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Free Flap Surgery

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BACKGROUND

Reconstructive free flap surgery involves the transfer of free tissue (skin, muscle, bone, bowel, or a combination of them) to a distant site using microsurgical techniques. The defect may be caused by trauma, infection or extensive surgery (e.g. mastectomy, head and neck cancer). The site and size of the defect determines which flap is used. The most commonly used flaps are the gracilis muscle for lower leg trauma, latissimus dorsi and rectus abdominis for breast reconstruction, and pectoralis major and radial forearm flap for head and neck reconstruction. Many others are described and each patient is individualised.

The technique of free tissue transfer is complex and despite improvement in surgical skills, hypoperfusion and necrosis of transferred tissues represent major problems. The overall failure rate is usually quoted as 1 - 5 percent.

Anaesthesia can be an important factor in improving the success rate of this type of surgery by controlling the global haemodynamics and the regional blood flow. The changes in blood volume, the use of vasoactive drugs and regional anaesthesia etc. may influence the blood flow in the free flap's microcirculation.

Microcirculation

The blood flow through the microcirculation is crucial to the viability of a free flap. The microcirculation is a series of successive branchings of arterioles and venules from the central vessels ranging in size from 7 to 100μm. Regulation of blood flow and oxygen delivery are accomplished by three functionally distinct portions of the microcirculation: the resistance vessels, the exchange vessels and the capacitance vessels.

- The resistance vessels are the muscular arterioles that control regional blood flow. Arterioles range in diameter from 20 μm to 50 μm and contain a relatively large amount of vascular smooth muscle in their walls. Alterations in vascular smooth muscle tone are responsible for active constriction and dilation in arterioles and thus control resistance to blood flow.

- The capillaries constitute the network of vessels primarily responsible for the exchange function in the circulation. Small bands of vascular smooth muscle, the precapillary sphincters, are located at the arterial end of many capillaries and are responsible for the control of blood flow within the capillaries.

- The venules act as the capacitance vessels, which collect blood from the capillary network and function as a reservoir for blood in the circulation.

The vascular bed of skeletal muscle has rich adrenergic innervation and therefore has a marked vasoconstrictor response to neural stimulation, primarily through the resistance vessels. Precapillary sphincters also constrict in response to sympathetic stimulation, but are sensitive to local factors such as hypoxia, hypercapnia and increases in potassium, osmolality and magnesium, which may cause relaxation. Other vasoactive hormones (e.g. renin, vasopressin, prostaglandins and kinins) also play a role in microvascular control.

Transplanted vessels in a free flap have no sympathetic innervation but are still able to respond to local and humoral factors, including circulating catecholamines.

Why is the Free Flap a unique piece of Tissue?

- It has no lymph drainage, at least initially.
- Denervated with respect to the sympathetic nervous system
- Usually only a single (and damaged) feeder artery and vein.

The Stages of Flap Transfer

- Initial dissection and then flap elevation and clamping of vessels. The free flap is transferred with its accompanying artery and vein, which are then reattached to vessels at the recipient site using microvascular techniques.
- Primary ischemia develops as blood flow ceases and intracellular metabolism becomes anaerobic (this is dependent on surgical time and lasts in the region of 60–90 minutes)
- Reperfusion occurs as the arterial and venous anastomoses are completed and the clamps released.
- Secondary ischemia is subsequent to hypoperfusion of the flap due to varied causes, but reperfusion injury being a central component. This can be minimized by appropriate anaesthetic management.

A staged technique is sometimes employed, the “vascular delay.”
The staging of vascular delay involves a surgical reduction of the vascular supply to tissue, usually by undermining the flap and dividing the perforating vessels. This produces a tissue flap that is sub-lethally ischemic. After a designated period of time, usually a few days to 3 weeks, the flap is transferred to its new site as a free or pediculed flap. This of course requires a second procedure, greater risk of related causes of morbidity and considerable extra cost. The mechanisms by which this improves flap survival are not fully elucidated, but involve angioneogenesis and probably some long term ischemic preconditioning.

To increase the chances of a successful reconstruction, it is necessary to consider all the known contributors to flap failure.

CAUSES OF FLAP FAILURE

Patient Selection

Successful free tissue transfer begins with proper patient selection. There are a number of patient characteristics which can additively increase the likelihood of failure.

Diabetes and other systemic illnesses such as hypercholesterolemia can increase the likelihood of microvascular disease and muscular artery atherosclerosis. In addition, poorly controlled diabetes often impairs proper wound healing. Microvascular disease delays healing and neovascularisation between the flap and surrounding tissues. It also increases the likelihood of infection with potential flap loss.

Atherosclerosis is most problematic when using lower extremity vasculature, but is less so with upper extremity, truncal, and visceral vasculature.

Patients with existing cardiac disease have increased morbidity and mortality with any large operation. This is particularly true in these reconstructions, where the surgery runs for an extended period of time. The use of free flaps requires significant operating time, although this has become less of an issue with the development of an increased number of distant donor sites which allow for a two team approach. Postoperative cardiac complications pose a major threat to the viability of free flaps, which are dependent on adequate blood flow. Cardiac function should be

optimized in these patients in the peri-operative period through invasive monitoring and appropriate medical management.

