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Skin perfusion pressure measured by radioisotope washout for predicting wound healing in lower limb amputation for arterial occlusive disease

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Dekan

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Dean

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- III. Holstein, P., Nielsen, P. E. & Barras, J.-P. (1979). Blood flow cessation at external pressure in the skin of normal human limbs. Photoelectric recordings compared to isotope washout and to local intra-arterial blood pressure. *Microvasc. Res.* **17**, 71–79.
- IV. Holstein, P., Sager, P. & Lassen, N. A. (1979). Wound healing in below-knee amputations in relation to skin perfusion pressure. *Acta Orthop. Scand.* **50**, 49–58.
- V. Holstein, P., Dovey, H. & Lassen, N. A. (1979). Wound healing in above-knee amputations in relation to skin perfusion pressure. *Acta Orthop. Scand.* **50**, 59–66.
- VI. Holstein, P. & Lassen, N. A. (1980). Healing of ulcers on the feet correlated with distal blood pressure measurements in occlusive arterial disease. *Acta Orthop. Scand.* **51**, 995–1006.
- VII. Holstein, P., Nielsen, P. E., Lund, P., Gyntelberg, F. & Lønsmann Poulsen, H. (1980). Skin perfusion pressure on the legs measured as the external pressure required for skin reddening after blanching: a photoelectric technique compared to isotope washout. *Scand. J. clin. Lab. Invest.* **40**, 535–543.
- VIII. Holstein, P. (1982). Level-selection in leg amputation for arterial occlusive disease. A comparison of clinical evaluation and skin perfusion pressure. *Acta Orthop. Scand.* **53**, 821–831.
- IX. Holstein, P., Trap-Jensen, J., Bagger, H. & Larsen, B. (1983). Skin perfusion pressure measured by isotope washout in legs with arterial occlusive disease. Evaluation of different tracers, comparison to segmental systolic pressure, angiography and transcutaneous oxygen tension and variations during changes in systemic blood pressure. *Clinical Physiology* **3**, 313–324.
- X. Holstein, P. (1984). The distal blood pressure predicts healing of minor amputations on the feet. *Acta Orthop. Scand.* **55**, 227–233.

Preface

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Chapter I: Introduction, aim

Introduction

According to Hansson (1964) dysvascular amputees constituted only 2 per cent of all patients fitted with prostheses in Gothenburg in 1926–1930. The corresponding figures for 1951–1955 were 57 per cent. To-day about 90 per cent of leg amputations are performed in dysvascular patients (Hierton & James 1973, Ebskov 1983). Hansson (1964) also reported an increase in leg amputation incidence from 34 to 93 per 100 000 inhabitants over 60 years of age from 1954 to 1962, and similar increasing figures have been published from other regions of Sweden by Hierton & James (1973) and by Liedberg (1983). In recent Danish studies, however, the incidence has been constant over periods of 10 and 8 years respectively (Christensen 1976, Mandrup-Poulsen & Steen Jensen 1982), and figures from the Danish Amputation Register show that the number of amputations a year during 1978 through 1981 has been constant at about 2000 in dysvascular patients (Ebskov 1983 and personal communication).

During the past 25 years there has been an increasing awareness that amputation for arterial occlusive disease (AOD), when inevitable, must be made as distally as possible to preserve function, and the main emphasis has been on preserving the knee (Bichel 1943, Schumacker & Moore 1951, Silbert & Haimovici 1954, Kelly & Janes 1957, Lim et al 1967, Murdoch 1967, Sarmiento et al. 1970, Burgess et al. 1971, Persson & Sundén 1971). It was pointed out by Pedersen, La Mont & Ramsey (1964) that arteriosclerosis was previously thought to be a generalized, relentlessly progressive disease and that once gangrene appeared in the toes, progressive gangrene would be imminent and a high above-knee (AK) amputation indicated. To-day it has been substantially evidenced that once a below-knee (BK) amputation has healed an ipsilateral re-amputation is rarely needed (Romano & Burgess 1971, Persson 1974, Ebskov & Josephsen 1980).

BK amputees can be rehabilitated as regards walking with a prosthesis in a larger number than AK amputees (Warren & Kihn 1968, Couch et al. 1977). In a review of the literature Warren & Record (1967) reported that between 50 and 92 per cent of healed BK amputees successfully wear a prosthesis, while only between 33 and 71 per cent of healed AK amputees reach this result. This might be due in part to the fact that in most series BK amputees are younger than AK amputees. But it has been demonstrated objectively that walking with an AK prosthesis is highly energy consuming (James & Nordgren 1973), i.e. more energy consuming than walking with a BK prosthesis (Waters et al. 1976). The gait velocity and the stride length also increase the more distal the level of the amputation. Moreover, even chairbound or bedridden patients are much better off when the knee joint is preserved or when a through-knee (TK) amputation is made than after an AK amputation (Persson 1974, Hirsch et al. 1975). The sitting patient achieves better balance with a longer stump, and for the patient confined to bed it will be easier to shift his position. To these facts we can add the importance of the better cosmetic result due to the lesser mutilation of a BK amputee.

Owing to the interest in preserving the knee the surgical technique has been improved. An atraumatic technique has repeatedly been emphasized (Lim et al. 1967, Burgess et al. 1971, Browse 1973, Fleurant & Alexander 1980), and osteomyoplasty (Ertl 1949) and myoplasty (Dederich 1967, Burgess & Romano 1968, Weiss 1969) have been introduced. Burgess (1968, 1971) popularized the technique of using a long posterior flap as suggested by Bichel (1943) and Ghormley (1946). Persson (1971, 1974) has renewed interest in using a sagittal incision and two side flaps as suggested by Robb, Jacobsen & Jordan (1965) and by Tracey (1966). The long posterior flap technique and the sagittal technique have proved equally suitable in a controlled trial (Termansen 1977). These techniques probably yield a better sta-

bilization of the muscles than the classical "fish-mouth" technique, and stabilization of the muscles facilitates vascularization of the stump (Hansen-Leth 1982). But there are no controlled trials to demonstrate the superiority of the long posterior flap or the sagittal incision to the classical fish-mouth technique. Also rigid postoperative plaster dressing (Berlemont 1961, Murdoch 1967, Weiss 1969, Vitali et al. 1969, Burgess et al. 1971) has been introduced. Mooney et al. (1971), in a controlled trial, demonstrated that this principle facilitates healing.

The importance of saving the knee has also stimulated interest in new methods for determining objectively the level of amputation. Preliminary studies on modern means of determining the arterial supply prior to amputation appeared about 10 years ago. The present author reported, in September 1972 (Holstein 1973), that skin blood pressure (skin perfusion pressure) correlated with healing after amputation, using an isotope washout technique designed by Nilsén et al. (1967) and advocated by Sejrnsen (1971). In November 1972 Kostuik (Kostuik et al. 1976) reported a correlation between healing of amputations and skin blood

flow, measured by ^{133}Xe -washout after epicutaneous labelling, extensively studied by Sejrnsen (1968). In June 1973 Moore (Moore 1973, 1974) published similar findings when using intracutaneously injected ^{133}Xe in saline as suggested by Bohr (1967) who was in fact the first to comment on a case of amputation in terms of isotope-washout technique. Since then, several papers have appeared on objective methods of level determination as recently reviewed by Burgess & Matsen (1981). These techniques will be discussed in chapter 5, which also reviews earlier methods.

Aim

The aim of the present study was to investigate the method of measuring the skin perfusion pressure (SPP), primarily by the isotope washout technique, and the relationship between the SPP and the healing of amputation wounds in dysvascular legs. The study also includes investigations on SPP as measured by a photoelectric technique and various distal blood pressure parameters in relation to healing of minor amputations and ulcers in dysvascular feet.

Chapter 2: Description of isotope washout technique for measurement of skin perfusion pressure (SPP)

Principle

When the washout from an intracutaneous depot of the freely diffusible radioactive isotope 4- ^{131}I -iodo-antipyrine (^{131}I -a.p.) mixed with histamine is recorded semilogarithmically, the resulting curve consists of three phases. During the first few minutes after the injection the washout is slow. The second, faster component is almost monoexponential and lasts until about 80–90% of the isotope has been washed out. In the third phase, the washout gradually decreases towards zero. The second component is used for pressure measurements. External pressure on the labelled skin area is applied by a cuff and increased stepwise until the washout stops (Fig. 1). It is assumed that this reflects cessation of effective blood flow in the labelled skin, and that the blood flow cessation external pressure (FCEP) is a measure of the skin perfusion pressure (SPP) (Holstein et al. I) (see below: Interpretation of method, p. 11).

Technique

^{131}I -a.p. dissolved in sterile water and histamine diphosphate (0.1% w/v in sterile isotonic saline) were drawn into the same syringe and mixed. A total of 0.1 ml of this solution, containing 10–30 μCi ^{131}I -a.p. and 50 μg histamine diphosphate, was injected intradermally with a fine needle (outer diameter 0.4 mm), so that a small papule was raised. Droplets of the solution arising from backflow along the needle track were removed with cotton wool. In order that additional back-flow should not contaminate the counterpressure device, a piece of Mylar membrane, 20 μm thick, was taped over the depot.

The gamma emission was measured by a NaI(Tl) scintillation detector (2×2") with a heavy lead collimator. The detector was placed vertically 10–15 cm directly above the depot to

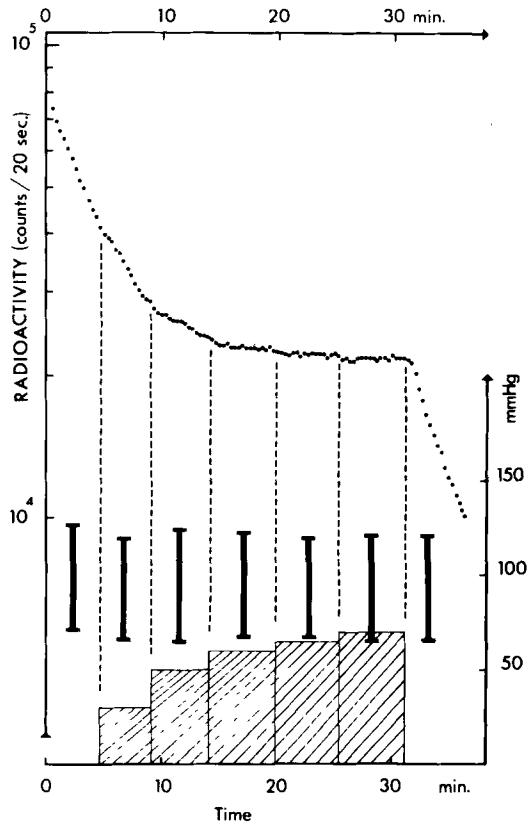


Figure 1. Recording of skin perfusion pressure (SPP) in a 21-year-old man on the calf with ^{131}I -antipyrine. The washout stops at 70 mmHg of external pressure (SPP = 68 mmHg). Auscultatory arm blood pressure 125/70 mmHg (vertical bars). The hatched bars indicate the external pressure. (From Holstein et al. I)

see a skin area larger than the radioactive field. The pulses were transmitted to a gamma spectrometer set to record the 0.364 MeV peak of ^{131}I . The initial counting rate was about 1000–5000 cps. The counting rate at flow cessation pressure was about 400–2000 cps. The recording was made semilogarithmically on a penwriter, paper speed 3 cm/min, one decade covering 15–20 cm. The standard technique

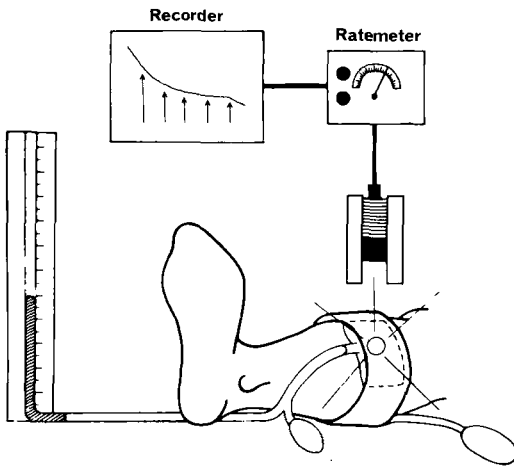


Figure 2. Measurement of the skin perfusion pressure (SPP) on the calf. The washout from an intra-dermal depot of ^{131}I -antipyrine mixed with histamine is recorded with a scintillation detector coupled to a ratemeter, the output from which is registered on a pen writer. External counterpressure to the labelled skin is applied with an ordinary blood pressure cuff. A slack air-filled plastic cushion is interposed between the skin and the cuff, and the pressure applied directly to the depot is measured by a mercury manometer connected to this cushion. (From Lassen & Holstein 1974)

implied evaluation of the tracing on the pen-writer by eye. The tracing was followed after the injection until the washout rate had been approximately monoexponential for about 3–5 min. The external pressure was then raised stepwise by a cuff (see below) which gave a stepwise decrease in washout rate. The first pressure increments were of 20–40 mm Hg and the corresponding curve segments were observed for about 3 min. The final pressure increments were of 5 mm Hg, and here the segments of the tracing were observed for approximately 5 min at each external pressure level. Accordingly, the FCEP was estimated as a pressure of 3 mm Hg above the last pressure where a minimal washout could still be discerned. After washout cessation, the external pressure was released to zero in order to ensure that the initial washout rate was re-established. When measuring low pressures the first pressure increments were adjusted according to the initial washout rate.

