Cessation of smoking in this group is of paramount importance and all available approaches should be considered. Other interventions to reduce cardiovascular risk should also be carefully considered (weight control and exercise may be of specific benefit in patients with LEAD). Although no specific recommendation is being made concerning aspirin use, evidence from secondary prevention trials in nondiabetic subjects indicates that aspirin has a protective effect on subsequent cardiovascular mortality and morbidity.24 Recent data from the Early Treatment of Diabetic Retinopathy Study suggest that aspirin is not harmful and may protect against myocardial infarction in diabetic subjects.25 Although it is suggested that risk factor modification be intensified in patients with an ABI of <0.90, it should be remembered that all people with diabetes are at increased risk for cardiovascular disease, and close control of blood pressure and serum lipids and smoking cessation are generally encouraged.

8. Other Complications of Diabetes

LEAD and medial arterial wall calcification are often associated (especially in patients with insulin-dependent diabetes mellitus) with an increased prevalence of nephropathy, proliferative retinopathy, and neuropathy.13 Therefore, it is strongly recommended that, at a minimum, existing guidelines for detection of these complications be followed. Guidelines currently exist for neuropathy26,27 and retinopathy.28 Distal sensory polyneuropathy is particularly important to detect at an early stage so that appropriate protective care of the feet can be initiated. The detection and/or presentation of any neuropathic foot lesion with good perfusion (ABI of >0.90 in all vessels) should lead to a referral to a specialist foot care team.

9. Detection, Management, and Follow-up of LEAD in Diabetic Patients

For a summary of recommendations, see the table.

10. Specific Observations on the Use of Primary Care Recommendations in Epidemiological Studies

Claudication. The current Rose questionnaire,29 if applied strictly, misses a significant number of patients with LEAD. This can be partly overcome by including as positive any exercise-related leg pain not present at rest. The current Rose questionnaire also does not permit assessment of whether one or both legs are affected.

Pulses and bruits. It is strongly advised that the detection of reduced or absent pulses and the presence of femoral bruits be confirmed by a second trained observer. These findings should not be used alone as primary end points in epidemiological studies.
Abbreviation:

• Full adoption of all recommendations contained in this report, including those in Appendix A, is strongly
advised.

• All observers should be trained so that the coefficient of variation over multiple measures for both
normal and diseased vessels is less than 15%.

• Interobserver variation should be assessed and mini-
imized so that measurement of ABI in the same indi-
gual by all observers is within 15% of all other
observers' readings. Use of a double-headed stetho-
scope, in conjunction with the ultrasound device, and
strict adherence to the protocol is recommended, as is
the recording of all blood pressures in duplicate and
calculating the mean of the two pressures.

• Although postexercise ABI is not recommended in
the primary care setting, the validity of this modality
and its relation to resting ABI, risk factors, and com-
plications and its predictive power for future morbidity
and mortality need to be studied further. Consideration
should therefore be given to using this test with a
standard work load (eg, 5 minutes walking at 2 mph on
a 12% incline), with ABI being measured at 1, 3, and 5
minutes postexercise.

Noninvasive Vascular Diagnostic Laboratory

Referral Categories

When the physician finds one or more of the following
conditions, as discussed in the primary care recom-
mendations, referral to a vascular laboratory or clinic for
further study may occur. The testing subsequently to be
done will depend on patient presentation, clinical find-
ings, and the results of preliminary screening done in the
physician's office.

Intermittent Claudication. It is recognized that exer-
cise-induced leg pain is a common sequela of arterial
narrowing and occlusion at one or more levels of the
arterial blood supply to the leg. The extent to which
further testing needs to be done will depend on the
severity of the problem, particularly as it relates to daily
activity. In general terms, those patients whose exercise-
induced pain affects their life-style will deserve the most
complete evaluation. The most common site for exer-
cise-induced pain is the calf, but it can also develop in the
thigh, hip, or buttock when the disease is localized
above the inguinal ligament. Often the pain will start in
the calf and then progress to the thigh and/or buttock if
exercise is continued despite the onset of pain. It must
be remembered that severe claudication is most often
the result of multilevel arterial disease, which can be
best evaluated in the noninvasive laboratory.

Critical Ischemia. The clinical definition of critical
ischemia is a clinical presentation that, if not reversed,
is likely to result in an amputation either at the level of
the foot or below the knee. In some rare cases ampu-
tation may be required at the above-knee level. Because
therapy is so critical for limb preservation, it is essential
that patients with critical ischemia have a complete
noninvasive evaluation before arteriography (unless
life-threatening infection is present, in which case im-
mediate arteriography may be indicated). The catego-
ries of presentation that are relevant to this subset of
patients are as follows:

• Ischemic rest pain: In this setting, the pain will be in
the toes and forefoot. It will, during its early phases, be
relieved by dependency. If it does not improve with
development of collateral circulation, amputation will
be inevitable unless some form of intervention (surgical
or endovascular) is carried out.