Smoking has been associated with decreased flap perfusion, hypercoagulability and impaired wound healing.

Obesity may also decrease the success of free tissue transfer as the increased adipose tissue makes dissection of the vascular pedicle more difficult and interferes with the microvascular anastomosis, insetting, and flap tailoring after transfer.

Collagen vascular disease can compromise the cardiovascular system, particularly in individuals with an active vasculitic process. These individuals have a much higher incidence of anastomotic thrombosis and thus may not be candidates for free tissue transfer.

Coagulopathies are another relative contraindication. Most are secondary to warfarin therapy for those who have a history of cerebrovascular disease, deep vein thrombosis, or mechanical heart valves. They can be managed with the replacement of clotting factors and temporary use of e.g. heparin. However, patients with a history of ethanol-induced hepatic insufficiency will often have a less - easily controlled coagulopathy. Severe intra-operative bleeding and postoperative hematoma increase the consequent risks.

Advanced age on its own is not a contraindication to this type of reconstructive surgery, as long as co-morbidities and general condition allows the patient to tolerate the long and extensive surgery.

The only absolute contraindication for free tissue transfer is a hypercoagulable state. In these patients (i.e. polycythemia, sickle cell disease) the risk of anastomotic thrombosis is too great to justify the use of free flaps.

Inadequate Anastomosis

The ultimate success of the procedure depends largely on the quality of the anastomosis and the ischemic time. This is of course dependant on the condition and size of the available vessels, as well as the surgical skill and equipment. Technical problems at the site of anastomosis compromise a considerable proportion of microsurgical free tissue transfers.

Patency of an anastomosis can be tested in various ways. Clinically the venous patency is mostly evident when the vessel is translucent. Direct

observation of arterial expansive pulsation is an indicator of vessel patency, whereas longitudinal pulsation usually indicates a partial or complete obstruction.

These conventional clinical tests of patency are unfortunately by no means foolproof.

Various monitors have been used with good results.
Doppler ultrasound, laser Doppler monitoring, transcutaneous O_2 tension monitoring, microdialysis and infrared venous saturation monitoring have been used as indicators of vessel patency. Doppler ultrasound is typically used to assess flow in the big vessels in the pedicle, and laser Doppler measuring is used to assess flow in the capillary network. Temperature monitoring of the flap is also employed because of ease of use, but problems are usually detected too late with this method. Microscope integrated near-infrared angiography has recently performed very well in a preliminary study[9].

Vascular Thrombosis

The overall thrombosis rate for free flaps is generally reported to be 10-12% although 50-85% can be salvaged by revision surgery or thrombolysis[11]. The chances of thrombosis are greatest at the site of anastomosis 15-20 minutes following closure. Therefore, it is customary to observe the anastomosis and test its patency during this period. If partial obstruction occurs, gently squeezing the vessel with forceps or massaging the vessel may break up the thrombus. A complete thrombus necessitates resection of the damaged segment and re-anastomosis. Vascular thrombosis is most commonly due to technical error in suture placement or pedicle kinking, or the use of a vessel with a damaged intimal layer. Thrombosis at the venous anastomosis accounts for 9 out of 10 thromboses and is more likely due to the slower venous flow and relative stasis of blood at this site.

After the first 20 minutes, the next critical period is within the first 3 postoperative days as 90% of vascular thromboses occur during this time. After this time, vascular thrombosis is more often associated with the late development of a hematoma, infection, or fistula. Neovascularisation may be complete in a short period of time in thin flaps, which have a large surface to volume ratio. Thicker flaps may take several weeks before they are independent of their anastomosed blood supply.

Interestingly, there are a small percentage of very late failures, i.e. years down the line, where the flap remained dependent on the pedicle and sufficient collaterals did not form. This possibility should be kept in mind when anaesthetising and positioning such a patient.

Poor flap Perfusion

The general causes of poor flap perfusion may be classified as arterial, venous or related to Ischemia-reperfusion injury oedema. If the flap is too large for its blood supply, partial flap loss will occur.