The application and measurement of the external counterpressure was standardized in

the following way (fig. 2): The labelled skin was covered by an air-filled slack cushion of 12×12 cm (inflatable part 11×11 cm) made of 0.2 mm thick polyvinyl-chloride (PVC). In the middle of one of its edges the cushion had a tubular outlet connected to a mercury manometer by which the external pressure on the skin was measured. When filled with approximately 200 ml of air, this cushion moulded smoothly to the labelled area when compressed by a 12 cm wide cuff encircling the limb (see page 15).

Experimental conditions

To standardize the technique 4 different sites of measurement were chosen: 1) on the anterolateral side of the thigh 10 cm proximal to the upper margin of the patella, 2) on the anterolateral side of the calf 10 cm distal to the knee-joint, just superficial to the proximal attachment of the anterior tibial muscle, 3) on the anterolateral side of the lower leg 10 cm proximal to the ankle joint, and 4) on the dorsal side of the foot midway between the ankle joint and the bases of the digits. The measurements were performed with the subjects in the supine position. Thus, the three proximal areas were investigated at the same level, i.e. at about heart level.

The foot was supported so that the point of measurement here was 10 cm above heart level. Sand bags were used to immobilize the legs. The auscultatory arm blood pressure was measured repeatedly by a 12×26 cm cuff around the left arm. The diastolic blood pressure was taken at the cessation of the Korotkoff sounds, and the mean blood pressure was calculated as the diastolic pressure plus one-third of the pulse pressure.

Before the measurements, each examinee received 0.5 g potassium iodide in solution by mouth to block the thyroid uptake of iodine. They were in a condition of thermal neutrality, experiencing neither heat nor cold. The room temperature was $23 \pm 3^\circ\text{C}$. All methodological studies, however, were done at $25 \pm 1^\circ\text{C}$. The skin temperatures at the sites of measurement were $28\text{--}34^\circ\text{C}$.

Comments on technique

The stepwise inflation of the cuff may result in an artifact on the curve, which could influence the slope for about half a minute. This artifact should be excluded when evaluating the slope. Involuntary movements in the patients may cause similar artifacts, and in these cases the tracing must be observed for a prolonged period. Histamine causes local vasodilation, and thus a high washout rate, which facilitates the evaluation of the curves. In fact, the technique does not work without histamine. Sejr-sen (1967) used 20 μg histamine (as base) per injection, but this dose was increased due to occasional failure of inducing visible skin reddening. 50 μg histamine diphosphate always causes a bright skin reaction in normal subjects, and larger doses are likely to cause unpleasant itching.

Interpretation of method

The FCEP is considered a measure of the skin perfusion pressure (SPP). This will be explained in detail.

The blood flow, as evidenced by the isotope washout, pertains to the exchange vessels, i.e.

to the microcirculation. The lowest intravascular pressure, viz. where the microcirculation is most easily collapsed by external pressure, is at the venous end of the capillaries. As measured directly by puncture, it is in the range of 4–25 mm Hg (Carrier & Rehberg 1923, Landis 1930, Wiederhielm et al. 1964, Intaglietta, Pawula and Thompkins 1970). The blood flow is, however, maintained at external pressures which far exceed these low pressures. Histamine raises the pressure in the capillaries (Landis 1930), but not to the level of the systemic arterial pressure, to which the FCEP corresponds (see below, normal material). Thus, the application of external pressure changes the local haemodynamic situation.

With increasing external pressure, and thus increasing tissue pressure, the local venous pressure – and the pressure in the microcirculation – rises to overcome the external pressure. When the blood flow stops, the perfusion pressure of the tissues reaches zero, and this means that the venous pressure now equals the arterial pressure. Therefore, the FCEP is a measure of the pressure head in the main feeding artery under compression, i.e. an *indirectly measured wedge pressure in this artery*. Hence, if the pressure in the local veins is close to zero when no compression is applied, the FCEP is a measure of the local perfusion pressure.

Chapter 3: Methodological investigations on SPP by isotope washout technique

Washout cessation as a measure of blood flow cessation

The basic assumption of the method is that cessation of washout of isotopes represents complete blood flow cessation. However, the possibility exists of underestimating the flow cessation external pressure, e.g. because of difficulties in recording a washout rate close to zero or because the washout stops even though a minimal flow persists, i.e. if major fixation of the isotopes in the tissues injected and/or re-fixation by diffusion across the venous walls has taken place. For these reasons the microcirculation of ^{133}Xe labelled skin was studied by capillaroscopy (Bolund & Holstein II). In 12 rat skin flaps the flow cessation external pressure as determined by isotope washout was 46.3 mm Hg, and as determined by vital microscopy it was 45.1 mm Hg (SD_{Diff} 2.7 mm Hg).

Discussion: Earlier investigators (Lassen et al. 1972) have employed the washout of isotope for measuring systolic blood pressure in humans. The tracer solution ^{133}Xe mixed with histamine, was injected distally to a miniature blood pressure cuff placed on the big toe. The flow cessation pressure in the cuff was practically equal to the systolic pressure as measured by a mercury in silastic strain gauge. During measurement of systolic blood pressure, venous stasis is, however, massive distal to the cuff. The study thus demonstrates that when the vascular bed is congested the washout of ^{133}Xe is as sensitive in detecting blood flow distal to the occluding cuff as the strain gauge technique, viz. yielding an estimate of the systolic blood pressure.

When measuring the FCEP the microvascular situation is entirely different. The vessels are progressively emptied of blood, as clearly seen by the vital microscopy. No venous distention takes place. The experiments thus demonstrated that even in such conditions a

minimal blood flow can be detected by the washout of ^{133}Xe , as the flow cessation is rather precisely determined.

Accuracy in reading the curves

The estimation of FCEP is based upon visual evaluation of the tracing. However, it may be difficult to determine when the tracing is horizontal. Therefore, a numerical analysis was carried out using the recorded digital counts (Holstein et al. I).

By means of the recorded digital counts the slopes were calculated for the washout segments considered as FCEP and the slopes of the segments representing FCEP minus 5 mm Hg. Moreover, in order to obtain a zero reference point the slopes were calculated for segments obtained by raising the external pressure another 20 mm Hg after FCEP, i.e. a situation with absolute flow stop in the microcirculation.

This showed that in 17 out of 100 cases the FCEP was overestimated by one external pressure step, i.e. 5 mm Hg, and underestimated by one pressure step in another 5 cases, meaning that the standard deviation in estimating the end point of the tracing was approximately 2.5 mm Hg.

Discussion: The inherent difficulty of the present method consists in defining the end point of the tracing, i.e. estimating when the curve is horizontal. The digital analysis showed, however, that the reading of the curves was satisfactory.

The digital analysis of the isotope washout also demonstrated that the slopes at the external pressure, estimated as the FCEP, were in fact slightly negative. This small washout may be due to a very small intermittent blood flow caused by the periodical, and perhaps the pul-

satile, variations in the systemic blood pressure. However, even at FCEP + 20 mm Hg, where such a mechanism seems very unlikely, a minimal decrease in radioactivity was found (median slope value: -0.044 per cent/min.). The physical decay accounts for a slope of $-0.0026\%/min.$ and cannot explain these findings, which are most probably caused by shrinkage of the tissues, labelled tissue fluid being squeezed away. Diffusion of the tracer into deeper layers may also occur. The phenomenon of minimal escape of isotopes, even at FCEP + 20 mm Hg, was also found in rat skin flaps measured with ^{133}Xe (Bolund & Holstein II) and in ^{99m}Tc -pertechnetate (^{99m}Tc) investigations (Holstein et al. IX). In the ^{99m}Tc curves, however, it could be explained by the physical decay. The residual decrease in the count rate was invisible in the tracings obtained with ^{131}I , ^{131}I -a.p. and with ^{133}Xe , but it could be discerned in the ^{99m}Tc tracings (fig. 3). If this phenomenon is a problem in reading the curves, the external pressure should just be increased by another step or two. The FCEP is then the minimal external pressure sufficient to cause a minimal decrease in count rate, which is not affected by increasing counterpressure.

Evaluation of different tracers

In an initial investigation using intra-dermal injection of ^{133}Xe mixed with histamine, occasional absurdly low values of FCEP were encountered. The washout in these tracings was not reestablished after relief of the external pressure, indicating that the tracer was trapped in the subcutaneous fat. For this reason, ^{133}Xe was replaced with ^{131}I -a.p. for measurements in humans. This isotope is equally soluble in water and fat, and after this modification the method worked satisfactorily. However, ^{131}I -a.p. splits off labelled iodide during storage (Munck & Andersen 1967, Kövamees 1968). Therefore, ^{131}I -a.p. as purified by chromatography was compared with free ^{131}I (as Na^{131}I) and moreover with ^{99m}Tc (Holstein et al. IX).

The shapes of the washout curves were almost identical for the three different tracers (fig. 3). There was no difference between the SPP values obtained with ^{131}I -a.p. and with Na^{131}I . When using ^{99m}Tc the values were on the average about 3 mm Hg higher than the values obtained by ^{131}I and by ^{131}I -a.p. ($P < 0.02$).

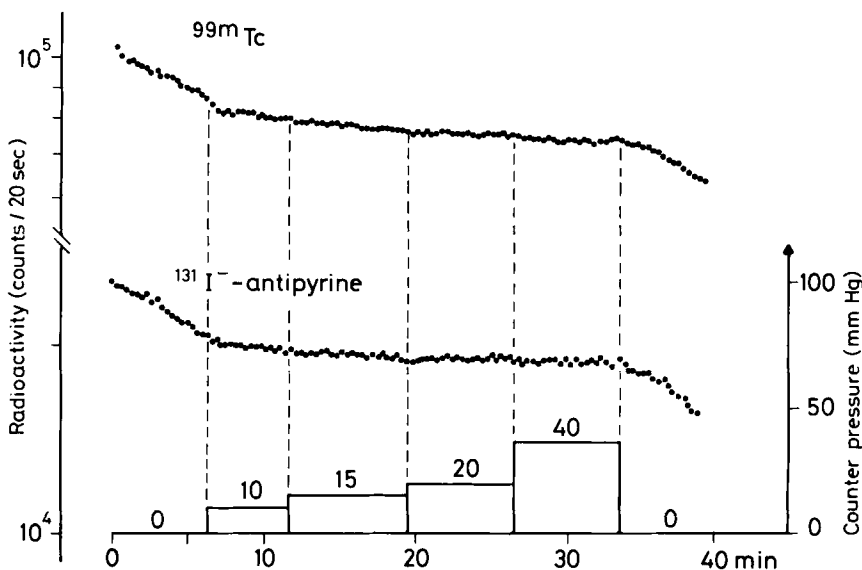


Figure 3. Simultaneous recording of skin perfusion pressure (SPP) with ^{131}I -antipyrine and ^{99m}Tc -pertechnetate. The washout ceases at 20 mmHg (SPP = 18 mmHg). A minimal decrease in count rate is seen in the ^{99m}Tc curve at 20 mmHg, but this is unaltered by the application of 40 mmHg of external pressure. This minimal decrease in the ^{99m}Tc count rate represents the physical decay of this short-lived isotope.

The skin blood flow measured with histamine-augmented isotope washout was almost equal for the three tracers.

