Chronic venous insufficiency and venous leg ulcers.

It has been estimated that chronic venous disease (CVD) accounts for 2 – 2.6% of the total health care budget in the US, France and UK (£400 million per year in the UK). In the Western Society, venous ulcers are found in 1% of the adult population and 3% of those over 65 years of age. Patients with CVD have worse quality of life scores than an age matched normal population which is improved by superficial venous surgery (Sam EJVES 2004).

The risk of developing an ulcer after an ileofemoral DVT is about 15%. In venous ulceration there is isolated deep venous reflux in 15%, combined deep and superficial reflux in 32% and isolated superficial reflux in 53%.

Blood samples from the common femoral vein in legs affected by CVD show raised levels of oxygen. This is thought to be due to the presence of AV fistulae. Venous hypertension is associated with an increased numbers of dermal capillaries and white cell (WBC) trapping in the capillaries. This may lead to increased peripheral resistance and tissue ischaemia plus white cell activation, proteolytic enzyme release and free radical activity. There are increased numbers of WBC in the dermis of patients with CVD.
In the fibrin cuff theory, large molecule capillary permeability due to widening of the endothelial gap junctions leading to leakage of fibrin into the pericapillary tissue was thought to be the cause of the skin changes. These cuffs may act as a barrier to diffusion of oxygen and nutrients. More recently it has been found that the cuff consists of extracellular matrix proteins – collagen types I, III and IV, fibronectin, vitronectin, laminin, tenascin and fibrin and macrophages and t lymphocytes. It may be that the cuff is due to a response by the endothelial cells to maintain vascular architecture in the presence of an increased mechanical load. The skin primary injury appears to be extravasation of macromolecules and red cells. Red cell degradation and protein extravasation are potent chemoattractants, resulting in leucocyte diapedesis and migration. Activated leucocytes traverse the perivascular cuffs and release transforming growth factor beta (TGF β), which binds to interstitial dermal fibroblasts. This stimulates collagen production, leading to tissue fibrosis. Excessive proteolysis may be responsible for the decreased healing rates seen with venous stasis ulcers.
Protracted healing in chronic venous ulcers is thought to be due to a disorder of normal wound cytokines.
Lipodermatosclerosis thus appears to be a chronic inflammatory condition of unknown cause. White cell trapping and activation may initiate tissue damage.

Clinical features.
Flat feet, a fixed ankle and reduced hip and knee mobilisty reduce the calf muscle pump function and this increased venous hypertension. The leg oedema can be exaccerdated by lymphoedema, cardiac failure, renal disease, hypoproteinaemia. The oedema fluid takes the path of least resistance resulting in ulcers exuding a lot of fluid and potentially delaying wound healing.
Perthes test – historical – leg wrapped in elastic bandage. Patient then exercises. Sever pain suggests deep venous occlusion.
Brodie Trendelenberg test – leg elevation, torniquet at SFJ and other sites down leg. Patient then stands and pattern of reflux noted.

Differential diagnosis.
Kaposi's sarcoma –
Rheumatoid ulcer
Arterial ulcer

Skin manifestations.

Dermatitis.
CVD cause increased venous pressures on ambulation leading to dilatation of vessels and extravasation of blood constituents with subsequent irritation of the skin. This is followed by thinning of the epidermis, erythema and development of thin scale with occasional vesicels and crusts. Scratching may exacerbate the changes.

Lipodermatosclerosis.
Pronounced skin induration and inflammation. In the acute form, inflammation predominates leading to pain and erythema. Differential diagnosis – cellulitis, morphea (cutaneous scleroderma), erythema nodosum.

Malignancy.
Marjolins ulcer – squamous cell carcinoma. 25% are metastatic at presentation.

Investigations.
Ankle brachial pressure index.
Venous duplex scan.
Ulcer biopsy.
Routine microbiological swab is not required unless there are clinical signs of infection.

Treatment.
Pharmacology.
Pentoxiffylin (trental) has been shown in some but not all studies to be more effective than placebo in healing venous ulcer althought the effect is small. No evidence to support flavinoids, oral zinc or oral antibioics.

Wound management.
Wounds should be washed with tap water. No dressing material has been shown to be superior to any other. The simplist and cheapest is paraffin tulle over which compression bandages can be applied. If there is bacterial colonisation is present, SSD cream can be placed on the ulcer. His is particulary effective for pseudomonas.
Systematic review of antimicrobial agents for chronic wound (O'Meara BJS 2001):
Antibiotics for bacterial colonisation of venous ulcers does not improve healing rates.
The following topical agents have been investigated and shown not to improve healing rates:
Polynoxylin paste
Mupirocin
Povidine iodine solution
Silver activate charcoal dressing
Tripeptide copper complex

The following were shown to improve healing rates:
Dimethyl sulphoxide
Allopurinol
Silver sulphadiazine

Compression bandaging.
Thought to work by decreasing ankle oedema, softening lipodermatosclerosis, decreasing venous volume, increasing deep venous velocity, shifting blood into central compartments, improves venous pumping, improves microcirculation and improves lymph drainage. 30 – 40mmHg of compression is required at the ankle. 3 months wound healing rates of 70% but recurrence rate is high. Elastic compression is more effective than non elastic compression. Multilayered compression is more effective than single layer compression. My preference is for 4 layer compression bandages:

    - Single layer orthopeadic wool in spiral from toe to knee
- Crepe bandage in spiral
- Elastic long stretch bandage, figure of 8
- Cohesive bandage applied in spiral
- 50% overlap throughout
- Profore (Smith and Nephew), Ultra Four (Robinson), System 4 (Senton) and K Four (Parema)

ABPI should be more than 0.8 for compression therapy and is certainly contraindicated if 0.6 or less.
Once the ulcer has healed, patients should have compression stockings for at least 5 years as these reduce recurrence rates. Preferably use class III below knee stockings.