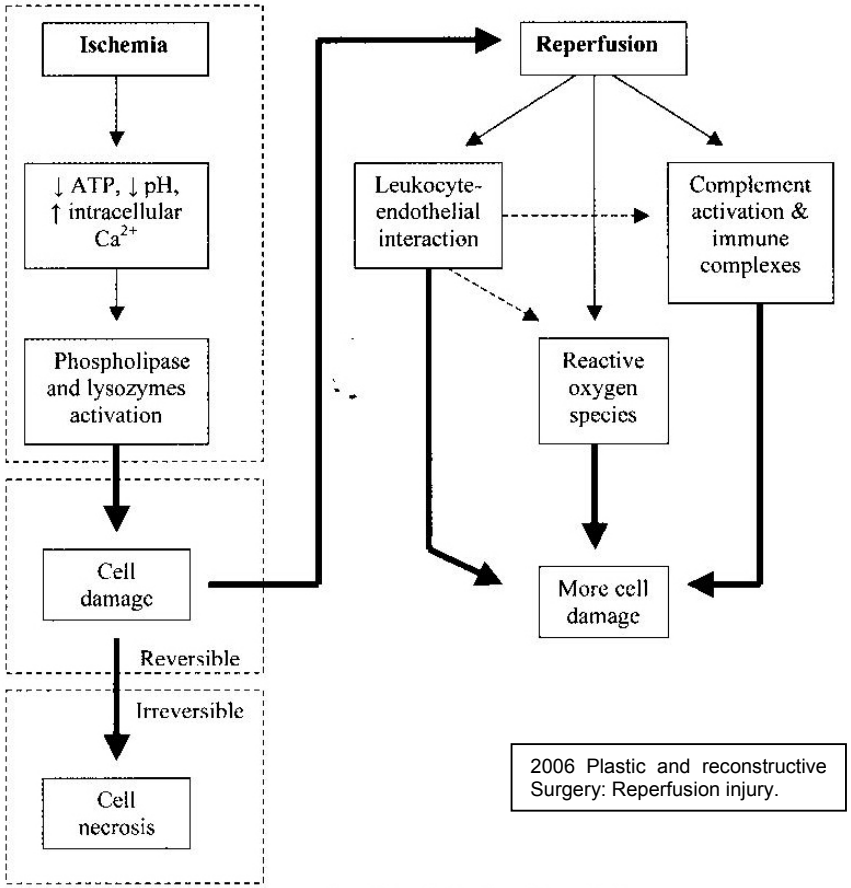
The arterial anastomosis may be inadequate, in spasm or thrombosed. The venous anastomosis may similarly be defective, in spasm or compressed (e.g. by tight dressings or poor positioning).

Oedema reduces flow to the flap and may be a result of excessive crystalloids, extreme haemodilution, trauma from handling or a prolonged ischemia time. Flap tissue has no lymphatic drainage and is therefore more susceptible to oedema.

Ischemia-Reperfusion (I/R) Injury

Tissue damage occurs as a result of ischemia and restoration of blood flow. This phenomenon has been extensively studied in other tissues as well, but is also of great interest in free flap transfers. Tissues differ in their ability to withstand primary ischemia, with skin and bone being much more resistant than muscle or intestinal mucosa. “Safe” periods are difficult to determine. Although some areas of patchy necrosis are visible in normothermic muscle after 2 hours,[4] obligatory ischemia of 1,5 to 3 hours is generally well tolerated.

The structural and metabolic changes seen in ischemia include: narrowed capillary diameter, sequestration of leucocytes and dysfunction of endothelial and general cell membranes. One of the important results of this is the increase in intracellular calcium adding to upregulation of many other enzyme systems to produce inflammatory mediators.



Mechanisms of ischemia/reperfusion injury[3][4][5]

1. Free oxygen radicals: The main source of these reactive oxygen species varies between tissues, but post-ischemic endothelium may be one of the main sources of superoxide radicals. Usually the harmful effects thereof are prevented by superoxide dysmutase (SOD), catalase and glutathione. During reperfusion these defences can be overcome. These free radicals damage a wide range of molecules including amino acids, membrane transport proteins, cytochrome enzymes and nucleic acids. Treatment with exogenous SOD has met with some, but limited success and it is clearly not the only contributor to reperfusion injury.

Recombinant human manganese-superoxide dismutase attenuated skeletal muscle dysfunction after I/R injury at 24 and 48 hours, but the protective effect was not maintained by day 7.

2. Leucocytes and endothelium: Neutrophils were once considered the trigger of ischemia/reperfusion injury, but are now thought to be the final pathway through which much of the destruction occurs. They are drawn to the site by chemotactic signals produced by platelets, endothelial cells and other leucocytes during the primary ischemia phase. Once activated they undergo diapedesis in an orderly three step process, rolling to firm adhesion mediated by glycoproteins of the selectin family, then followed by migration into the tissues. Here they cause injury by proteolytic enzymes, further production of free radicals via respiratory bursts and probably physical obstruction of the microcirculation at capillary level, thus leading to further ischemia. The consequences are shutdown of functional capillaries, thrombosis, and occlusion of microvessels, leading to the no-reflow phenomenon.

3. Complement: Complement activation is a major component of the events leading to injury after ischemia. It can be activated through three mechanisms. The classic, lectin and alternative pathways, although these are not be as independent as previously thought. They all use C3 to cleave C5, resulting in the powerful proinflammatory C5a and C5b-9, which are believed to be largely responsible for I/R injury. After the role of complement activation in tissue injury during I/R was established it became a target for experimental work.

- Recombinant soluble complement receptor type 1 (sCR1) showed significant benefit in cardiac, lung, liver and gut I/R and some protection in skeletal muscle.
- C1 Esterase inhibitor suppressed endothelial adhesion molecule expression during myocardial I/R suggesting a direct influence on neutrophil mediated injury.
- Antibodies to C5 significantly inhibited neutrophil infiltration and necrosis in rat myocardium.