Discussion: Estimation of FCEP by isotope washout was originally described by Nilsén et al. (1967) who used ^{133}Xe and decreasing external pressure in muscles. The method was advocated by Sejrsen (1971) for measuring perfusion pressure in the skin, and the present author modified the technique by using increasing external pressure and ^{131}I -a.p. as the tracer. Since equal values were found when comparing ^{131}I -a.p. with ^{131}I , the split-off phenomenon cannot influence the SPP values. The slightly higher values as estimated with $^{99\text{m}}\text{Tc}$ are probably a result of the physical decay barely visible on the curves. This phenomenon might perhaps be expected to influence the critical values of healing after amputations. But healing in 82 BK amputations done after SPP determinations with ^{131}I -a.p. did not differ significantly from healing in 67 BK amputations done after SPP determination with $^{99\text{m}}\text{Tc}$ (Holstein et al. 1979). Consequently, the favourable physical properties of $^{99\text{m}}\text{Tc}$ make this isotope the best choice in clinical routine.

Application and measurement of external counterpressure

Measurements of the SPP by using an ordinary blood pressure cuff showed that with decreasing cuff width the SPP values increased (Holstein et al. I). After interposition of a slack, airfilled 12 by 12 cm plastic cushion between skin and cuff the SPP values became independent of the cuff size. The values obtained on the calf with this cushion were between values as measured with a 16 cm and with a 12 cm wide cuff, viz. appropriate cuff sizes for this leg segment.

Discussion: Ordinary blood pressure cuffs invariably wrinkle on the inner surface when inflated. This may cause uneven external pressure to the small isotope depot, which occasionally may escape along a wrinkle. Measurement with an ordinary blood pressure cuff

also implies the risk of measuring erroneously low values, i.e. if the blood pressure cuff is inadvertently tightened too much. These problems were eliminated by interposing the cushion, which moreover measured the external pressure by the attached manometer. The SPP values obtained with this device were equal to SPP values obtained with cuffs appropriate according to the 20 per cent rule applying to cuff widths for systolic blood pressure measurements (Kirkendall et al. 1967)-

Normal values and correlation to intra-arterial blood pressure

In a series of 20 normal subjects evaluated by ^{131}I -a.p. (Holstein et al. I) the average SPP lay between the diastolic and the mean blood pressure on the thigh, calf and ankle. On the foot the average values were 9 mm Hg lower, which could be ascribed to the difference in hydrostatic pressure. The results were confirmed in a later series of 13 normal legs measured with ^{131}I on the ankle (Holstein, Nielsen & Baras III). Comparison to the intra-arterial blood pressure measured with micro-cannulas in the posterior tibial artery showed the average SPP to lie 9.8 mm Hg above the diastolic blood pressure and 10.9 mm Hg below the mean blood pressure. Similar results were found, moreover, in 5 normal subjects, where the SPP on the calf was compared to the intra-arterial femoral blood-pressure (Holstein et al. VII).

Discussion: Blood flow cessation at external pressure has been measured in the brain of baboons (Symon et al. 1973). During cisternal infusion the cerebral blood flow ceased at intracranial pressures of 0–40 mm Hg below the systemic mean blood pressure (no values for diastolic pressure were given). Dahn, Lassen & Westling (1967) induced cessation of the washout of a ^{133}Xe – histamine depot in the anterior tibial muscle in normal recumbent persons using a 17 cm wide plethysmograph. Flow cessation occurred at the level of the intra-arterial diastolic blood pressure.

Photoelectric recording of skin reddening after skin blanching by a technique very similar

to the isotope washout technique has revealed values in between the diastolic and the mean systemic blood pressure on the legs as well as on the upper arms (Nielsen, Lønsmann Poulsen & Gyntelberg 1973, Gyntelberg, Nielsen & Lønsmann Poulsen 1974, Holstein, Nielsen & Barras III, Holstein et al. VII). By a simple technique with inspection by eye of a histamine flared skin area through a transparent blood pressure cuff, Chavatzas & Jamieson (1974) observed that "skin blood pressure" values of normal legs ranged from 60–105 mm Hg (systemic blood pressure values were not stated).

Thus the results of the above-mentioned studies are consistent with the SPP values as found with the isotope washout technique.

Segmental SPP compared with segmental systolic blood pressure

Segmental SPP measured on the 4 different, standardized skin areas were compared with segmental systolic pressures measured with a strain gauge plethysmograph (Holstein et al. IX). Thirty-nine legs in 59 patients with AOD of different severity were investigated. Eleven patients (16 legs) had diabetes mellitus. A statistically significant correlation was found between the two different segmental blood pressure parameters. As could be expected, the systolic blood pressure was on the average significantly higher than the SPP values.

The SPP on the forefoot was also significantly correlated to the systolic blood pressure on the ankle, but the scatter was great, indicating that the systolic ankle blood pressure is not suitable as a measure of forefoot perfusion. In diabetic legs the systolic blood pressures were higher as compared to non-diabetic legs, but only at the ankle and on the calf.

Discussion: Segmental systolic blood pressures have been recommended for determining the amputation level as will be discussed in chapter 5. Although systolic ankle blood pressure has gained widespread acceptance in the diagnosis and in the monitoring of patients with AOD, it is a drawback that falsely high values may be encountered in diabetic pa-

tients, as noticed by several investigators (e.g. Nielsen & Munkgaard Rasmussen 1973, Emanuele, Buchanan & Abaira 1981, Burgess & Matsen 1981). This phenomenon is caused by medial sclerosis which prevents proper transmission of the cuff pressure. Rigid arteries do not seem to be a problem in measuring the systolic digital pressures, which have proved suitable especially in evaluating the healing prognosis in ulcers on the feet and in minor amputations on the feet (Holstein & Lassen VI, Holstein X).

The relation between segmental systolic blood pressure and the SPP is consistent with the findings in a series published by Støckel & Brøchner-Mortensen (1981). Segmental systolic pressures in amputation level determination will be discussed in chapters 5 and 7.

SPP compared with transcutaneously measured oxygen tension

Forty-seven measurements of the SPP and of the transcutaneously measured oxygen tension ($tc\ pO_2$) were made in 43 patients with AOD of the legs (Holstein et al. IX). The results of these two methods were significantly correlated, but the scatter was great. Thus, $tc\ pO_2$ of 0–45 mm Hg was found at SPP of 20 to 30 mm Hg.

Discussion: According to Wyss et al. (1981) $tc\ pO_2$ decreased to zero when the arterio-venous pressure difference dropped to 10–30 mm Hg. Tønnesen (1978) found $tc\ pO_2$ values of zero in feet with rest pain when the systolic digital blood pressure was in the range 10 to 30 mm Hg. In spite of the scatter in the present author's investigation, the above findings were confirmed, since zero values of $tc\ pO_2$ occurred at SPP of 20–30 mm Hg. $tc\ pO_2$ in amputation level determination will be discussed in chapter 5.

SPP compared with angiography

The SPP and the systolic blood pressure on the ankle were compared with angiograms in 35 legs (Holstein et al. IX). The SPP was consis-

tently decreased only in legs with occlusion of the main arterial pathway at two or more levels distally to the ankle. In legs with a single stenosis or occlusion the SPP failed to reveal the arterial narrowing in 7 out of 17 legs, whereas the systolic ankle blood pressures were decreased in 16 out of the 17 legs. Thus, the SPP is inapplicable in the diagnosis of occlusive arterial disease.

Discussion: The above findings are not surprising. Slight arterial narrowing decreases the systolic blood pressure, but has little influence upon the mean pressure. When the stenosis is severe the mean blood pressure is also decreased (May, DeWeese & Rob 1963, Young, Cholvin & Roth 1975). For this reason, the SPP should not be used in the diagnosis of AOD.

Reproducibility

The reproducibility was calculated as the SD_{Diff} of SPP determinations on two different days. Twenty double determinations made at each of the four standard levels demonstrated the best reproducibility on the thigh: SD_{Diff} : 5.9 mm Hg. The highest SD_{Diff} was found on the foot: 7.7 mm Hg. When the SPP values were divided into different pressure intervals, the best reproducibility was found at low pressures (SPP 0–30 mm Hg: SD_{Diff} 5.2 mm Hg). (Holstein et al. I).

Discussion: With the photoelectric technique of measuring the SPP on the calf the SD_{Diff} was 7.6 mm Hg (Holstein et al. VII). This is consistent with an SD_{Diff} of 6.6 mm Hg reported in another study with photoelectric technique (Stöckel & Brøchner-Mortensen 1981) – and consistent with the SD_{Diff} findings for the SPP measured with isotope washout technique. For systolic blood pressures on the thigh and ankle Carter (1968) found an SD_{Diff} of 7 mm Hg. Nielsen, Bell & Lassen (1973) found an SD_{Diff} of 8 mm Hg for digital systolic pressures. Paaske & Tønnesen (1980) observed that low pressures were remarkably constant: the SD_{Diff} of the toe blood pressure index was 0.06, i.e. about 8 mm Hg and that of the ankle pressure index 0.065, i.e. about 8 to 9 mm Hg. Thus, statistically sig-

nificant changes (2 SD = 95 per cent) of low pressures are in the range 10 to 15 mm Hg.

SPP during variations in systemic blood pressure

To be able to compare SPP values measured over a period of time in the same patient it is necessary to have guidelines to correct for changes in systemic blood pressure. In 5 normal legs (5 subjects) and in 12 legs in 7 patients with AOD distal to the inguinal ligament the SPP on the calf or on the foot was measured repeatedly during induced variation in the systemic blood pressure and during continuous recording of the intra-arterial blood pressure. Moreover, in the legs with AOD the systolic blood pressure on the ankles and on the toes was measured by the strain gauge technique (Holstein et al. I, Holstein et al. IX). In the normal legs the SPP varied *parallel* with the systemic mean blood pressure and in the legs with AOD it varied in *proportion* to the systemic mean blood pressure. The ankle and toe blood pressures varied on an average in proportion to the systemic systolic blood pressure (legs with AOD). There were considerable individual deviations from this average proportional rule, but the investigation suggests that for groups of patients corrections of blood pressures distal to arterial occlusions can be made *in proportion* to variations in the systemic blood pressure.

Discussion: Ehrenfeld et al. (1970), Fourcade et al. (1970) and Boysen, Engell & Henriksen (1972) investigated the stump pressure during carotid clamping for endarterectomy of the carotid artery during induced variations in the systemic blood pressure. The stump pressure, i.e. the *perfusion pressure* in the ipsilateral hemisphere varied in proportion to the systemic mean blood pressure, but only on an average basis with considerable individual deviations. Carter (1968) found a better reproducibility when using the index systolic *ankle* blood pressure divided by systolic brachial blood pressure instead of the systolic ankle blood pressure itself. This suggests that the systolic ankle blood pressure varies in propor-

tion to the systolic brachial blood pressure. Noer, Tønnesen & Sager (1978) were able to predict the systolic ankle blood pressure increment after segmental arterial reconstruction by assuming this proportional relationship. Concerning the systolic *digital* blood pressure Gundersen (1972) found that this parameter varied approximately parallel with the systemic systolic blood pressure; in his 5 patients, however, the digital blood pressures were only slightly decreased. Noer, Tønnesen & Sager (1978) found that digital pressures increased by an average of 12 mm Hg less than the ankle blood pressure after arterial reconstruction, but the individual data varied considerably. The above studies are in good agreement with the results in the present series, i.e. a proportional relation seems to exist. It is not surprising that the average rule does not always pertain to the individual case, since the haemodynamic effect of an arterial narrowing depends on several factors, such as the characteristics of the stenosis, the flow velocity, the peripheral resistance, the pulsatility, the turbulence and the viscosity (Young & Tsai 1973). Moreover, the present study concerns *induced acute* variations in the systemic blood pressure, and the possibility exists that such variations influence the blood pressures distal to arterial narrowings in another way than spontaneous variations.

General discussion on the SPP by isotope washout technique

The flow cessation external counterpressure measured in the skin in human legs is in the same order of magnitude as in other organs, i.e. the brain (Symon et al. 1973), the skin on the back (Larsen, Holstein & Lassen 1979), leg muscles (Dahn, Lassen & Westling 1967) and skin on the upper arms (Nielsen, Lønsmann Poulsen & Gyntelberg 1973, Gyntelberg, Nielsen & Lønsmann Poulsen 1974, Holstein et al. IX). It can be interpreted as the local effective perfusion pressure (see also Interpretation of method, p. 11).

Apart from the technique of applying and measuring the external pressure and the problems related to evaluation of the washout trac-

ing, which have previously been discussed, there are other factors which might influence the recorded values. This concerns the "critical closing" phenomenon, which implies arterial or arteriolar shut-down at distending pressures above zero caused by wall tension (Burton 1951, Ashton 1963). However, it is not likely that any vascular tone persists after the prolonged ischaemia in the tissues exposed to external counterpressure. Moreover, the effect of histamine probably ensures maximal vasodilation. The relation between external pressure and isotope washout rate also was almost linear, without any abrupt deflection towards zero flow values at low distending pressures (Holstein et al. I, Bolund & Holstein II).