• Ulceration: When a break in the skin occurs at any
location of the foot or lower leg, healing might not occur
unless some form of intervention is carried out. The
single exception may be for a patient who has an ulcer
over a pressure point or site of direct injury that is
secondary to neuropathy. However, it must be remem-
bered that ischemia and neuropathy may coexist making
patients in this subset candidates for amputation, unless
the areas of occlusion are either bypassed or eliminated
by transluminal angioplasty.

• Gangrene: Tissue death, when it involves one or
more toes or the forefoot, will require amputation that
may be limited to the involved areas if direct inter-
vention can bring more blood to the ischemic area.

• Skin Changes: Although not as definitive as the
preceding three categories, skin atrophy, nail changes,
and dependent rubor occur in some patients who may
require further evaluation. This is particularly true if the
ABI is found to be abnormal.

Abnormal ABI. In the absence of any of the above
conditions, a referral to a vascular laboratory is recom-
mended for patients whose ABI is confirmed to be
<0.50 in one or more vessels. This will permit confirma-
tion, localization of the lesion, and possible assess-
ment of toe systolic blood pressure index (TSPI) and
will provide a more accurate picture of vascular status
independent of medial arterial wall calcification.

The finding of incompressible arteries (ie, systolic
blood pressure >300 mm Hg) at the level of the ankle
makes it impossible to estimate the systolic pressure. In
some cases the arteries may be compressible but give
falsely high levels of recorded pressure. If the ankle
systolic pressure is ≥75 mm Hg higher than the arm
systolic pressure and/or the ABI is >1.30, medial arte-
rial wall calcification is virtually certain and measure-
ment of the TSPI in the vascular laboratory should be
performed.

Recommended Vascular Laboratory Studies

Studies done in the resting state. It is possible to
determine the severity of the occlusive disease by a
combination of measurement of the ABI and the TSPI.
It is recommended that both tests be done to provide
confirmation of the vascular status. There are various
cutoff levels that must be considered in conducting
these tests. These are as follows:

• ABI: If the ABI is <0.90, occlusive arterial disease
can be present. If a value of <0.80 is noted, it is highly
likely that vascular disease will be found. ABIs between
0.50 and 0.80 are likely to be found in patients with
single segment occlusions, while ABIs <0.50 are com-
monly found in patients with multileg disease.

• TSPI: When measurements are made at the level of
the toes, there are two cutoffs of clinical value. Firstly,
for screening purposes a TSPI of >0.60 is normal. The
variability in this measurement is ±17%. Secondly, the
absolute levels of systolic pressure are of great value in
estimating healing potential when an ulceration is
found. If the absolute pressure is ≤30 mm Hg, healing is
unlikely to occur unless some form of direct intervention is carried out.

- Alternative forms of study: The ABI is an overall indicator of obstructive disease in the legs, the aorta, or both. Thus, other supplemental modalities are desirable. Measurement of segmental systolic pressures permits, to some degree, the localization of sites of arterial occlusion in the limbs and may provide a more sensitive indicator of progression. Similarly, pulse volume recording taken at several levels of the limb is largely a qualitative testing procedure that provides data on the pattern of volume changes in response to pressure changes. The waveforms recorded will reflect underlying occlusive disease but are rarely specific as to exact sites of occlusion.

Another widely used method is velocimetry using continuous wave Doppler techniques. By using systems that permit an accurate display of the velocity patterns (fast fourier transform spectral analysis) it is possible to confirm the presence of arterial disease at or proximal to the recording sites. The procedure can be used at the femoral, popliteal, and tibial arteries at the ankle. Loss of the normal triphasic waveforms normally seen can be taken as certain evidence of arterial disease.

Because the ABI and TSPI provide quantitative indexes, they are to be considered the definitive diagnostic studies. The more qualitative tests can be added to provide additional information.

Exercise testing. Not all patients with exercise-induced leg pain will have arterial occlusive disease as the cause. It is well known that neuropathal disease and musculoskeletal disorders can also lead to leg pain and can be confused with true vascular intermittent claudication. When the etiology is uncertain, the cause can be elucidated by exercise testing.