None of these has yet been accepted in routine clinical use.

It is postulated that the limited success of all the above mentioned pharmacological interventions (and there have been many more) is probably due to the fact that all these pathways leading to I/R injury are integrated at many levels. Targeting just one component at a time has always had limited success. The current research is thus focused on finding and inhibiting more "upstream" triggering events, rather than trying to treat an effector.

Activated protein C (APC) is now thought to be the new agent with the most potential. It has emerged as a promising therapy in countering microcirculatory injury. The potential benefit in free flaps is not limited to its anticoagulant and indirect profibrinolytic properties.

Of special note are its anti-inflammatory properties. APC signalling on endothelial cells leads to the inhibition of NF-κß expression and activity, as well as other transcription factors, such as activator protein-1, c-Fos and FosB. Via the ability to downregulate these producers of pro-inflammatory mediators and adhesion molecules, it can dramatically inhibit leucocyte trafficking. Apoptosis of endothelial cells also plays a role in I/R injury, and APC has been shown to limit this.

Early experimental work in animals (rats) on APC in I/R injury appears very promising[3]. The effect of APC in I/R injury has been investigated in several organ systems, including liver, kidney, intestine and skeletal muscle. In a rat model of hind limb ischemia-reperfusion injury, investigators showed reduced myeloperoxidase levels and protected electrical muscle activity in animals treated with APC.

At present there are unfortunately no studies in humans, but this is likely to be a new avenue of research.

INTRA-OP MANAGEMENT

The basic intra-anaesthetic goal is to maintain an optimal blood flow for the vascularised free flap.
The "problem" with research in this field is the relatively low failure rate, together with a multitude of patient and procedure variables that are difficult to control for. Much of what we "know" is actually extrapolated from related research or from animal models. Among the various animals used are rats, pigs and dogs. Adult pigs are generally preferred because their circulation closely approximates that of humans.

Although obviously integrated, the main practical considerations are discussed separately.

Temperature and Glucose Control

Temperature control is probably much more important than in most other procedures and because of the prolonged surgery and sometimes extensive exposure it can be difficult to achieve. Even though anaesthesia abolishes some of the vasoconstriction associated with hypothermia during the procedure, it is still a major cause of vasoconstriction and flow through the flap will still be compromised. This can be severe in the post-op period.

Hypothermia has been shown to be effective in temporary storage of free flaps and severed extremities (can be viewed as a very uncontrolled "free flap"). However in the intact human body cooling has many deleterious effects: rise in viscosity, vasoconstriction, platelet aggregation etc. These effects reduce flow in the free flap. In animal models[8], the post occlusive blood flow and reactive hyperaemia in the flap are significantly reduced in hypothermic subjects.

Although hypothermia is used with success in cardiac and neurosurgery, it is generally believed to be deleterious if the re-anastomosis is going to be within the "ischemic time" of the tissues involved. This period is not well defined, but after roughly 2 hours areas of patchy necrosis can be seen in muscle.

The general recommendations[2] are therefore to maintain patient temperature with warming blankets pre- and intra-op and for the first 24-48 hours. Ambient theatre temperature should be relatively high: 24 - 25˚C, and the temperature differential between skin and core should be kept to less than 2˚C. (An exact recommendation widely quoted, always without a reference.)

Glucose control: This has not been studied specifically in free flaps. From related research regarding albumin leak it would seem that acute and chronic hyperglycemia is associated with vascular leakage and tissue oedema is more likely to be formed. Good glucose control is possibly still recommended in this setting.[2]

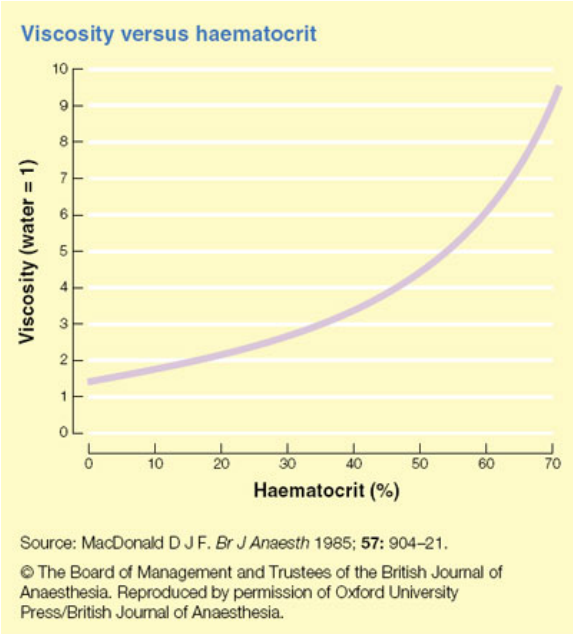
Hematocrit and Viscosity

The rheology of blood in the microcirculation is determined by the cell concentration, plasma viscosity, red cell aggregation and deformability as well as the vessel characteristics.

$$\text{Laminar flow} = \frac{\Delta P \times r^4 \times \pi}{8 \times \eta \times l}$$

Hagen-Poiseuille: Laminar flow

Flow in the small vessels can be approximated by the above formula. Flow is thus proportional to the fourth power of the radius, and even small decreases in the vessel lumen will result in a big decrease in flow. (Hypovolaemia, hypothermia etc.) Decrease in intraluminal pressure (hypotension, hypovolemia) or increase in extravascular pressure (oedema, haematoma) will reduce vessel diameter.