A yield pressure phenomenon, i.e. the lowest arterio-venous blood pressure difference required to maintain blood flow, when the vascular pathway is just open, is probably of minimal importance. Experimental studies (Levy, Philips & Brind 1954, Haynes & Burton 1959) have shown, that the yield pressure does not exceed 5 mm Hg.

The tissue pressure is another factor to be considered. Intracutaneous values of about 4 to 7 mm Hg have been found (Wells, Youmans & Miller 1938).

Finally, because some external pressure is absorbed by deformation of the cushion and the tissues, a gradient must exist between the pressure in the cushion and that in the compressed vessels. This gradient, however, must be very small, since the distensibility of the rigid PVC cushion is negligible and the tissues are soft; this is considered an important advantage of the present method and in contrast to the problems in systolic blood pressure measurements, which may be distorted by rigid arterial walls (see discussion on "Segmental SPP compared with segmental systolic blood pressure", p. 15).

In conclusion, the existence of a pressure gradient between the cushion and the vessels tends to an overestimation of the true arterial pressure, whereas the phenomena critical closing pressure, yield pressure and tissue pressure tend to an underestimation.

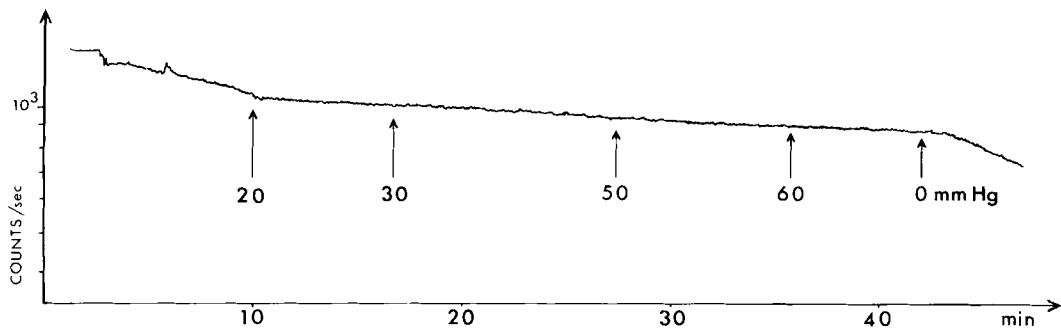


Figure 4. Artifact caused by oedema. The application of 20 mmHg of external pressure causes a decrease in washout rate, but further steps of external pressure do not stop the washout rate. The (labelled) oedema is squeezed away.

Technical notes and sources of error

It is a drawback of the method that it is time-consuming: one measurement takes about half an hour. This makes it difficult to map out an extremity. However, in the situation where a major amputation has been planned its level can be determined in most cases by measurements at one or two levels.

It has been argued that the measurement of the SPP is too painful. True, a patient with rest pain cannot lie quietly with external pressure on the ischaemic limb for about half an hour, but pain can be treated. Repeated doses of Demerol (pethidine) 25–35 mg given intravenously completely control the pain. It is a technical error to continue the measurements in spite of pain, because the blood pressure may rise considerably, causing high SPP values not representative of the patient's situation. The systemic blood pressure should always be measured every 5–10 minutes. Support with sandbags should be employed to secure stable geometry.

When measuring very low pressures it may take time until the washout from the depot of isotopes is constant, viz. suitable for measurement. About 5 minutes may elapse before the washout starts, and it may take another 5 minutes before the acceleration has ceased. The external counterpressure should be postponed until this point, because otherwise the SPP will be underestimated. This delay of the washout, present in particular at low pressures, is probably due to a high initial pressure in the isotope-

histamine depot and, moreover, to a slow histamine reaction.

The presence of oedema at the site of injection involves a risk of overestimating the SPP, because the oedema which has become labelled is pushed away by the external counter pressure. This artifact, however, is easily recognized on the tracing: the usual characteristic stepwise decreasing washout is replaced by a smooth decreasing washout, not influenced by an increasing external counterpressure (fig. 4) until the oedema has been squeezed away. In most cases the problem can be solved by squeezing the oedema away *before* injecting the isotope solution.

Another artifact arises if the external counterpressure is increased in steps of too short duration. Each increment will always disturb the counting geometry for about 30 seconds, and if each external pressure level is kept constant, for example about 1 minute only, a series of small artifacts will arise. This may resemble the oedema curve. In the present investigation each level of external pressure was kept at about 3 minutes in the first steps and at 5 minutes close to and at the flow cessation external pressure. It must be pointed out that if the curve becomes horizontal sooner than expected and the washout has to be reestablished for further measurements, it may take 2 to 3 minutes to reestablish the washout. For this reason, the original principle of measuring with stepwise *decreasing* external counter pressure – as is suitable for muscles (Nilsén et al. 1967) – was abandoned.

Chapter 4: SPP measured by photoelectric technique

Principle, method

Another physical principle of measuring skin perfusion pressure is photoelectric recording of skin reddening after blanching by external counterpressure. A series of investigations on this rapid technique has been carried out (Holstein, Nielsen & Barras III, Holstein & Lassen VI, Holstein et al. VII). The results further elucidate the physiological background of recording the SPP by external counterpressure.

Red blood cells have a high adsorption of light as compared with other soft tissues (Kramer et al. 1951, Jarløv 1957). The photoelectric probe has an incandescent lamp sending white light into the skin. Any change in the amount of red cells is subsequently recorded by the photocell as a change in the light reflected from the tissues. For example, pulsations in normal skin can be recorded by this equipment (Thune 1971).

The photoelectric probe is placed underneath a blood pressure cuff as described by Nielsen, Lønsmann Poulsen & Gyntelberg (1973) or underneath the counterpressure equipment as used in the isotope washout method (Holstein, Nielsen & Barras III, Holstein et al. VII). When the counterpressure is applied suddenly, the blood is squeezed out of the tissues. This can be recorded by the photocell and results in a new baseline on the tracing representative of blanched skin (fig. 5, upper panel). When this baseline is stable the external counterpressure slowly decreases, and at a given external pressure the tracing starts to return towards the original baseline; at this point too pulsations usually appear. The external pressure corresponding to this point is denoted the skin blanching threshold external pressure (BTEP) (Holstein, Nielsen & Barras III, Holstein et al. VII). This pressure is close to the external pressure that allows a measurable minimal washout of isotopes, i.e. a phenomenon that takes place in the microcirculation. For this reason, the deflection of the baseline of the blanched

skin is considered a sign that the microcirculation fills with red blood cells, and the BTEP is taken to be an approximate measure of the SPP.

Normal values

Twenty-four normal legs were measured on the thigh, calf and ankle at the same sites as used in the isotope washout technique (Holstein et al. VII). On the average the BTEP was slightly below the auscultatory brachial mean blood pressure. A slight, but statistically significant increase in the average BTEP in the distal direction was found, the ankle BTEP being 5 mm Hg higher than the thigh BTEP. Measurements on the dorsum of the foot were tried, but this region proved unsuitable for BTEP recordings. Then, a new equipment was developed for measurements on the heel. In 13 normal heels (Holstein, Nielsen & Barras III) the average BTEP was 4 mm Hg below the auscultatory brachial diastolic blood pressure. Thus, normal values of BTEP were in the same order of magnitude as normal FCEP values.

Comparison to isotope washout technique

BTEP and FCEP were compared over a wide range of pressures (18–187 mm Hg) (Holstein et al. VII). This revealed that at low pressures, viz. below 60 mm Hg, the BTEP was on the average 8 mm Hg lower than the FCEP ($P \leq 0.05$). Between 60 and 119 mm Hg the values of the two methods were equal, and at 120 mm Hg or more the BTEP exceeded the FCEP by an average of 13 mm Hg ($P < 0.01$).

Measurements of BTEP and FCEP on the calf in patients treated for arterial hypertension disclosed that at very high pressures the BTEP increased to values above the systemic

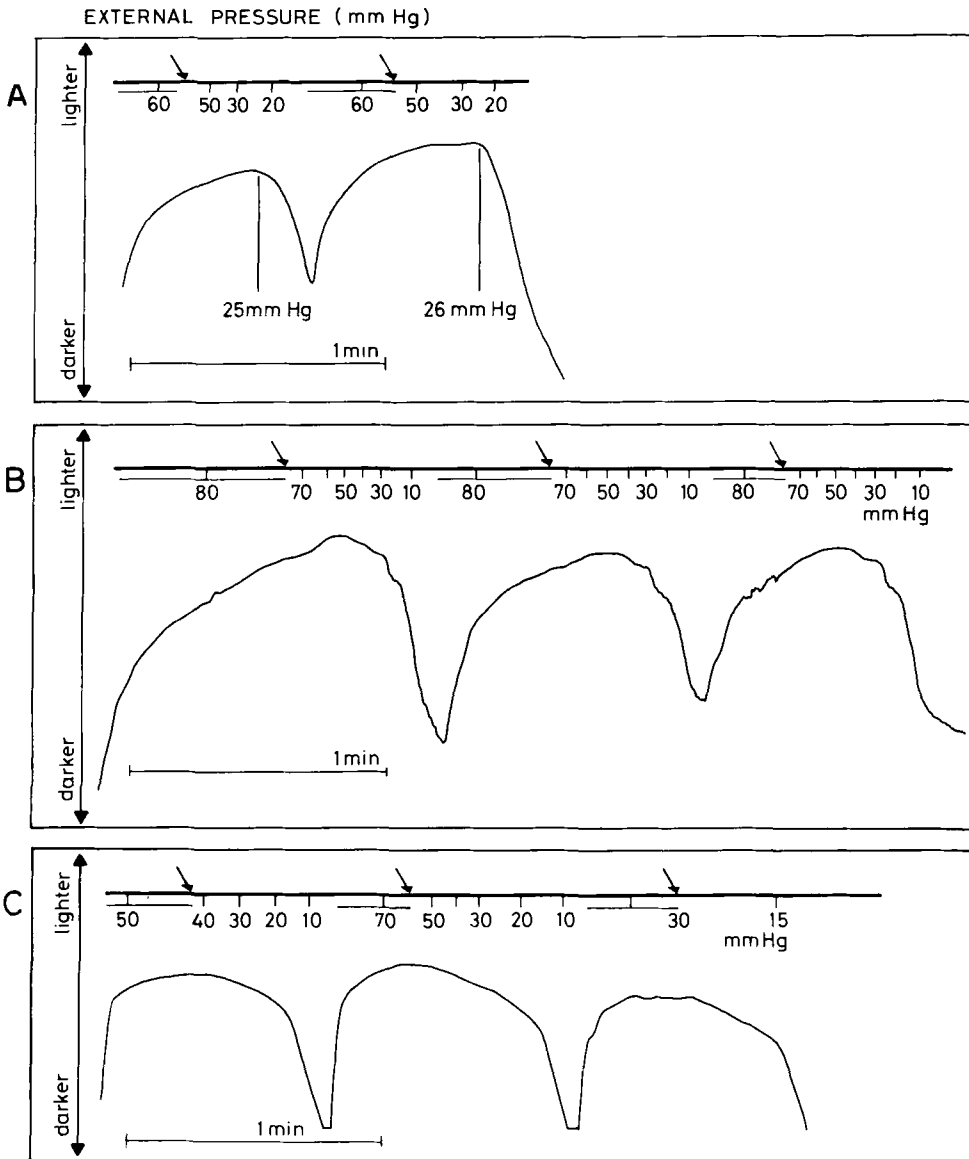


Figure 5. Different types of photo-electric curves. The arrows on the scales indicate the points where deflation of the cuff starts after stabilization of the baseline during skin blanching at high external pressure.

(A) Clear-cut curve indicating BTEP = 25 mmHg and 26 mmHg as measured repeatedly on the calf in a patient with severe occlusive arterial disease.

(B) Tracing recorded over irregular structures. No clear-cut endpoint can be identified.

(C) Artifacts consisting in deflections of the curves at the points of initiating the deflation of the cuff. The repeated measurements demonstrate the irreproducibility of this false endpoint. The artifact is seen in case of atrophy of the subcutaneous tissue.

(From Holstein et al. VII)

mean blood pressure, whereas the average FCEP was below the systemic mean blood pressure.

