The ageing of the blood supply and the lymphatic drainage of the skin

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Abstract
The anatomy and functions of the blood and lymph vessels of human skin are described. Variation in these due to site, ageing and events during life consequent to exposure to a threatening environment are emphasised. Gradual atrophy and greater heterogeneity are features of ageing. Responses to injury and repair are complex and the interaction of mechanical signals distorting skin cells with numerous chemical signals are referred to. The lymphatics are part of an immunosurveillance system to monitor skin barrier penetration. The review attempts to draw attention to key recent advances in our understanding of the cytokine and growth factor production of the skin in the context of previous mainly physiological reviews especially influenced by 50 years of clinical practice as a dermatologist with an eye on both the skin and the fields of microcirculation and lymphology.

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1. Introduction
This brief patho-physiological review will focus on the interaction of the blood vessels and lymphatics of the skin with the organ they supply and drain against a background of accumulating effects of endogenous and exogenous injury. A full review of the vast increase in biochemical knowledge of how blood vessels and lymphatics behave must be read elsewhere. Cines et al. (1998) in one of many such, write about the physiology and pathophysiology of endothelial cells in vascular disorders to which this review adds a dermatological perspective with the skin as its focal point and Singh and Swerlick (2003) can be read to provide the view of a contemporary North American skin biology perspective. Previous reviews over several decades (Ryan, 1966, 1973, 1976, 1978a,b, 1993, 1995a,b) are valid since they address several aspects that are not now state of the art but include information on anatomy, blood flow, inflammation and blood rheology that are no longer the focus of research but aid interpretation of contemporary observations. The role of blood supply unpinning

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thermoregulation including arterio-venous shunting and the effects of cold injury, to which the elderly are so susceptible, was covered in those earlier reviews. The observations of blood vessels in animals, including man, skin windows and the detailed studies using the electron microscope are unlikely to be repeated or surpassed. The significant advances of today are all about cytokines and growth factors, or nitric oxide and other mediators of vessel function identified during the last few decades, but they need to be interpreted on the basis of what was discovered in earlier days. This review will therefore provide a perspective on the relevance of earlier studies on the vasculature in old age. These newer mediators have yet to be comprehensively focussed on a role in ageing.

The skin is not a homogeneous organ. There is too much regional variation in its structure and function and the ageing processes are a determinant of increasing heterogeneity with the passage of time. It is important to understand that the function and adaptations of the blood vessels and the lymphatics take place in both a physico-mechanical and a chemical environment and this interaction will be especially emphasised in this review.

1.1. Functions and structure of the skin affected by ageing

The functions of the skin are to communicate by display, protect and repair, thermoregulate and to perceive touch itch and pain. These are compromised by ageing. The rosy cheeks of youth give way to the pallor and patchy telangiectasia of old age. Senile pruritus and burning legs or ischaemic pain trouble the elder’s sleep. The grossly thin skin over the shin tears easily and repairs with difficulty. When exposed to extreme environmental temperatures the elderly vessels show a reduced capacity to constrict dilate or shunt. The skin failure that is so common in old age presents as pressure ulcers in the prone and leg ulcers in the upright and as ischaemic toes in diabetes mellitus or in atherosclerosis.

In old age there is an overall tendency for atrophy especially of the upper dermis but it is punctuated by patchy hypertrophy as in ‘cherry’ angiokeratomata (Fig. 1) or in the blood supply of keratoses or in the repair of frequent minor injuries. Throughout life, the response of the vasculature to growth stimuli and repair is seen in wounds but also in the cyclical regeneration and regression of the life of the hair bulb in the dermis or in the rich blood supply and later regression of the lactating breast. There are diseases such as psoriasis and skin cancer in which angiogenesis may be prominent in all age groups. There are also ‘birth marks’ such as the port wine stain or strawberry naevus subject to their own pattern of growth and regression with the passage of time. Thus ageing of the skin vasculature produces changes in structure. These can be detected by direct vision of that organ when they are still very small; an advantage less available for internal organs.