Source: MacDonald D J F. *Br J Anaesth* 1985; **57:** 904–21.

Upstream of the capillaries the viscosity of blood depends on the hematocrit and the velocity of the flow. The higher the hematocrit and the lower the flow velocity, the higher the viscosity and vice versa. Blood viscosity is a quadratic function of the hematocrit in larger blood vessels, whereas microvascular viscosities are a weak function of systemic hematocrit.

The principles of the Hagen-Poiseuille equation break down at the capillary level and other regulators become more important. In the microcirculation the viscosity is sensed by the endothelial cells, via the plasma layer between the red cells and the glycocalyx on the cell surface. In moderate haemodilution, the reduction in viscosity is compensated for by increased flow, thus the shear stress sensed by the endothelium is increased because of the increased flow. This is essential for the local control of blood flow in the capillaries and excessive haemodilution can lead to dysfunction of these local regulators and a decrease in flow, seemingly independent (and on top of) the lowered O_2 carrying capacity.

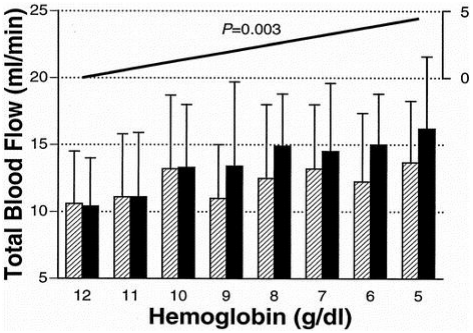
The role of viscosity in maintaining microcirculatory conditions is much more important than previously thought. This mechanical shear in the vessel wall seems to be a more potent local regulator of capillary perfusion than the O_2 carrying capacity of the blood. This has been demonstrated by comparing normal blood with blood composed largely of methaemoglobin and dilution with a plasma expander.

Thus on a microcirculatory level the positive effects seen after transfusion are more a function of the restoration of viscosity rather than just an increase in O_2 carrying capacity.[16]

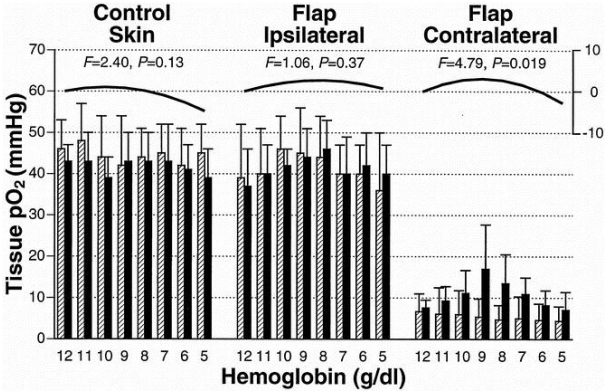
There are no studies specifically investigating the optimum Hb and its effects on O_2 - carrying capacity and rheology in relation to free flaps in humans.

In a pig model[15] normovolemic haemodilution was investigated by the administration of 6% Hydroxyethyl starch (200 / 0.5) A flap was raised that was partially well - perfused and partially ischemic and the effects of haemodilution on total and regional blood flow as well as O_2 tension in the respective parts of the flap were measured. The gradual haemodilution caused a linear increase in blood flow to the flap, but this is linked to a reduction in the O_2 carrying capacity.

The principal finding of this study was that in the ischemic and hypoxic part of the flap (Contralateral on the graph), the oxygenation and metabolism was improved with moderate haemodilution, with the optimum Hb being around 9 and Hct just less than 30.



Schramm S. Wettstein R. et al. June 2002 Anesthesiology: Acute normovolemic haemo-dilution improves oxygenation in ischemic flap tissue.



Extrapolating from known physiology and other research on the microvascular flow during shock (in humans), the “best guess” target to aim for seems to be moderate haemodilution with haematocrit ~30% and thus viscosity ~3.5 to 4cP.[2]

Vasoactive Drugs

The aim is to increase flow through the flap, via maintenance of cardiac output and creating favourable vasomotor conditions in the flap. Free flap surgery results in the disruption of the autonomic nerves running around the feeder vessels of the flap. In the short term, sympathectomy may reduce vascular tone and improve microcirculation. On the other hand, experimental studies and clinical observations suggest that denervation supersensitivity can develop after sympathectomy, leading to excessive vasoconstriction in response to catecholamines. The onset of this supersensitivity is roughly 48 hours in rats, but is not clearly known in humans.