The separation becomes possible because intermittent claudication secondary to arterial disease is always accompanied by a decrease in ankle systolic pressure after exercise. This is a stress test, but the levels of exercise required to make this distinction are minimal. Although several methods of exercise can be used to bring out the abnormality associated with arterial disease, it is recommended that a treadmill be used with a standard elevation and speed. A speed of 2 mph at a 12% elevation is most commonly used. This speed and elevation can be tolerated by nearly all patients but can be decreased if the user desires. Regardless of the speed and elevation, it is important that the patient walk to the point of pain and preferably to the point of being unable to continue or for a full 5 minutes. It has been found that periods of walking in excess of 5 minutes provides little further information.

The patient with true claudication will sustain a fall of >20% in the ankle systolic pressure with a recovery time that exceeds 3 minutes. It is also possible to express the postexercise results in terms of ABI. Either approach is acceptable as long as the vascular laboratory has experience with the testing procedure. At the recommended low work load, patients with normal limbs or those with pain secondary to nonvascular causes will not have a fall in ankle pressure as noted above.

Concern must be given to the patients with known coronary artery disease who have angina pectoris. There are no firm guidelines for this group of patients. However, adverse cardiac events at this workload are extremely rare. Some laboratories may wish to combine the testing procedure with electrocardiographic monitoring, but this is not absolutely necessary.

Ultrasound duplex scanning. The introduction of duplex scanning has added a new dimension to the field of vascular testing. Although the technology is evolving, it clearly will play an increasingly important role in vascular testing. Based on current evidence, the following recommendations are made:

1. There is no justification for its use as a routine screening procedure. It is not necessary in order to establish the presence or absence of arterial occlusive disease.

2. If information is desired as to the exact location of arterial disease, duplex scanning can provide this information. However, it cannot be used as an index of severity, which is best determined by the clinical presentation and the ABI and TSPI.

3. In some centers, duplex scanning is being done as the method of selecting the appropriate interventional therapy. If available, it can be so used, but this is not at present widely practiced, even though there are indications that this use will become more important in the future.

Tissue PO2. The likelihood of healing of ischemic skin lesions may be assessed by the measurement of tissue PO2. It is generally believed that values below 20 mm Hg indicate questionable capacity for healing and those below 10 mm Hg are not compatible with healing. Therefore, the need for additional medical or surgical referral will become apparent when this test indicates nonviability of injured tissue. The PO2 is also a sensitive indicator of improvement in blood flow due to either collateral flow development or surgical treatment. Another possible use of this measurement is determination of the level of amputation when this becomes necessary.

Arteriography. Though invasive, arteriography remains the definitive diagnostic procedure prior to any form of surgical intervention. However, it should not be used as a diagnostic procedure to establish the presence of arterial disease. There are several considerations relative to its use that must be kept in mind. These are as follows:

1. Patients with diabetes mellitus may also have renal disease, which places them at high risk for renal failure secondary to the use of contrast material. This risk must be taken into account whenever arteriography is contemplated. The volume of contrast material used must be limited as much as possible.

2. It is strongly recommended that arteriography be done prior to an amputation to assess the exact status of the arterial supply. Although it is recognized that there are patients with neuropathy and irreversible tissue damage who do not have arterial disease, confirmation of the status of the arterial supply is necessary, particularly when the ABI and TSPI indicate that arterial disease is present.

Vascular Laboratory Accreditation

Because the quality of vascular diagnostic laboratory studies is key to the evaluation process, it is strongly recommended that vascular laboratories participate in the voluntary accreditation process currently in place. The Intersocietal Commission for the Voluntary Ac-
creditation of Vascular Laboratories, which is sponsored by several societies, has established rigid criteria and procedures for certification. This will provide assurance to the user that procedures for optimal performance are followed. Further details can be obtained by writing to the Intersocietal Commission for Accreditation of Vascular Laboratories, 11200 Rockville Pike, Suite 205, Rockville, MD 20852-3139.

**Future Research Needs**

During the course of deliberations, a number of research needs were identified. These are specified below in no specific order of priority except the first. The recommendations that intensive risk-factor intervention be instigated in those with LEAD, as outlined above, are based on the strength of risk factor associations and extrapolation of results from clinical trials in the general population that have generally excluded diabetic subjects. The absence of clinical trial data (especially in terms of correction of disturbed lipoprotein profiles) in diabetes is most worrisome, and the National Institute of Diabetes and Digestive and Kidney Diseases, the National Heart, Lung, and Blood Institute, the American Heart Association, and the American Diabetes Association are strongly urged to mount appropriate research initiatives in this area.

**Recommendations for Research**

1. Clinical trial evidence of the benefit (eg, cardiovascular disease prevention, limb preservation) of risk factor modification for the prevention of macrovascular disease in diabetic patients, especially focusing on lipids and lipoproteins. To date, most prospective trials of cardiovascular disease prevention have excluded diabetic patients. Both primary and secondary prevention studies should be considered.

2. The Rose questionnaire needs to be revised for epidemiological use to minimize false-negatives and obtain data on laterality.