1.2. Endogenous and exogenous auxiliary factors contributing to ageing

A study of skin blood flow over the deltoid in the age groups of both sexes from 20 to 72 years showed a fall of 40% and this was significantly associated with a high blood cholesterol and a low blood pressure (Tsuchida et al., 1996). Ashimaoui et al. (2002) using laser Doppler technology found that the elderly had lower basal blood flow and considerable impairment of maximal blood flow even when the effects of high blood pressure or cholesterol were excluded. They believe that ageing carries a risk of endothelial dysfunction.

The passage of time leads to changes which alone are attributed to ageing. These same effects are enhanced by some additional influences such as exposure to ultraviolet irradiation, or, in the legs, to the effect of gravitationally induced venous hypertension, and to the accumulation of scars from repetitive injury. Smoking contributes to loss of elasticity of the skin and exaggerates wrinkling besides it’s other effects on the cardiovascular and respiratory system. Noble and Clough (2002) observed that pressure-induced hyperaemia over the skin of the sacral region was much
reduced in smokers. In a recent study, examining age, sun exposure, and smoking, destruction of elastic tissue was related to age and sun exposure in both sexes but telangiectasia was predominately acquired by males. (Kennedy et al., 2003) Thus it is that the worst effects of ageing are seen in the skin of the lower leg in the smoking sun exposed, perhaps obese, white skinned Texan or Australian, who is employed in an occupation requiring prolonged standing. Maybe diabetes mellitus will add to his or her accelerating problems of old age. Hormonal factors must explain why telangiectasis is more prominent in the facial skin of men although some protection may be provided by the greater use of cosmetics in women (Kennedy et al., 2003). It has long been known that some angiomata (spider naevi) are oestrogen dependent, and disappear in old age. Oestrogen receptors have a role in vessel growth and regression of cutaneous haemangiomata (Sasaki, 1987) and the thinning of the skin, which in older females can be 80% (Tan et al., 1982) can be reversed by oestrogen therapy (Brincat et al., 1987). Of course, some elderly look young for their years, even beyond three score and ten, having protected themselves or because of their genetic make up. Genes are a major determinant and their effects are seen in those who have a biochemical defect such as Albinism or Xeroderma Pigmentosum or in syndromes of progeria, (Pesce and Rothe, 1996). The therapeutic application of steroids is another common hormonal cause of transparency due to its atrophic effect on the upper dermis.

1.3. Anatomical changes attributed to ageing

The distribution of the capillaries and the initial lymphatics is determined by the needs of the tissues supplied, which is mostly epithelium. The pattern of perpendicular blood capillary loops draining into a horizontal venular plexus lies mostly immediately superficial to the initial lymphatic network of vessels (Fig. 2). In normal young skin there are approximately 60 loops to every cm². With aging there are many less loops, the upper dermis is thinned and may be transparent so that a poorly supported and dilated subpapillary plexus is visible to the naked eye of an observer (Fig. 3). Pearse et al. (1994) reported a 40% reduction of papillary loops in the forehead and 37% in the forearm and since the exposed skin of women may be thinned by up to 80% (Tan et al., 1982) a diminution in demand and of the support of its vasculature can be no surprise. In the foot, atrophy of the vasculature is less a feature than great heterogeneity with, in one study of 17 subjects with a mean age of 70 years (Lamah et al., 1996) some areas having low numbers and others having higher than expected capillary density, The adnexal structures such as the hair follicles, sebaceous glands and sweat apparatus, atrophy at different rates. Thus, atrophy associated with baldness can occur early in the genetically predisposed. Even the regression of blood supply of the antler, which plays such a significant role in seasonal shedding, is worth revisiting (Goss et al. (1964) as an indication of the role of the deep dermis as a stimulus to a vascular bed when it meets epithelial invaginations.