Phenylephrine is the drug commonly used in theatre and is the drug most commonly included in these studies. It is an α_1 agonist and is known to constrict mainly larger arterioles (110 µm in diameter) but has virtually no effects on terminal arterioles that respond more to α_2 agonists (such as norepinephrine, which is a mixed α_1 and α_2 agonist) and metabolic factors (acidosis and hypoxia).

Animal studies[10] have shown that at least in the short term there is a reduced response to circulating vasoconstrictors post sympathectomy. (Phenylephrine and noradrenalin in rats) The flow in the flap was proportional to the increase in MAP, while the cutaneous flow in normal tissue was reduced. The exact mechanism is uncertain.

2008 Jul Microsurgery: Effect of adrenergic stimulation of cutaneus microsirculation immediately after surgical adventitiectomy in a rat skin flap model.

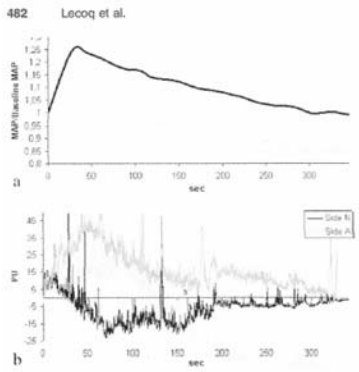


Figure 1. Changes in mean arterial pressure (MAP) over time expressed as the ratio of MAP over baseline MAP (a); changes in cutaneous microcirculation expressed in perfusion unit (PU) over time (b) after the administration of 10 µg kg^{-1} phenylephrine. The curves shown are the average of all the individual curves after each treatment. Side N (dark curves) = side with intact pedicle; Side A (pale curves) = side with adventitiectomy.

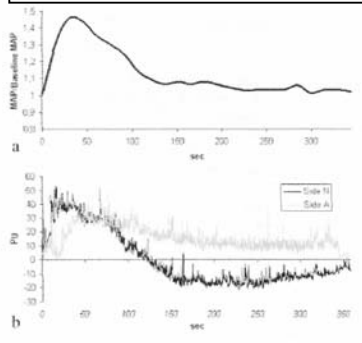


Figure 3. Changes in mean arterial pressure (MAP) over time expressed as the ratio of MAP over baseline MAP (a); changes in cutaneous microcirculation expressed in perfusion unit (PU) over time (b) after the administration of 10 µg kg^{-1} norepinephrine. The curves shown are the average of all the individual curves after each treatment. Side N (dark curves) = side with intact pedicle; Side A (pale curves) = side with adventitiectomy.

The following study[12] showed quite different and much worse results for Phenylephrine in pediculed flaps in a swine model:

	Cardiac output	Flap flow	Flap flow relative to cardiac output
Phenylephrine	↓	↓	↓
Dopamine	↑↑	↔	↓
Dobutamine	↑↑	↑	↓

The unfavourable result with regard to the effect of phenylephrine relative to the other studies is not easily explained.

One of the few studies in humans also showed results similar to the above for both dopamine and dobutamine.[14]

Another study[13] also in pigs showed better results with phenylephrine.

	MAP	CO	Flow in flap	Flow in skin	Flow in muscle
Phenylephrine	↑30%	↔	↔	↔	↔
Systemic Na-Nitroprusside	↓30%	↔	↓40%	↓23%	↓30%
Local Na-Nitroprusside			↑20%		

A study[18] in pigs designed to evaluate the effects of an epidural on microvascular flow also evaluated the effects of a phenylephrine infusion. In that study the phenylephrine infusion significantly improved MAP, but left cardiac output and flow in the flap unchanged.

The other "inodilator" studied in humans was milrinone. In a randomised double blind trial in humans investigating milrinone vs. placebo, there was no influence in graft survival or surgically graded vasospasm and an increase in the need for other vasopressors.[23]

Adrenaline: Increases MAP, CO and flow in rotational (as opposed to free) muscle flaps, where there is no sympathectomy. What happen in a free flap is uncertain.

The general recommendation if an inotrope is needed, is to use dobutamine, and although there is some conflicting evidence, phenylephrine might not be as dangerous as once thought.

Regional Technique or Not

Most of the research on this topic was done using epidural anaesthesia. Whether the same effects are seen with e.g. brachial block is not certain.
It was generally believed that the sympathectomy from an epidural will vasodilate and improve blood flow to the region. A retrospective review[17] in humans in 1993 seemed to show improved flap survival and general outcomes. This was assumed to be attributed to improved blood flow to the region. The first experimental studies done in the late 1990's did not confirm this assumption.

A study[18] in 1997 in pigs to evaluate the effects of epidural anaesthesia and phenylephrine in normovolemic and slightly hypovolemic (10% blood loss) pigs found the following:

Normovolemic: after onset of epidural

MAP	CO	Flow in muscle	Flow in skin
↓10%	↓10%	↓20%	↓20%

These changes were not statistically significant though.