General discussion on SPP by photoelectric technique

With minor discrepancies the BTEP proved practically identical with the FCEP. The first discrepancy consisted in slightly lower values at low pressures in patients with AOD of the legs. This may be related to the differences between the two techniques: BTEP is recorded as an opening pressure and FCEP as a closing pressure; the measurements might be influenced by "critical opening" and "critical closing" pressures (see also General discussion on the SPP, p. 23). Ashton (1962) found no substantial difference between critical opening and critical closing pressures, and in the present investigation the local arterial wall tension was probably reduced by histamine. However, the vasodilation during the long-lasting registration of the FCEP is probably more complete and extensive due to the induced ischaemia than during the rapid recording of the BTEP. This could explain the finding of slightly lower BTEP values at low pressures. Another possibility is that external pressures are transmitted more evenly to the skin during the isotope washout recordings, since the soft cushion moulds smoothly and directly to the skin, viz. without the photoelectric surface probe interposed. Tissue pressure and yield pressure phenomena probably influence the two methods equally (see discussion p. 17).

The second discrepancy was the tendency of BTEP to exceed the FCEP and even the systemic mean arterial blood pressure in hypertension. In this connection it should be mentioned that the BTEP has previously been interpreted as the systolic blood pressure in small skin vessels with a diameter of less than 300 to 400 μm (Nielsen, Lønsmann Poulsen & Gyntelberg, Nielsen and Lønsmann Poulsen 1974). The application of external pressure, however, must change the local haemodynamic situation: the intravascular pressure of all compressed vessels will approach the arterial pressure head of the main feeding artery

under compression. Since the BTEP (and the FCEP) are only slightly below the mean arterial blood pressure, it is more likely that the BTEP is a measure of the arterial pressure in the local main artery.

Nevertheless, the systolic blood pressure peak probably influences the BTEP. When the systolic pressures are excessive, it is likely that the systolic peaks at high pulse pressure penetrate so far into the compressed vessels that the red blood cells are recorded by the photocell at external pressures higher than that permitting a measurable washout of isotopes.

This could explain the high BTEP values recorded in hypertension. Furthermore, it might explain the finding that the BTEP values increase distally in normal legs (Holstein et al. VII), viz. in agreement with the phenomenon that the systolic peak increases in the distal direction in normal subjects (Hamilton, Woodbury & Harper 1936, Nielsen, Barras & Holstein 1974).

Technical notes and sources of error

Rapid changes in skin perfusion pressure can only be measured by the photoelectric technique as used in studying the haemodynamic effect of mimicking a surgical amputation by inflating a blood pressure cuff (Lassen & Holstein 1974) and in studying the hemodynamic effects of drugs and of physical exercise (Nielsen, Lønsmann Poulsen & Gyntelberg 1973, Nielsen et al. 1976). Moreover, the SPP can be measured on the arm by the photocell (Gyntelberg, Nielsen & Lønsmann Poulsen 1974, Holstein, Nielsen & Barras III), as used in studying patients with arterial hypertension. This is difficult by the isotope washout technique because the inherent venous stasis distal to the cuff is too painful. It may also be a problem in measuring on the legs of hypertensive subjects, and in these cases the photocell is preferable.

The drawback of the method is that the curves may be difficult to interpret. Pulsations on the curves may represent pulsations in the skin vessels, but in some situations it may be difficult to exclude that the tracings demonstrate seismographic recordings instead, i.e. the probe is rocked by the pulse volume. The

endpoints of the curves are not always clear-cut (fig. 5, intermediate and lower panel), implying the possibility of misinterpretation. Investigations on the different components were carried out in the attempt to eliminate these drawbacks. Different wavelengths, different intensity of light, and different photocells were tested (Holstein et al. VII), but no significant improvements were obtained. A careful standardization of skin areas used for measurements was more helpful. Careful attention must be paid to the quality of skin as regards the thickness of the subcutaneous layer, especially in limbs with AOD. Measurements were recorded only when the skinfold – picked up between the thumb and the index finger – was at least 5 mm thick as measured with a Harpenden skinfold caliper (Tanner 1959). They could not be carried out in dehydrated patients whose skinfolds subsided slowly when picked up at the site of measurements. Moreover, skin over osseous or tendinous prominences, such as the dorsum of the foot and the fibula, should be avoided (Fig. 5, intermediate and lower panel). Conic parts of the extremities caused the counterpressure equipment to

slide sideways, stretching the skin and leading to falsely low values. Oedema of the limb, however, did not seem to influence the BTEP.

Owing to these limitations some 5 per cent of the patients with ischaemic limbs could not be measured on the calf; measurements on the thigh in patients with AOD were more often impossible to perform.

Recently, Støckel and Brøchner-Mortensen (1981) have presented a modification of the photoelectric technique using systolic blood pressure determination in defining the baseline of blanched skin. In a comparison with the isotope washout method over the range of pressures from 18 to 100 mm Hg they found no difference between the two methods. Healing results in amputations as compared with BTEP measured by this modification did not deviate from the results obtained with the isotope washout technique. According to Støckel et al. (1982) 4 per cent of the measurements had to be made with the isotope washout technique because of thin skinfolds. It was concluded that the isotope washout technique was necessary in such difficult cases.

Chapter 5: Clinical applicability of SPP in below-knee amputations

Correlation with healing

In two prospective series (Holstein, Sager & Lassen IV, Holstein VIII) studies were made of the relationship between healing of amputation wounds and the SPP measured preoperatively as well as postoperatively by the isotope washout technique.

Preoperative SPP: The healing figures of the two series, derived from 3 different orthopaedic departments (table 1), were consistent, demonstrating that healing rarely took place when the SPP was below 20 mm Hg (3/17 = 18 per cent). On the other hand, SPP above 30 mm Hg indicated a good healing prognosis (96/102 = 94 per cent).

Postoperative SPP: The healing figures of postoperative measurement (Holstein, Sager & Lassen IV, Holstein VIII) (table 2) show that none of the stumps healed when the SPP was below 20 mm Hg. In the SPP range 20–30 mm Hg 39 per cent of the stumps healed as against 93 per cent at SPP above 30 mm Hg. In both series the postoperative SPP was significantly higher than the preoperative SPP, but the average increase was in the range of only 5 to 8 mm Hg, explaining why the preoperative SPP correlated so closely with healing.

Diabetes mellitus: In both series the average SPP below the knee was higher in diabetic than in non-diabetic legs. However, the healing figures in relation to the SPP were equal for diabetics and non-diabetics (table 1).

Infection: Surprisingly, infection was about equally frequent in diabetics and non-diabetics (Holstein VIII). Wound healing failed in 14 out of the 24 infected BK amputations. Infections were treated with antibiotics and surgical revision when necessary, but antibiotics were not given pre- or peroperatively.

Clinical selection of amputation level compared with SPP: Out of 102 major leg amputations 18 cases were selected for AK (or through knee (TK)) amputations and 84 cases were selected for BK amputations (Holstein VIII). The selection was made on the basis of clinical examination – and the preoperative SPP values were sealed. Fifteen out of 18 cases selected for AK amputation had below knee SPP of less than 30 mm Hg. In 13 out of these 15 cases there were signs of ischaemia at the usual site for below knee amputation. The other AK (or TK) amputations were made for reasons other than ischaemia. These figures suggest a good clinical judgement of the arterial insufficiency

Table 1. Healing rates of BK amputations in relation to preoperatively determined skin perfusion pressure (SPP) in 3 different orthopaedic departments (144 cases)

SPP	< 20 mmHg	21–30 mmHg	> 30 mmHg
Surgical Dept. M Bispebjerg Hospital	2/8 = 25%	8/12 = 67%	36/40 = 90%
Dept. of Orthopaedic, Surgery O Frederiksberg County Hospital	0/5 = 0%	4/8 = 50%	32/33 = 97%
Dept. of Orthopaedic, Surgery T-2 Gentofte Hospital	1/4 = 25%	2/5 = 40%	28/29 = 97%
Total	3/17 = 18%	14/25 = 56%	96/102 = 94%
Without DM	2/13 = 15%	8/16 = 50%	48/51 = 94%
With DM	1/4 = 25%	6/9 = 67%	48/51 = 94%

Table 2. Healing rates of BK amputations in relation to postoperatively determined skin perfusion pressure (SPP) in 132 evaluable cases

SPP	< 20 mmHg	21-30 mmHg	> 30 mmHg
Surgical Dept. M Bispebjerg Hospital Depts. of Orthopaedic Surgery O and T-2	0/3 = 0%	3/7 = 43%	38/44 = 86%
Total	0/8 = 0%	7/18 = 39%	97/104 = 93%
Without DM	0/6 = 0%	4/12 = 33%	41/45 = 91%
With DM	0/2 = 0%	3/6 = 50%	46/49 = 94%

based on the presence of signs suggesting ischaemia.

Nevertheless, there were 15 failed primary BK amputations with SPP below 30 mm Hg. Only in one of these cases did a skin lesion on the calf suggest ischaemia.

Thus, the lack of clinical signs of ischaemia does not guarantee that the arterial supply is sufficient for wound healing.

Clinically useful parameters were the presence of a temperature demarcation line as felt by hand at the BK level. This sign and also the presence of cyanosis reliably indicated poor circulation. Palpable pulsations in the popliteal artery, on the other hand, effectively indicated that circulation was adequate for healing of BK amputations. Pulsations in the femoral artery were not useful. Poor bleeding during the operation led in only one case of the series to a

decision to change from BK to AK level. SPP was below 20 mm Hg in this case. Ulcerations on the calf did not necessarily indicate ischaemia.

It must be concluded that cyanosis and the presence of a skin temperature demarcation line at the BK level indicate that healing will not take place, whereas pulsations in the popliteal artery indicate healing. However, such reliable clinical signs were present in only 25 out of the 102 cases (Holstein VIII).

Discussion on selection of amputation level by systolic blood pressure, skin blood flow and skin perfusion pressure

The following discussion concerns primarily methods of level determination with special

Table 3. Healing of BK amputations in relation to systolic blood pressure on the calf or distally on the thigh

Investigators	No.	No. with DM	Poor arterial supply		Borderline arterial supply			Good arterial supply			
			Criterion	Healed No.	Failed No.	Criterion	Healed No.	Failed No.	Criterion	Healed No.	Failed No.
Dean et al. 1975	26	12	<50 mmHg	0	1	Not indicated			>50 mmHg	22	3
Barnes, Shanik & Slaymaker 1976	53	30	Undetectable Signal	0	5	Undetectable to 70 mmHg	12	4	>70 mmHg	32	0
Raines et al. 1976	27	?	Undetectable Signal	0	3	Undetectable to ≤65 mmHg	No amputations		>65 mmHg	24	0
Wagner & Buggs 1978	10	10	No amputations below 70 mmHg			>70 mmHg			10	0	
Gibbons et al. 1979	47	47	No amputations below 65 mmHg			>65 mmHg			42	2	
Burgess et al. 1982	26	?	Undetectable Signal	7	3	Undetectable to <70 mmHg	6	3	>75 mmHg*	7	0
Nicholas, Myers & De Muth 1982	54	38	<70 mmHg	19	6	Not indicated			>70 mmHg	33	1

* Values proposed as criterion by the author after analysis of the data.

reference to the BK level. Since the appearance of the preliminary reports on amputation level selection by isotope washout methods (Bohr 1967, Holstein 1973, Moore 1973, Kostuik 1976) several papers on different methods have been published. However, only a limited number of the methods have been studied to a major extent, i.e. segmental systolic blood pressure, skin blood flow and skin perfusion pressure.

Segmental (or "distal") systolic blood pressure: The most widely investigated method is determination of the segmental systolic blood pressure by Doppler ultrasound technique (see survey in table 3). It appears that a systolic blood pressure as measured on the calf or on the lower thigh exceeding some 50–75 mm Hg indicates a high rate of success. However, this parameter cannot reliably predict failures. Even at undetectable signal, healing is not uncommon. Exact limits for healing or failure could perhaps not be expected either, first of all because of rigid arterial walls yielding falsely high pressures, especially in diabetics, and secondly because an undetectable signal is often found in a vital limb, viz. the lower range of circulation is not properly graduated.

Systolic ankle blood pressure, viz. measurements quite far from the amputation site, have also been proposed. Raines et al. (1976) reported good healing results at ankle pressures above 30 mm Hg. This was confirmed by Nicholas, Myers & DeMuth (1982) who found 91% healing with ankle pressures exceeding 30 mm Hg. However, healing also occurred in 60 per cent of those with ankle pressures less than or equal to 30 mm Hg and in 6 out of 9 cases with undetectable pressure. Pollock & Ernst (1980) suggested that 70 mm Hg was the critical value of wound healing; 2 out of 7 cases with lower ankle pressures healed.