The skin includes adipose tissue which has projections into the dermis around the sweat coil and the hair bulb. It is well endowed with blood capillaries but not by lymphatics, which are found passing deeply through the septa with the arterioles supplying the dermis and the veins that drain it (Ryan and Curri, 1989). The adipose tissue also shows increasing heterogeneity with ageing (Fig. 4) much of it showing gender differences and the effect of sex hormones. This affects its function as a determinant of body shape, pressure dispersal as in the palm, sole, or buttock and as insulation. In each of these functions, blood supply participates. When it ages, body shape, thermoregulation and pressure from weight bearing are all casualties. The vasculature of the breast also is a special model of growth and atrophy, which, like adipose tissue, merits a review to itself (Ryan and Curri, 1989).
1.4. The response to irritants and to wounding

The weal and flare response to the inoculation of histamine varies with both age and site (Tur, 1983) as does the response to the inoculation of saline (Aschner, 1960) and in old age a diminished response has been observed to stripping the skin with sellotape, to the application of irritants to the skin surface (Grove et al., 1981) and to the initiation of blisters (Grove et al., 1982), the fluid of which is derived from blood vessels and the size of which can be influenced by factors controlling vascular permeability. Gilchrest et al. (1982) showed that ageing diminished the response to the damaging affects of ultraviolet light usually measured by the intensity of the erythema, the most often used test of the therapeutic effectiveness of agents protecting against sun burn such as tocopheral and ascorbate. But Podda and Grundmann-Kollmann (2001) considered that inhibition of erythema as an end-point for measuring oxidative damage as inappropriate. There are chronic alterations in structure, which explain why old skin may not manifest erythema. Sandblom et al. (1953) inflicted 5 cm incisions in the forearms of volunteers aged 22–87 to demonstrate that the mechanical properties of the healed wound were impaired in the elderly. Since this observation, in vivo ultrasound analysis has revealed the importance of the water content in the upper dermis as a factor in its pliability, resilience and elasticity (Gniadecka et al., 1994a) (Fig. 5). The redistribution of water and diurnal variation must be taken into account especially in the elderly (Gniadecka et al., 1994b) and at sites of mechanical stress such as the sole of the foot (Ryan et al., 2001) and this depends as much as anything on the exchange between blood vessels and lymphatics (Ryan, 1995a,b). Strigini and Ryan (1996) examined the healing of a 3-mm annular wound on atrophic skin of exposed sites in women aged 55 and over. They assessed its blood supply using a scanning Laser Doppler and video microscopy. Blood supply was maximised using topical nicotinate since this had been previously shown to reveal an enhancement of blood supply after the prescription of Retinoids (Kligman et al., 1986). The study included measurements over a period of three months of the effects of the application of topical tretinoin (a known anti-ageing agent) compared to vaseline. Both these agents promoted a significant improvement in resting blood supply. Resting temperature measurements at the surface of the skin correlated with resting blood flow. Maximal blood supply improved only in the tretinoin treated legs. In such legs their was a visible increase in upper dermal capillary vessels later confirmed by histology. In another study, lymphatic flow was also increased by the application of retinoids to the skin (Kaiser and Ryan, 1991). One must be aware that where skin is thinned technologies measuring from the surface will have increased depth awareness and furthermore technologies seeing only blood columns will not record empty vessels (Ryan, 1985). Such vessels can be filled for counting by local obstruction to outflow (Ryan, 1985). Histological confirmation of the above can be informative. Strigini and Ryan (1996) also found a reduction in arteriolar supply as previously demonstrated by Braverman et al. (1990); Pasyk et al. (1989) but in the thinned skin of elderly lower legs that have experienced lifelong gravitational stresses the hypertrophy of the walls of venules complicates identification.