Slight Hypovolemia: after onset of epidural

MAP	CO	Flow in muscle	Flow in skin
↓24% p<0.01	↓31% p<0.01	↓22% p<0.05	↓20% p<0.05

This prompted a follow up study[19] in humans:
In 21 patients surgery was performed under general anaesthetic only, and the epidural commenced only after re-anastomosis. Musculocutaneous, fasciocutaneous and free muscle flaps were evaluated, and the same results found in all.

After commencement of the epidural:

MAP	Flow in intact tissue	Flow in the flaps
↓from 85 to 68mmHg P<.01	↔	↓20 to 30% p<0.01

Other similar studies[21] in dogs further confirmed this "steal phenomenon"

The problem is now one of weighing up the relative risks and benefits: Epidural anaesthesia has many potential benefits i.e. less risk of DVT,

pulmonary complications etc. The excellent pain relief might limit the stress response and decrease circulating catecholamines. These other beneficial effects on the often elderly patients might indirectly benefit the flap.

A recent article[20] reported on the successful use of epidural anaesthesia alone in three patients that were considered too high risk for general anaesthesia, and by inference, at high risk for flap failure. All the flaps survived. This just makes the point that a regional technique still has a place in selected patients.

Volatile vs. IV Anaesthetic agents

Propofol has been shown to limit neutrophil infiltration relative to ketamine, and the assumption is made that this might be of benefit in limiting I/R injury. The beneficial effects of the inhalational agents in ischemic preconditioning are well documented in other tissues and there is some evidence of benefit here as well. Both Propofol infusions and the inhalational agents can be readily titrated during the protracted surgery that often has widely varying intensities of surgical stimulation. Some articles suggest that the inhalational agents are used more often, but there is no clear evidence of benefit over a TIVA technique.

ANTICOAGULATION

The use of various anticoagulants and volume expanders is employed by some to reduce the probability of vascular thrombosis. Some have been shown to produce an advantage in experimental models, and also potential clinical benefit in retrospective analysis. However, because the rate of thrombosis is quite low with good techniques, detection of a difference between groups is difficult. Despite considerable research on thrombosis in e.g. cardiovascular disease, antithrombotic regimens in microvascular surgery are generally empiric and few randomised blinded controlled studies exist.[11]
The three most commonly used substances include heparin, aspirin, and low molecular weight dextran (also a volume expander).

Heparin
Heparin is used in microvascular surgery both systemically and topically in irrigation solutions.[11] In rat models, both fractionated and unfractionated heparin significantly improved anastomotic patency and flap perfusion compared to controls.

Heparinised irrigation fluid has been investigated in numerous studies, with mixed results. Some found platelet aggregation to be decreased, but no difference in patency rates. A study in rats using heparin irrigation at 100 IU/ml showed significantly inhibited thrombus formation without altering coagulation profiles. In another study a concentration of 250 IU/ml also inhibited thrombus formation, but not without causing an increase in partial thromboplastin time.

Aspirin
Human studies showing an improvement in flap success rates do not exist, but 5mg/kg worked well in rats. However, clinical studies did not show an increase in complications when using aspirin. Based on this good safety profile, low dose aspirin is usually recommended for prophylaxis in microvascular free flap surgery.[2][11]

Dextran
This is available as dextran 40 and 70, and is thought to decrease platelet adhesiveness and aggregation by increasing the negative charge of platelets, erythrocytes and endothelial cells, resulting in the destabilization of fibrin polymerization. It is also a volume expander and decreases blood viscosity. Results in animal studies (rabbits for a change) were conflicting.

It was widely used though, and enough human data has become available.
A prospective study of 100 consecutive patients showed the following.[11]
The complications included being: CCF, MI, pulmonary oedema, pleural effusion and pneumonia.

	Flap survival	Ratio of Systemic complications
Aspirin 325mg/day for 120 hours.	All	1
Dextran 40 at 20ml per hour for 48 hours	All	↑3.9 times
Dextran 40 at 20ml per hour for 120 hours	All	↑7.2 times

They concluded that the routine use of dextran was not warranted in microvascular free flap surgery.

When a thrombus does form, the surgeon has various options, mostly mechanical i.e. re-exploration, but thrombolysis can also be considered. Case series of successful use of tPA etc. exist.[11] An added advantage of attempted thrombolysis in a pediculed flap is that the thrombolytic agent can often be delivered directly into the only feeder artery, and can be drained via the venous side.

The possibility of systemic anticoagulation and thrombolysis should also be kept in mind when considering a regional technique.

POST-OP MANAGEMENT

The general principles of keeping patients warm, pain free and adequately hydrated apply.
As an α_2 agonist, dexmedetomidine might be expected to induce vasoconstriction in denervated flaps. It is otherwise a very attractive drug for use especially in the postoperative period, and this possibility was thus investigated in pigs. They compared deep sedation with dexmedetomidine vs. propofol, and found a higher MAP with dexmedetomidine, but no difference in flap tissue metabolism as measured by microdialysis. They concluded that even if used for deep sedation, dexmedetomidine does not have a deleterious effect on local perfusion or tissue metabolism in denervated free flaps.[22]

CONCLUSION

Anaesthesia for free flaps has some unique problems and challenges, with many uncertainties regarding the best management. It is also an exciting and expanding field with great promise in improving quality of life for many.