Thus, the figures reported on systolic ankle and calf blood pressures are not quite consistent.

Skin blood flow: Skin blood flow determination by ^{133}Xe (Bohr 1967, Sejrnsen 1967) was used by Moore (1973, 1974) who injected ^{133}Xe in saline intradermally. Thirty BK amputations with skin blood flow in excess of 2.6 ml/min/100 g

tissue healed. BK amputations with lower flow did not heal. Malone et al. (1979) reported 100 per cent primary healing in cases with skin blood flow in excess of 2.6 ml/min/100 g tissue and 50 per cent healing when the flow was between 2 and 2.6 ml/min/100 g tissue. However, Holloway & Burgess (1978) found healing in cases with flow values as low as 0.01 ml/min/100 g tissue, and there was no significant difference between the average skin blood flow in cases that healed and in cases that failed. One would expect this technique to be less precise, since no histamine was added in the injection and because ^{133}Xe is trapped in the subcutaneous fat. Kostuik (1976), using epicutaneous labelling with gaseous ^{133}Xe , found 22 amputations to heal at flow values of more than 1.5 ml/min/100 g tissue and 2 failures out of 10 cases at lower values. Unfortunately, normal values ranged down to 1.1 ml/min/100 g tissue. If skin blood flow by isotope washout is employed, it is desirable to use an isotope which is not trapped in the subcutaneous fat, such as ^{131}I -a.p., ^{131}I and $^{99\text{m}}\text{Tc}$ (Holstein et al. IX). Moreover, histamine should be applied to eliminate the influence of the injection trauma (Sejrnsen 1967) and to obtain the local maximal blood flow, i.e. the capacity of blood flow.

Skin perfusion pressure: A survey of the results obtained by techniques of measuring the SPP is given in table 4. The results of the different series are consistent with SPP above 30 mm Hg, indicating over 90 per cent healing and with SPP below 20 mm Hg only 35 per cent healing.

The most significant deviation was seen in the series of Hammersgaard & Baadsgaard (1977) in which healing was obtained in 4 out of 6 cases at SPP below 20 mm Hg. It should however, be noted that ^{133}Xe (which later proved not to be suitable for SPP measurements) was used in parts of the study (Trap-Jensen, personal communication).

Discussion on selection of amputation level by other methods

Skin temperature: Clinical examination includes estimates of relative skin temperature

Table 4. Healing of BK amputations in relation to skin perfusion pressure (SPP)

Investigators	SPP	Surgical technique	No.	No. with DM	Poor arterial supply		Borderline arterial supply		Good arterial supply				
					Criterion mmHg	Healed No.	Failed No.	Criterion mmHg	Healed No.	Failed No.	Criterion mmHg	Healed No.	Failed No.
Holstein 1973 (preliminary report)		Mainly "fishmouth" technique											
Holstein, Sager & Lassen 1979	^{131}I -a.p.		60	30	<20 mmHg	2	6	21-30 mmHg	8	4	≥ 30 mmHg	36	4
Lund & Sager 1977	^{131}I -a.p. and ^{85}Tc	Sagittal	41	18	<40 mmHg	10	6	Not indicated			>40 mmHg	21	4
Hammersgaard & Baadsgaard 1977	^{133}Xe and ^{99}Tc		56	?	<20 mmHg	4	2	Not indicated			>30 mmHg	49	1
Kolind-Sørensen & Marquersen 1979	^{131}I	Sagittal	56	17	≤ 20 mmHg	7	10	21-39 mmHg	6	3	≥ 40 mmHg	26	4
Støckel et al. 1981	^{131}I		29	14		No amputations below 20 mmHg					>30 mmHg	27	2
Holstein 1982 (VIII)	^{131}I -a.p.	Sagittal or long posterior flap technique	84	34	<20 mmHg	1	8	21-30 mmHg	6	7	>30 mmHg	60	2
Støckel et al. 1982	Photoelectric technique	Fishmouth or long posterior flap	31	?		No amputations below 20 mmHg		21-30 mmHg	0	1	>30 mmHg	26	4

in ischaemic limbs. Skin temperature has been extensively studied (e.g. Ipsen 1936, Kövamees 1968). Systematic evaluation in relation to amputation level determination, however, seems to be lacking. Walheim (1945) initiated a study but soon gave up this parameter in severe ischaemia. Kövamees (1968) found elevated skin temperature in ischaemic limbs; even in the contralateral limbs the temperature was increased. Body heating resulted in a paradoxical drop in distal skin temperature in some cases. These findings might explain why temperature measurements are perhaps difficult to interpret in level selection. And although thermography has been suggested (Murdoch 1975) and blood flow can be measured as a function of local skin temperature (Hensel & Bender 1956, Mathiesen 1971), materials on level determination by these methods do not appear to have been published.

Histamine- and morphine puncture: The response in skin to histamine was described by Eppinger in 1913 and studied intensively by Lewis (1927). This reaction was suggested as a circulation test, either by intradermal injection or "pricking" (Starr 1928, 1934, deTakats 1931, deTakats & Reynolds 1940). Nyström (1937) described freezing of the skin yielding a histamine response, and Gröbel (1929) observed that morphine induced a similar reaction. Haxthausen (1938) advocated the morphine puncture as a diagnostic test, and Walheim (1945) found this method equally effective as oscillography in determining the level of amputation. The morphine puncture test, however, has recently been found to be inadequate (Bek, Mikkelsen & Lauritzen 1982, Møller & Lucht 1983). In the latter study the test was compared with measurements of SPP. The lack of histamine-induced skin reddening did not reliably indicate ischaemia. Histamine is considered an important adjunct to measurement of the SPP, but only in facilitating the applicability of a physical principle of objective measurement. Chawatzas and Jamieson (1974) have suggested measurement of skin perfusion pressure with a translucent cuff compressing a skin area reddened by histamine. Their application of histamine by an injection-gun is

perhaps more reliable in causing skin reddening.

Oscillometry: This was introduced by Pachon in 1909 and evaluated by Harris, Schwartz & DeWeese (1961). Pulsations in the calf on the oscillogram were a favourable finding, but their lack did not rule out healing. Moreover, Eraklis & Wheeler (1963) found healing in 13 out of 16 consecutive BK amputations carried out in patients with no trace of calf oscillations. Recently, oscillometry has appeared in new modifications, one of which is very sensitive to mild arteriosclerosis, i.e. the digital pulse plethysmography (Zetterquist et al. 1971). The other one, i.e. the pulse volume recorder (PVR), has been introduced in level determination (Darling et al. 1972). Out of 27 cases of BK amputations healing failed in 3 (Raines et al. 1976), and in these cases the pulsations were poor. However, 6 cases healed despite the same poor category of pulsations. In level determination the PVR has until now been used only in combination with Doppler pressures (Darling et al. 1972, Raines et al. 1976, Fleurant & Alexander 1980).

Fluorescein uptake: This was used in 1882 by Ehrlich (Myers 1961) in studies of the eye. Circulation studies were facilitated by the development of the fluorodermometer (Lange & Krewer 1943), which has now appeared in modern versions, presented by Lund (1977) and by Wagner (1982) (Silvermann & Wagner 1983). In a recent series Tanzer & Horne (1982) found that 3 out of 14 healed BK amputations had been doomed to failure by this method and that two out of three failed BK amputations were correctly predicted. Recently, fatal reactions to fluorescein have been published (Buchanan & Levine 1982).

Angiography: Level determination by this means was advocated by Tolstedt & Bell (1961). Baddeley & Fulford (1964) were able to predict a successful outcome in 23 out of 26 BK amputations. However, later investigators (Lim et al. 1967, Burgess et al. 1971) have abandoned the method. The latter investigators found healing in 14 out of 15 cases with no

contrast filling of the trifurcation on the calf and with poor collaterals.

Leg scanning: This can be made by different physical principles. Murdoch advocated thermography (1975), and the old fluorescein method has recently been re-introduced (see fluorescein uptake p. 27). Fee, Friedman & Siegel (1977) injected ^{99m}Tc labelled microspheres through a translumbar aortic catheter, but have only reported three cases. Similar techniques have been used for predicting healing of skin lesions on the feet (see chapter 7).

Tissue viability according to muscle pH: Young et al (1978) used a metabolic approach in measuring the muscle pH with a glass electrode during BK amputation surgery in 20 cases. None of the 6 amputations with pH below 7.0 healed, but there was no statistically significant difference between the average values for cases that healed and cases that failed.

Transcutaneously measured oxygen tension: This method was studied in amputation level determination by Franzeck et al. (1982) and by Burgess et al. (1982). The preliminary results suggested that values of 0–5 mm Hg indicated failures, whereas values of above 40 mm Hg indicated healing. When tc pO_2 was compared with SPP (Holstein et al. IX) there was a statistically significant correlation, but the scatter was great. tc pO_2 values of above zero indicated that SPP was above 25 mm Hg, which is consistent with the above findings. More data, however, are necessary for assessing the predictive value of tc pO_2 measurements.

Skin blood flow by laser-Doppler-technique: By this method blood flow in the skin is measured by using a laser beam (Yeh and Cummings 1964, Watkins & Holloway 1978).

The blood flow correlates significantly with values obtained by ^{133}Xe washout (Holloway & Watkins 1977). Very few data are available as regards the healing of amputations (Holloway and Burgess 1983). It is tempting to try this physical principle in determining the flow cessation external pressure, viz. the SPP.

Discussion on level selection by clinical examination

The selection of amputation level based on clinical examination implies consideration of the patient's general condition and situation as well as a number of local anatomical and functional findings. The attitude to level selection, however, has changed much over the years (see also p. 7). In 1939 Homans stated that "amputation below the knee can almost never be expected to offer a healthy stump". In 1964 Glattly reported a study of 12000 new amputees from different areas in the U.S. In 7 of the areas 34 to 46 per cent of major amputations were made at the BK level. In 3 areas 51 to 58 per cent were at the BK level, Oleiniczak (1967) and Warren & Kihn (1968) reported 27 and 33 per cent BK amputations, and in the Scandinavian countries the proportion was much the same, with 20 to 43 per cent BK amputations (Hansson 1969, Lindahl & Bolund 1969, Hierton & James 1973, Christensen 1976). In the U.K. surgeons compromised at intermediate levels: the through knee (TK) amputations (Howard, Chamberlain & MacPherson 1969), the TK level according to Gritti-Stokes (Martin, Renwick & Thomas 1967) and the supracondylar AK level (Weale 1969).

The new surgical techniques have greatly influenced the pattern of level selection in some centres. Thus, Sarmiento et al. (1970), Burgess et al. (1971) and Persson (1974) demonstrated about 80 per cent retainment of the knee in those cases which required a major amputation. In larger population studies, however, the pattern is not much changed. Warren et al. (1973) reported 41 per cent BK amputations as the community practice in Boston. Malone et al. (1979) reported 50 per cent BK amputations in The Veteran Administration system. Netz, Stark & Ringertz (1983) reported 50 per cent BK amputations in 1976 in the Stockholm area. In Denmark nation-wide studies from the years 1976 and 1980 have been published (Eickhoff 1981, Ebskov 1983): amputations at the BK level were performed in 32 and in 45 per cent of the major amputations respectively. The mean age of the patients and the relative number of diabetics are not the same in the dif-

ferent series, which are thus not comparable. Nevertheless, these figures suggest that clinical evaluation and level selection differ from one centre to another, which in turn means that there is a great need for objective measurements to predict healing.

Physical signs indicating adequate versus inadequate circulation are qualitative rather than quantitative. As regards palpable pulsations several authors have found that the rate of healing increases when the distance between palpable pulsations and amputation level decreases (Silbert & Haimovici 1954, Harris, Schwartz & Weese 1961, Wheelock 1961, Lempke et al. 1963, Stahlgren & Ottemann 1965, Warren & Kihn 1968, Burgess et al. 1971, Holstein, Sager & Lassen IV, Holstein VIII). Moreover, the SPP on the calf is significantly correlated to the level of pulsations (Holstein, Sager & Lassen IV, Holstein VIII).