1.5. The interplay of mechanical stresses with chemical mediators

The endothelial cell responds to the mechanical forces of blood pressure and flow by regulating vascular tone and by shape change. There are rapid changes in
the passage of ions, calcium concentration, and the release of many of the agents normally made by this cell (Davies, 1995); adhesion proteins and grip and stick (Ryan, 1990) have proved of especial interest for the skin (Ryan, 1989). Some variation in flow and blood pressure is age related, but for the continuously exposed skin external pressures and shearing forces complicate the interpretation of age related pathology. The capillaries become less well supported by the epidermal rete ridges and dermal connective tissue, and senile purpura tears and pressure ulcers are a consequence.

In earlier reviews (Ryan, 1973) the clear relationship between the range from atrophy to hypertrophy of blood vasculature to the range in size shape and demands of epithelial tissues was emphasised. It was proposed that angiogenic factors were released as a by-product of growth injury and repair. Their effect depended on ease of passage through ground substance, activation of receptors, and the confounding effect of other cell systems such as macrophages the Mast cell or melanocyte. The balance of activators and inhibitors of plasminogen was one system investigated (Ryan et al., 1971). During the last decades the discovery of the role of the eicosanoids cytokines and growth factors has demonstrated just how rich is the productivity of the epidermis and the responsiveness of the endothelium.

1.6 The lymphatic system

The lymphatic system has long been known to remove macromolecules and to be an essential route for the traffic of the immune system but exactly how it responds to the cytokine system and the full effects of its failure are only now becoming clear. This has been stimulated by the discovery of genetic influences and cytokines and receptors specific for the lymphatic, reviewed by Mortimer and Browse (2003). The grotesque effects of lymphatic failure on the behaviour of the skin shown in Fig. 6 has previously stimulated little interest.

The extent lymphatic vessels atrophy with age has similarly received little contemporary interest but a review by Huth (1983) referred to many studies that emphasised a greater density and wider lumen in youthful subjects and mid-20th century confirmation by anatomists that involution of lymphatics occurs with age. Since sclerosis and varicosity of the main lymphatic trunks was well documented by these authors it would be surprising if there were not a knock on effect on the lymphatics of the skin. To function effectively the lymphatic endothelial cell is sensitive to the deforming stresses of the movements of the tissues so essential if lymph is to be encouraged to enter the lymphatic and then to flow along it. In healthy skin, this is helped by the snap back provided by a closely applied and appropriately orientated elastin fibre network (Fig. 7) (Ryan and De Berker, 1995). The orientation of elastin in the upper dermis allows it to take up some of the strain in an expanded upper dermis and to restore it rapidly to its normal width. The replacement by more inflexible material as in elastosis (Fig. 8) provides rigidity instead of pliability and elasticity. Age related changes are much associated with overload of the lymphatics by a failing venous system (Mortimer and Browse, 2003; Vaqas and Ryan, 2003).

1.7 VEGF—a key player

Currently the angiogenic factor produced by the epidermis that excites most interest is Vascular Endothelial Growth Factor (VEGF). There are several variants and several receptors (Ferrara, 2000). The epidermis produces especially a form that is a very potent Vascular Permeability...
Factor. One effect, therefore, is an outpouring of serum from the papillary loops, an expansion of the upper dermis and a consequent stretch effect on the endothelium (Fig. 9; Ryan, 1995a,b, 2003). Indeed, in the upper dermis any other permeability factor such as the secretions of the Mast cell or the prostaglandin generation by the epidermis may have the same effect. Some have supposed (Dvorak, 1986) that the inflammatory effects of leakage of proteins and of fibrin cuffing of blood vessels is one explanation of the angiogenesis induced by VEGF. The role of mechanical forces as a transducer of biochemical signals also has especial relevance for the endothelial cell. It has to be sensitive to the shear forces of flow and to high blood pressure due to its siting in the blood vascular bed. More recently, the study of transgenic mice producing VEGF without its permeability inducing properties casts doubt on the significance of the permeability effect (Eliceiri et al., 1999) as a requirement for angiogenesis. But a distinction has to be made between embryonic and neonatal growth and the needs of repair in the adult.