REFERENCES

1. Francis B. Quinn, Jr., MD and Matthew W. Ryan, MD. May 22, 2002 : Grand Rounds Presentation, UTMB, Dept. of Otolaryngology Free Flap Reconstruction of Head and Neck Defects.
2. Natalia Hagau, Dan Longrois. 2009 Microsurgery 29(2) Anaesthesia for free vascularised tissue transfer.
3. Liwski R, West K: 2008 24(5) Journal of reconstructive Surgery: Activated Protein C: An emerging therapeutic agent in prevention of Ischemia-reperfusion injury.
4. Khalil AA, Hall JC: 2006 Plastic and reconstructive Surgery: Reperfusion injury.
5. M. Siemionow, E. Arslan: 2004 (24) Microsurgery: Ischemia / Reperfusion Injury: a review in relation to free tissue transfers.
6. I Kinnunen, E. Laurikainen, A Schrey, P Laippala, K Aitasalo.: 2002 18(1) Journal of reconstructive microsurgery: Effect of Acute Ischemic Preconditioning on blood-flow response in the Epigastric Pediculed Rat flap.
7. Anaesthesia UK: Anaesthesia for Reconstructive free flap. Created 6/01/2006.
8. Kinnunen I. Laurikainen E. Schrey A. Laippala P. Aitasalo K.: Dec. 2002 British Journal of Plastic Surgery: Effect of hypothermia on blood flow responses in pedicled groin flaps in rats.
9. Holm C. Mayr M, Dornseifer U, Ninkovic M: March 2009. Assessment of the patency of microvascular anastomosis using microscope-integrated near-infrared angiography: A Preliminary study.
10. Jean-Pierre H. Lecoq, JL Joris, X Nelissen, M.L. Lamy O.Y. Heymans: 2008 Jul Microsurgery: Effect of adrenergic stimulation of cutaneous microcirculation immediately after surgical adventitiectomy in a rat skin flap model.
11. MM Hanasono, CE Butler: 2008 24(5) Journal of Reconstructive Microsurgery: Prevention and Treatment of Thrombosis in Microvascular Surgery.
12. Cordeiro PG, Santamaria E, Hu QY, Heerdt P. 1997 Nov. Annals of plastic surgery: Effects of Vasoactive medications on the blood flow of island musculocutaneous flaps in swine.
13. Banic A, Krejci V, Erni D, Wheatley AM, Siqurdson GH. 1999 Jan. Anesthesiology: Effects of sodium nitroprusside and phenylephrine on blood flow in free musculocutaneous flaps during general anaesthesia.
14. Souminen, Sinikka, Svartling, Nils, Silvasti et al. 2004 Nov. Annals of plastic surgery: The Effect of Intravenous Dopamine and Dobutamine on blood circulation during microvascular TRAM flap operation.

15. Schramm S. Wettstein R. Et al. June 2002 Anesthesiology: Acute normovolemic haemodilution improves oxygenation in ischemic flap tissue.
16. P Cabrales, J Martini, M Intaglietta, A.G. Tsai. March 2006 Am J Physiol Circ Physiol: Blood viscosity maintains microvascular conditions during normovolemic anemia independent of blood oxygen carrying capacity.
17. Scott GR, Rothkopf DM, Walton RL: April 1993 Plastic and Reconstructive surgery: Efficacy of epidural anesthesia in free flaps to the lower extremity.
18. Banic A. Krejci V. Erni D. Peterson-Felix S. Siqurdsson GH: Sept 1997 Plastic and Reconstructive surgery. Effects of extradural anesthesia on microcirculatory blood flow in free latissimus dorsi musculocutaneous flaps in pigs.
19. Erni D. Banic A. Signer C. Sigurdsson GH: Okt. 1999 European Journal of Anaesthesiology: Effects of epidural anaesthesia on microcirculatory blood flow in free flaps in patients under general anaesthesia.
20. Alam NH. Haeney JA. Platt AJ: March 2006 Journal of Reconstructive Aesthet Surgery. Three episodes of gracilis free muscle transfer under epidural anaesthesia.
21. Lanz OI, Broadstone RV, Martin RA, Degner DA: Jul-Aug 2001 Veterinary surgery: Effects of epidural anesthesia on microcirculatory blood flow in free medial saphenous fasciocutaneous flaps in dogs.
22. Nunes S, Berg L et al. Sept 2007 Anesthesia and Analgesia: Deep sedation with dexmeditomidine in a porcine model does not compromise the viability of free microvascular flap as depicted by microdialysis and tissue oxygen tension.
23. Jones SJ, Scott DA, Watson R, Morrison WA. 2007 Oct: Anaesthesia and Intensive Care: Milrinone does not improve free flap survival in microvascular surgery.