Palpable pulsations in the popliteal artery are the most valuable clinical sign. They indicate that a BK amputation will heal in about 90 per cent of the cases (Lempke et al. 1963, Lim et al. 1969, Cranley et al. 1969, Burgess et al. 1971, Holstein, Sager & Lassen IV, Holstein VIII). However, there is substantial evidence of successful BK amputation also in the absence of popliteal pulsations (Warren & Kihn 1968, Burgess et al. 1971, Romano & Burgess 1971, Holstein, Sager & Lassen IV, Holstein VIII), and not even the lack of pulsations in the femoral artery rule out healing at BK level, accomplished in this situation in about one-third of the cases (Lempke et al. 1963, Holstein, Sager & Lassen IV, Holstein VIII). Sarmiento et al. 1970 virtually disregarded the level of pulsations, focusing only on the bleeding during operation. However, palpable pulsations in the popliteal artery remain the best predictor of healing at BK level, but they are present in only a limited number of the cases.

Severe physical signs of poor circulation at the site considered for amputation are claimed to be valuable in clinical level selection. This pertains to skin temperature demarcation lines, cyanosis, lividity, dependent rubor, skin necrosis, ulcerations and rest pain. In a systematic evaluation (Holstein VIII) it was found that skin temperature demarcation lines and cyanosis are reliable signs of inadequate cir-

ulation for healing, whereas the presence of a skin lesion does not necessarily indicate ischaemia. Dependent rubor, lividity and rest pain were not evaluated.

Bleeding at skin edges during operation was used by Sarmiento (1970) as the only indicator of the circulatory situation. Burgess et al. (1971) analysed the bleeding, finding correlation with healing time. On the other hand, the lack of bleeding from muscles did not justify revision to AK level. Only in one case of the present author's series (Holstein VIII) did poor bleeding lead to AK amputation instead of the planned BK amputation, and the evaluation of bleeding did not prevent failures. Beyond any doubt, pulsatile bleeding is a favourable sign, but poor bleeding is difficult to evaluate. In this connection it should be noted that the local perfusion pressure depends among other things on the systemic blood pressure, which may be quite varying during anaesthesia.

Discussion on infection and diabetes mellitus

Infection: This factor was high-lighted by Lempke et al. (1963), finding that failure of healing in 28 cases was due to ischaemia in 76 per cent and to infection in 24 per cent of the cases. All patients had treatment with antibiotics initiated preoperatively, which seems to have been unusual at that time. In the present author's series (Holstein, Sager & Lassen IV, Holstein VIII) infection frequently occurred in ischaemic as well as in non-ischaemic failures. Surprisingly, the rate of infection was about equal in diabetics and non-diabetics (Holstein VIII).

In 1978 Persson pointed out that there were still no controlled studies on the impact of prophylactic antibiotics. But such studies are now appearing, and Sonne-Holm et al. (1983) have demonstrated a substantial decrease in postoperative infections as well as in re-amputations by this means.

Diabetes mellitus. Diabetic patients are often better candidates for BK amputations than non-diabetic patients (Cranley et al. 1969, Condon & Jordan 1970, Persson & Sundén

1971, Romano & Burgess 1971, Termansen 1977, Holstein, Sager & Lassen IV, Holstein VIII, Ebskov 1983), and early advocates of BK amputation were dealing primarily with diabetic patients (Maes 1930, Silbert & Haimovici 1950, 1954, Smith 1956, Hoar & Torres 1962). This may be due to the fact that diabetics are younger when they come to amputation than non-diabetics (Lempke et al. 1963, Burgess et al. 1971, Holstein, Sager & Lassen IV, Holstein VIII), but a better circulation on the calf must also be taken into account. Objective measurements of the local arterial supply have made a contribution to the problem. Diabetic patients have better circulation in the calf when they come to amputation (Barnes, Shanik & Slaymaker 1976, Holstein, Sager & Lassen IV, Holstein VIII), but there is no difference in healing in relation to pressure between diabetics and non-diabetics (table 2). The finding of higher SPP at the BK level in diabetic legs is a natural consequence of the vulnerability of the diabetic foot caused by AOD, peripheral neuropathy and liability to infection (Oakley 1954) and that AOD in diabetics involves to a large extent the medium-sized and smaller arteries of the foot and calf (Gensler et al. 1965, Strandness, Priest & Gibbons 1964), (see also: Diabetic foot lesions, p. 36).

Discussion on postoperative measurements, postoperative treatment and rehabilitation

Postoperative measurements: In investigations on rabbits Hansen-Leth (1982) found that the blood flow increased after amputation, in particular when the level was proximal on the calf and when the muscle function was preserved. On the other hand a mid-thigh amputation was unfavourable for post-operative increase in stump blood flow. Holloway and Burgess (1978) found an increase in postoperative skin blood flow in BK amputation stumps as compared to preoperative values. These findings are in agreement with the recorded increase in postoperative SPP in BK amputations (Holstein, Sager & Lassen IV, Holstein VIII) as compared to preoperative values. No increase was found after AK amputations (Holstein,

Dovey & Lassen V). The increase in SPP after BK amputation may be due to new collateral arteries or to the effect of the amputation itself, viz. the elimination of a major part of the low pressure vascular bed. An attempt to mimic this effect preoperatively has been made by a tourniquet around the leg (Lassen & Holstein 1974). Although a rise in SPP could be measured in some cases, the values obtained during such a "pseudo-amputation" did not show an increased accuracy in predicting whether healing would take place (unpublished observations). In this context it should be noted that the commonly used technique of measuring the SPP includes an element of pseudo-amputation, explaining why the preoperatively measured SPP values correlated so closely with the healing after the amputation.

Renström (1981) found that blood flow measured with strain-gauge in BK stumps was less than that measured on the contralateral leg. In agreement with this finding, the SPP on the BK stump was less than that on the contralateral leg (Holstein, Sager & Lassen IV, Holstein VIII).

Postoperative treatment: Bandaging techniques after closure of the amputation wound can be dangerous. This is illustrated by the technique of measuring SPP: With increasing external pressure the isotope washout (blood flow) decreases until cessation. Isherwood, Robertsson & Rossi (1975), in reviewing the subject, outline dangers of bandaging and review more recent techniques such as the pressure sock (Puddifoot, Weaver & Marchall 1973) which exerts very low sustained pressures as compared with the higher pressures produced by both skilled and unskilled bandagers. Since the work of Berlemont (1961), the use of rigid plaster casts instead of classical elastic bandaging has gained widespread use, and Mooney et al. (1971) in a controlled study demonstrated its superiority over soft dressings. The extension of the rigid plaster dressing to include a pylon and foot (immediate post-surgical limb fitting) has not gained the same acceptance (Vitali et al. 1969). Readhead (1973) devised an equipment for "Controlled Environment Treatment" which encloses the stump in a chamber which controls pressure, sterility,

humidity and temperature, and which allows inspection of the wound.

For BK amputations a loose soft dressing was used in the present author's first series (Holstein, Sager & Lassen IV) and rigid casts in the second (Holstein VIII). The studies were not, however, planned for comparison of post-operative managements.

Rehabilitation: In only one case in the present author's series (Holstein, Sager & Lassen IV) did a BK stump break down during prosthetic training. This stump had preoperatively an SPP of 18 mm Hg. The ability to walk with a BK prosthesis was attained in 50 per cent of the first series (Holstein, Sager & Lassen IV)

and in 69 per cent in the next series (Holstein VIII). The ability to tolerate a prosthesis was not related to pre- and postoperative SPP measurements, but more data on this subject are needed, for example the load on the prosthesis, the type of prosthesis prescribed and the number of walking hours per day. However, the observation of only one break-down after healing is consistent with reports by other investigators who have found very little risk of ipsilateral amputation after healing of a BK amputation (Glattly 1964, Romano & Burgess 1971, Persson 1974). The most substantial evidence of this resistance of an amputation stump has appeared from "The Danish Amputation Register" (Ebskov & Josephsen 1980).

Chapter 6: Clinical applicability of SPP in above-knee and through-knee amputations

AK amputations

In a study of 59 cases of AK amputations the healing was compared with the SPP measured on the standard site on the thigh (Holstein, Dovey & Lassen V). Below 30 mm Hg only one case out of 11 healed primarily (9 per cent). Another case healed by second intention, but in 9 cases there were severe wound complications, fatal in three. Above 30 mm Hg 36 out of 48 cases healed primarily (75 per cent). Another 8 cases healed rapidly by second intention, and in 4 cases there were major wound complications, fatal in 2. The difference in the wound complication rate at different pressures is highly significant.

The indications for sacrificing the knee in the present series were failed BK (or TK) amputations in 15 cases, and ischaemia or a poor general condition in 44. Out of these 44 cases the SPP below the knee was less than 30 in 32 cases. In the remaining 12 cases the general condition was poor.

Postoperative measurements were made in 47 cases: on an average 53.2 mm Hg which was only slightly above the preoperative values: on an average 52.0 mm Hg ($P > 0.1$). Thus, no increase in SPP was found after the AK amputations.

Discussion: Very little has been published on objective methods in AK amputation, and preliminary reports on new methods include only small numbers (Holstein 1973, Dean et al. 1975, Wagner & Buggs 1978). The healing of AK amputations with poor results below 30 mm Hg is in accordance with the results in BK amputations (Holstein, Sager & Lassen IV, Holstein VIII). However, poor results in AK amputations constituted major wound complications, in some cases fatal, whereas poor results in the BK series meant re-amputations above the knee. Very low SPP values at BK level indicate in most cases that a BK amputa-

tion must be abandoned. Very low SPP values measured above the knee at the standard site lead to the following considerations: In frail patients, who have lost the ability to walk for reasons other than peripheral ischaemia, wound complications must be avoided. For this reason, a very short AK stump – or perhaps a hip disarticulation – has to be made. More proximal SPP measurements ought to be helpful in this decision. In patients with a possible capacity for walking with a prosthesis a long stump facilitating walking and sitting must be considered, even despite the risk of wound complications.

TK amputations

Recently, a series of 20 TK amputations have been compared with preoperatively measured SPP at the standard site below the knee (Thyregod, Holstein & Steen Jensen 1983). Of 4 cases with SPP below 20 mm Hg 2 failed to heal. At above 30 mm Hg one stump out of 10 failed to heal. The 14 successful stumps with SPP above 20 mm Hg healed by primary intention.

Discussion: TK amputations are done a little more proximally than BK amputations, and if no specific complications related to the TK level appear, a slightly better healing rate would be expected. In fact, the healing figures were better, with 67 per cent healing below 30 mm Hg against 32 and 50 per cent healing at this same pressure zone in the BK amputation series (Holstein, Sager & Lassen IV, Holstein VIII). Moreover, rehabilitation as regards walking with a prosthesis has been found to be almost equal in BK and TK amputees and considerably better than in AK amputees (Steen Jensen, Mandrup-Poulsen & Krasnik 1983). At present the relative number of TK amputations is only about 1 to 2 per cent (Ebskov

1983, Netz, Stark & Ringertz 1983). However, the TK amputation must be considered an alternative to BK amputation in cases where the SPP is below 30 mm Hg. If the healing figures

as reported above hold true on a larger scale, a considerable reduction in AK amputation would seem possible, and measurements of the SPP at the level of the knee joint ought to be valuable.

Chapter 7: Clinical applicability of SPP in minor amputations and in ulcerations of the feet

Amputations on the feet

The healing of transmetatarsal forefoot amputations and amputations on the digits were studied in 134 cases, 102 of which were diabetic feet (Holstein X). The healing was compared with the SPP as measured on the dorsum of the foot by isotope washout technique, with the systolic digital blood pressure measured on the first or second toe, and with the systolic ankle blood pressure.

For the SPP measured in 43 cases the healing rates were: SPP < 20 mm Hg: none of 4 (0 per cent); SPP 20 to 30 mm Hg: 7 out of 18 (38 per cent); SPP ≤ 40 mm Hg: 12 out of 21 (57 per cent) ($P < 0.05$). However, closer correlation with healing was found for ankle blood pressures and in particular for digital pressures.

The relatively larger number of major amputations done in spite of adequate arterial supply at the time of measurement was due to invasive infection in the diabetic legs and to progressive ischaemia in the non-diabetic legs. There were no statistically significant differences in healing ratios related to pressure between diabetics and non-diabetics, but the healing was very slow in diabetic feet.

Ulcers on the feet

Closely related to the prediction of healing of minor amputations on the feet is the prediction of healing of a foot lesion. This was studied in a prospective series of chronic ulcerations on 66 feet 35 of which were in diabetic patients (Holstein & Lassen VI). The healing was correlated with the systolic digital and ankle blood pressure and SPP as measured by the photoelectric technique on the heel (Holstein, Nielsen & Barras III). The measurements were repeated until healing was obtained or until a major amputation had to be carried out. The predictive value of the three parameters was quite sim-

ilar to that in the above study (Holstein X), and repeated measurements demonstrated that the systolic digital pressure was particularly valuable. Limb loss from invasive infection did not occur in this study, but the foot lesions were chronic, viz. they had passed over into a relatively quiet phase, in which infection was effectively controlled. There was no difference between diabetics and non-diabetics in healing results related to pressures.