Exercise.
A program of compression stockings and exercise has beneficial effects on patients with CVD. It can reduce reflux. (Zajkowski Phlebology 2006).

Intermittent calf compression.
May be used in those that do not tolerate compression bandaging or in those in whom compression bandaging has failed. Ulcer healing rates 62%. 45mmHg at foot and 30mmHg at thigh for one hour per day. In a randomised study, rapid inflation and deflation of the device improved healing rate and success over slow inflation and deflation (Nikolovska, Medical Science Monitor 2005). However, other randomised traisl have shown no advantage for intermittent compression.

Skin grafts
Dermagraft – human fibroblast derived dermal replacement. Origin of cells – human newborn foreskin. Consists of a bioabsorbable scaffold containing growth factors, matrix proteins and glycoaminoglycans on which fibroblasts are cultured. Does not reject. Improve ulcer healing rates at 12 weeks (50% vs. 12%).

In an analysis of the effectiveness of skin grafting to treat chronic venous leg ulcers by Vytautas Jankunas, (Wounds 2007), he compared patients treated by skin grafting (n = 40) to patients treated non operatively (n = 31). The analysis evaluated the influence on the speed of epithelization (healing) of ulcers. Ulcers did not heal completely in any patients in the non operative group (100%) - ulcer size increased in 17 patients and decreased in 14 patients. The average area of ulcers in this group C was 171.12 cm^2 (range = 8 cm^2-720 cm^2). Compared to the area before treatment (m = 182.29 cm^2), the reduction in average area was not significant. The contamination of ulcers did not change much in either group over the course of the study. Staphylococcus aureus and Pseudomonas aeruginosa were the most commonly found pathogens. In the skin graft group, the skin epithelized completely in 27 cases (67.5%) and did not epithelize in 13 cases (32.5%). The average ulcer area was 16 cm^2 (range = 6 cm^2-52 cm^2).

Ulcers that fail to heal after compression or surgery may be treated by skin grafting.

Cochrane review in 2005 of skin grafting for venous leg ulcers revealed 9 randomised trials which were described as being of poor methodology. They concluded that a bilayer artificial skin used with compression increased the chance of healing a venous ulcer.

In 2007, Abisi (BJS) reported that wide local excision and meshed skin graft benefited 55% of patients with refactory ulcers. Recurrence was most likely to occur in the first 2 months.

Autologous platelet gel.

Blood is centrifuged (Magellan, Boston Scientific) and platelets extracted. Fibrin is added. The platelet concentrate has high levels of multiple growth factors.

Surgery.
ESCHAR study (n = 500), surgical correction of superficial venous reflux followed by compression bandages reduced the 12 month ulcer recurrence rate from 28% to 12% when compared to compression alone, but there was no effect on healing rate. 12 month mortality 10%. 20% of patients in the surgical arm refused surgery. Ulcer recurrence at 12 months is 15% with surgery and bandaging, 34% with bandaging alone. NNT = 5. No benefit for surgery in those with total deep reflux and segmental superficial reflux (Lancet June 2004). At 4 years recurrence rate in the surgery group was 31% vs. 56% in the compression group.

In another study, the ulcer recurrence rate was 38% with compression alone and 9% in those who had surgery plus compression after 3 years and healing rates were improved with surgery. (EJVES April 2003).

Direct surgical repair of deep venous valves. Small numbers in any series.
Kistner – valve repair
Raju – supravalvular approach.
Surgical treatment of superficial venous disease results in inmprovement in deep venous disease in 30% of patients. So only in the resence of deep venous occlusion is superficial venous surgery contraindicated.

Venous transposition and valve transplant – axillary or brachial valve

Procedures for venous obstruction:
- Venous bypass
- Cross pubic bypass- Palma Dale procedure. Patency aided by AV fistula and anticoagulation. Fistula ligated after 6 months
- Ileocaval or femorocaval bypass – patency aided by fistula
- Venous angioplasty plus stenting.

In patients with combined superficial and deep vein incompetence standard varicose vein surgery reduces deep vein reflux (Coistek EJVES 2004). This is less likely to occur with post thrombotic damage.

Cochrane reviews:
Surgery for deep venous incompetence – Ligation and limited anterior plication produce moderate improvement for patients with mild to moderate deep venous incompetence secondary to primary valvular incompetence. However there is insufficient evidence to recommend this treatment.
Horse chestnut seed extract for chronic venous insufficiency – efficacious and safe in the short term for treatment of CVI.

Chronic venous obstruction.
Best treated with endovascular stenting.