3. Further study is needed on the prognosis of arterial calcification and, in particular, its association with nephropathy. Could it be used as an early marker?

4. Further study is needed to determine whether there is a gender difference in ABI measures.

5. Further research is needed to evaluate why there is such a poor association between abnormal resting ABI (eg, <0.9) and abnormal postexercise ABI (eg, <0.8).

6. An evaluation of the efficacy and cost-effectiveness of establishing a foot clinic/foot-care team should be performed.

7. The interrelation of various noninvasive testing approaches and their relations to arteriographically defined LEAD needs to be formally evaluated. It is recommended that duplex scanning, Doppler flow velocity, magnetic resonance arteriography, and exercise and resting ABIs, claudication, palpation of pulses, and detection of femoral bruits all be studied in terms of their relations to each other and to the gold standard of arteriographically defined LEAD.

**Appendix A**

**Protocol for Measurement of the Ankle Brachial Index**

*Instrumentation.* The most practical device for the assessment of both ankle and arm systolic blood pressure is the continuous wave Doppler system. A hand-held device that has either a small speaker for the output or a stethoscope headset can be used to listen to the blood velocity patterns from the brachial, radial, dorsalis pedis, and posterior tibial arteries at the ankle.

Cuffs. The same cuffs used for measurement of arm blood pressure should be used at the ankle. Similar concerns with regard to the need for appropriate-size cuffs for obese arms apply also to the ankle, and an appropriate cuff the width of which approximates 40% of the limb in circumference should be used at both sites. In most cases a regular arm blood pressure cuff will be adequate.

*Method of measurement.* There are several aspects of pressure measurement that must be observed if the examiner is to obtain the best and most reproducible results. The recommendations are as follows:

1. The pressures should be measured in both arms; use the higher of the two.

2. It is preferable to have the patient rest, quiet and supine, for at least 5 minutes before the pressures are measured. This ensures that any changes in pressure that might have occurred due to previous walking have a chance to stabilize.

3. The Doppler transducer should be placed at an angle of 60° to the artery being tested so that the best velocity signals will be obtained. If the transducer is at right angles to the artery, the detected velocity (frequency shift) will be at a minimum and often difficult to hear, particularly if the velocities are reduced secondary to arterial disease proximal to the recording site. In addition, care must be taken to maximize the Doppler signal by moving the probe back and forth over the artery to obtain the loudest signal. Failure to do so may result in underestimation of the arterial pressure measurement.

4. To obtain the most reproducible and accurate measurements, the following rules must be followed:
   - The pressure must be taken at the point at which the Doppler signal first appears during deflation of the cuff (ie, pressure is never taken during cuff inflation).
   - The cuff should be inflated to at least 20 mm Hg above arm systolic pressure levels to ensure complete collapse of the dorsalis pedis and posterior tibial arteries.
   - The pressure that is recorded is taken at the point at which flow returns as detected by the Doppler system.
   - Cuff deflation must be slow (2 mm Hg/second) to accurately determine the point at which flow is restored.
   - It is mandatory that the Doppler system also be used to measure the arm systolic pressure. To determine the arm pressure, the examiner may use either the brachial artery distal to the cuff or the radial artery at the wrist.

When the arterial signals at the level of the ankle cannot be obliterated by cuff inflation (pressure is >300 mm Hg), this is conclusive evidence that medial calcification is present. Similarly, when the ankle pressure is >75 mm Hg above the arm pressure or the ABI is >1.3, partial incompressibility due to medial calcification is likely to be present, giving rise to falsely high ankle pressure.

**Appendix B**

**Protocol for Measurement of Toe Systolic Blood Pressure**

*Instrumentation.* A strain gauge or a photoplethysmograph can be used as a sensor. (The strain gauge is also practical for measurement of ankle blood pressure). The cuff used to measure toe blood pressure should be 2.4 cm wide by 10 cm long (encircling the first toe).

*Measurement.* To obtain useful and reproducible results, the following aspects must be observed:

1. It is preferable to have the patient rest, quiet and supine, for at least 5 minutes before the pressures are measured.

2. Room temperature should be comfortable (more than about 22°C) so the patient does not feel cold.
3. The skin temperature of the toes should be at least 25°C. If necessary, the feet should be warmed gently for 10 minutes in warm water (37 to 39°C). In case of a skin lesion a protective plastic bag can be drawn over the foot.

4. Before inflation of the miniature cuff the toe should be gently squeezed between the examiner’s fingers to empty the vessels of blood. This produces a more clean-cut curve. At very low pressures a stepwise deflation of the cuff will often facilitate reading of the tracings.

Appendix C

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References


Other Selected Readings


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