Discussion

Systolic ankle blood pressure: A number of publications in the past ten years have dealt with objective methods of predicting the healing of ulcers and amputations on the feet. Table 5 shows the results of the most commonly studied parameter, viz. the systolic ankle blood pressure measured by Doppler or strain-gauge. It appears that at ankle pressures below some 50 mm Hg healing on the feet is rarely accomplished. Controversy exists, however, over the role of higher pressures. It is difficult to identify a "grey zone", and failures at high pressures (exceeding 100 mm Hg) are not uncommon. Systolic ankle pressures are falsely high in a number of diabetic patients because of rigid arterial walls (Nielsen & Munkgaard Rasmussen 1973, Holstein, Collatz Christensen & Lassen 1975, Gibbons et al. 1979, Bone & Pomajzl 1981, Holstein et al. IX). Another difficulty in predicting healing on the feet is the frequent infection, all the more so as diabetic patients dominate the materials.

Some authors have investigated the index: systolic ankle blood pressure divided by the auscultatory systolic arm blood pressure as an adjuvant to the local systolic pressures (Verta et al. 1976, Johnson & Patten 1977, Wagner & Buggs 1978, Paaske & Tønnesen 1980, Burgess et al. 1982).

This index is an excellent tool in the diagno-

Table 5. Healing of ulcers and minor amputations on the feet in relation to the systolic ankle blood pressure

Investigator	Material	DM	No.	Poor arterial supply		Borderline arterial supply		Good arterial supply		
				Criterion mmHg	Healed Failed	Criterion mmHg	Healed Failed	Criterion mmHg	Healed Failed	
Carter 1973	Skin lesions on the feet	-	18	<55	0	5	Not defined	≥55	23	2
		+	43	<55	0	4		>55	48	15
Raines et al. 1976	Skin lesions on the feet	-	34	<55	?	?	55-65	>65	?	?
		+	40	<80			80-90	>90		
Verta et al. 1976	Transmetatarsal and digital amputations	±	31	<50*	1	3	Not defined	>50*	19	8
Baker & Barnes 1977	Transmetatarsal and digital amputations	±	57	<60	0	4	60-70	>70	38	6
Mehta et al. 1978	Digital and forefoot amputations	±	60	≤40	2	2	40-60	≥60	39	12
Wagner & Buggs 1978	Amputations on the feet	+	56	≤70	2	7	Not defined	>70	47	1
Gibbons et al. 1979	Digital and forefoot amputations	+	100	<70	31	5	70-100	>100	37	5
Holstein & Lassen 1980	Skin lesions on the feet	-	31	<50	1	6	50-99	≥100	8	0
		+	35	<50	0	2	50-99	≥100	15	0
Bone & Pomejzl 1981	Digital and forefoot amputations	-	6	<70*	0	2	Not defined	>70*	4	0
		+	24	<70*	1	1		>70*	15	7
Nicholas et al. 1982	Digital and forefoot amputations	±	72	≤70	8	15	Not defined	>70	32	17
Holstein 1984	Digital and forefoot amputations	-	29	<50	0	2	50-99	≥100	7	3
		+	90	<50	0	3	50-99	≥100	40	15

* Values proposed by the author after analysis of the available data.

sis and quantitation of arterial disease (e.g. Carter 1968), but it does not solve the problem of medial sclerosis. In principle, moreover, it does not yield information about the local perfusion which determines the healing. This is so because the potentiality of perfusion is determined by the local arteriovenous difference and not by the pressure drop across the arterial occlusion. In summary, ankle pressures are only moderately useful in predicting the healing of ulcers and amputations on the feet.

Systolic digital blood pressures: The literature on digital pressures is more scanty but also more consistent (Carter 1973, Holstein & Lassen VI, Barnes 1979 – in discussing the paper of Gibbons et al. 1979 –, Paaske & Tønnesen 1980, Holstein X). These papers show that digital pressures of below 10–25 mm Hg indicate poor healing. In the present author's series (Holstein & Lassen VI, Holstein X) healing is rarely accomplished at digital pressures of below 20 mm Hg, and digital pressures exceeding 30 mm Hg indicate that ischaemia is not a problem in wound healing. Consequently the "border line" zone is narrow, i.e. 20–30 mm Hg encompassing only a small number of the cases. In the majority of the series there were no differences between the pressures necessary for healing in diabetic and non-diabetic cases. Only in two papers has a digital pressure exceeding 45 mm Hg been required for healing in diabetic feet (Carter 1973, Bone & Pomajzl 1981).

Skin perfusion pressure: SPP measured on the foot seems to have been evaluated in only two papers (Holstein & Lassen VI, Holstein X).

The isotope washout method is technically difficult to employ in feet with infection and oedema. The SPP measured by photoelectric technique on the heel had only little predictive value as compared to systolic digital and ankle pressures. Thus, systolic pressures – and in particular repeated measurements on the digits – are preferable in predicting healing on the feet. Unfortunately, the digits may be necrotic or they may have been amputated and in this situation one of the other parameters must be used.

Other methods: Early attempts at predicting healing of foot lesions include the cutaneous histamine reaction (Starr 1934). According to recent investigations on this method (Bek, Møller & Lauritzen 1982, Møller & Lucht 1983, see p. 27) further use of this method is not tempting. Scanning procedures after *intra-arterial* injection of albumin microspheres or macroaggregates labelled with ^{99m}Tc have been tested (Gardner et al. 1972, Siegel et al. 1975, Johnson & Patten 1977). The results are promising, but the method is perhaps too invasive. Intra-venous injection of 201 thallium has been suggested, but only a few data are available (Siegel et al. 1983).

Diabetic foot lesions

The classification of Oakley (1954) was a major step forward in understanding the causes of foot problems in diabetic patients. He classified the causes as 1) ischaemia, 2) neuropathy, 3) infection and 4) combined.

Each of the three causes requires its own therapy (Holstein, Larsen & Sager 1976). The prognosis as regards healing is determined firstly by the arterial supply (Holstein & Lassen VI) and secondly by infection and neuropathy. When the arterial supply is adequate, infection can be treated with antibiotics and surgical drainage when necessary, and neuropathy can be compensated for in most cases by properly fitted shoes and insoles.

Early investigators have shown that amputation in diabetics can often be performed very distally, i.e. as digital or transmetatarsal forefoot amputations (McKittrick, McKittrick & Risley 1949, Wheelock 1961, Rosendahl 1972), and the majority of the patients in the present author's series of distal amputations (Holstein X) were diabetics. Wagner and his group (Wagner 1977) have renewed interest in Syme's amputation performed as a two-stage procedure (Hulnick, Highsmith & Boutin 1949), and by this disarticulation in the ankle joint it is possible to eliminate a foot which is too seriously damaged for toe or forefoot amputation and yet to avoid a BK amputation – i.e. if the arterial supply is adequate.

It may be difficult to assess the arterial sup-

ply of the diabetic foot by clinical examination alone, in particular in the presence of infection. Rest pain may be lacking even in severe ischaemia, and the skin may be pink and the foot quite warm in spite of inadequate circulation. Digital pressures can be used for predicting the result of digital and forefoot amputations. Wagner (1977) advocates the ankle pressure for Syme's amputation. Because of the problems related to medial sclerosis other predictors, however, are badly needed. It is likely that BK amputations in diabetics can to some

extent be replaced by Syme's amputations or even more distal amputations. The relatively high SPP values measured at BK level (Holstein, Sager & Lassen IV, Holstein VIII) in diabetics undergoing BK amputations also support this presumption.

Last but not least, because of the risk of loss of diabetic limbs, even in case of adequate circulation (Holstein X), frequent control of diabetic feet is seriously needed (Lippmann 1979, Runyan et al. 1980, Faris 1982).

Chapter 8: Final conclusions, future aspects

Final conclusions

The present investigations have shown that the isotope washout cessation external pressure in the skin can be taken as a measure of the local skin perfusion pressure (SPP). The SPP is significantly correlated to other measures of the local arterial supply. It is valuable in predicting the healing result in amputations below and above the knee in dysvascular patients. The SPP is less effective in predicting healing of minor amputations on the feet for which the systolic digital pressure is more suitable. Amputations in diabetic patients heal at the same rate as in non-diabetic patients at identical pressure levels, provided that infection can be controlled. Since the healing of wounds is only compromised at very low pressures these must be measured very accurately.

Future aspects

In future attempts at improving healing predictors a preoperative pseudo-amputation with local blood flow or local blood pressure should be explored. Postoperative monitoring of the stump circulation may possibly prevent ischaemic tissue damage. Continued improvement in amputation surgery implies continued efforts to replace AK amputations with BK amputations whenever possible and to do TK amputations in many of the remaining cases. In diabetic patients BK amputations can probably be replaced by Syme's amputations in a substantial number. Finally, studies on prophylactic antibiotics in amputation surgery deserve great interest.

Dansk resumé

Formålet med dette arbejde har været at udvikle en målemetode til lokalt kredsløb med henblik på vurdering af sårhelingsmuligheder efter amputation på benet eller foden på grund af svært nedsat blodforsyning (koldbrand). Man har valgt at anvende en teknik baseret på radioaktive isotoper, som indsprøjtes under huden.

Udvaskningen, som foregår som følge af kredsløbet i huden, måles og der lægges nu stigende grad af tryk på det radioaktive hudområde ved hjælp af en blodtryksmanchet. Det tryk, som lige akkurat er i stand til at standse udvaskningen, er hudens perfusionstryk. Hos normale i liggende stilling er hudens perfusionstryk 5 til 10 mm Hg højere end det diastoliske blodtryk, dvs. af størrelsesorden 75 mm Hg. Hudblodtryk, som er nedsat, er ensbetydende med blokerede pulsårer (i reglen på grund af åreforkalkning).

Hudperfusionstrykmåling er sammenlignet med en række andre metoder til at vurdere pulsårerne, dvs. det arterielle kredsløbs tilstand. Specielt er der foretaget undersøgelser, som viser, at hudperfusionstrykket også kan måles med en fotoelektrisk metode.

Der foretages årligt i Danmark ca. 2000 amputationer over eller under knæet på grund af dårligt kredsløb. Anvendeligheden af hudperfusionstrykket i denne situation er undersøgt ved målinger før og efter amputation. Resultaterne viser, at man med stor sikkerhed kan forudsige chancen for sårheling eller risiko for

manglende heling, dvs. risiko for, at der må amputeres igen højere oppe på benet. Denne risiko har hidtil været vurderet på grundlag af klinisk undersøgelse af patienten. Resultatet af denne undersøgelse, dvs. den beslutning, der er truffet vedrørende amputationsniveau, er også sammenlignet med hudperfusionstrykmålinger. Undersøgelsen viste, at kliniske tegn på meget dårlig eller på den anden side meget god blodforsyning er pålidelige i vurderingen af det arterielle kredsløb. Imidlertid er der kun sådanne pålidelige tegn hos de færreste patienter. Derfor er hudens perfusionstryk nyttigt i vurderingen af amputationsniveau.

Sårheling på fødderne efter mindre amputationer, dvs. på foden eller på tæerne, er ligeledes sammenlignet med hudperfusionstryk. Dette findes imidlertid mindre pålideligt ved disse amputationsniveau'er, og sideløbende undersøgelser har vist, at den bedste parameter her er det systoliske blodtryk målt med en miniaturemanchet på storetåen (eller 2. tå).

Helingsmuligheder ved kroniske sår på fødderne, blandt andet ved sukkersyge, vurderes også bedst ved tåblodtrykket.

Der argumenteres for, at amputation – når det er uomgængelig nødvendigt – foretages længere ude på benet eller foden end tilfældet er i øjeblikket, og at mulighederne bør udforskes under kontrol med objektive kredsløbsmålemetoder.

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Abbreviations

AK: above knee

BK: below knee

BTEP: blanching threshold external pressure

FCEP: flow cessation external pressure

PVC: polyvinyl-chloride

SPP: skin perfusion pressure

SD: standard deviation

SD_{diff} : standard deviation of the difference

TK: through knee

tc pO_2 : transcutaneously measured oxygen tension

^{131}I : $\text{Na}^{131}\text{I}^-$

^{131}I -a.p.: 4- $^{131}\text{I}^-$ -iodo-antipyrine

^{99m}Tc : ^{99m}Tc -pertechnetate