Studies of the life cycle of the hair follicle (Yano et al., 2003) show that the angiogenesis needed to support it is due to VEGF production. As the hair regresses there is downregulation of this stimulus. At the same time, thrombospondin upregulation provides strong vascular inhibition. Thrombospondin plays a role in the regression of granulation tissue, a requirement for completion of wound healing.

The new technologies available for studying human skin include its transplantation into immuno-compromised mice and then the intradermal injection with different adenoviral vectors inserted with different genes coding for growth factors cytokines, proteolytic enzymes and their inhibitors, adhesion receptors, oncogenes, and tumor suppressor genes (Gruss et al., 2003). Such technology has drawn attention to a role for plasminogen activator in the regulation of VEGF expression. The role of the epidermis in producing the inhibitor of plasminogen activator and its possibly greater production in adult rather than in foetal or new born skin was proposed many years ago as an explanation of the gradual loss of flexibility and increasing skeletal rigidity of ageing (Ryan, 1989).

Vascular regression in ageing must examine the field of tumour research into the key survival factors for endothelium. This is a complex field and the contributions of dermatologists studying the resolution of benign angiogenesis in psoriasis may have more relevance to ageing (Bhushan et al., 2002; Creamer and Barker, 1995). The induction of inhibitors wherever there are activators, and the presence or absence of receptors for either, are explanations of complexity. Apoptosis of endothelial cells is clearly relevant to ageing. VEGF induces the expression of anti-apoptotic proteins in human endothelium (Gerber et al., 1998). Also, from skin laboratory new technology, tissue engineered endothelialized dermis is promoted as highly efficient for assaying angiostatic as well as angiogenic compounds in vitro (Hudon et al., 2003). The field of angiogenesis has to be distinguished from that of vasculogenesis which is the initiation of vasculature. Angiogenesis is more concerned with maintenance of mature vessels. It requires interaction with angiopoietins and in order to establish lymphatics additional receptors must evolve of which VEGFR-3 is currently deemed the most important (Burnand and Mortimer, 2003).

1.8. The neural control of blood flow

The common observation that the elderly develop oedema of the lower leg towards the end of the day is explained in part by the poverty of the postural venoarteriolar reflex. Healthy young adults when changing from a supine to a standing position have a fall in limb blood flow due to constriction of the arterioles, which thus protects the capillary bed from overfilling. Without this baroreceptor reflex, due to the influence of gravity the venous system overfills (Tanner et al., 1989). This causes excessive leakage of blood giving rise to the diagnostic sign of venous disease likely to lead to ulceration, which is pigmentation from
haemosiderin especially above the medial aspect of the ankle (Fig. 10). This reflex is mediated by the sympathetic nervous system, which becomes less responsive in the elderly, who, as in younger persons with diabetes mellitus, show a high resting blood flow but an impaired neural control of flow. They can neither vasoconstrict when the leg is lowered nor vasodilate when minor injury requires an increase in blood supply for repair. The defect can be demonstrated by such stimuli as forced expiration or placing ice on the nape of the neck as well as changing posture from the supine to the prone (Gniadecka et al., 1994c). Disturbed blood flow regulation is particularly severe in those who are prone to leg ulceration (Junger et al., 1996).

Impaired responses to neural stimulus can also be explained by the effect of fibrosis causing increased stiffness of the tissues (Gniadecka et al., 1994a–d); a mechanical restraint to distensibility more marked in the lower leg (Mridha and Odman, 1985) that makes it difficult for vessels to respond. Both blood vessels and lymphatics lose elasticity as elastin becomes replaced by collagen.

1.9. The chemical control of blood vessels

The reduction of vascularity in the skin of old age could be due to a lesser stimulus from the epidermis and this could be a consequence of less production, greater inhibition of or a reduction of receptors, but also due to the above mentioned stiffness of the vessel wall much of this control of vascularity is chemically mediated, but physico/mechanical factors such as the above mentioned tissue stiffness (Daly and Odland, 1979), or changes in the diffusion properties or thickness of the ground substance, have also to be considered. The most obvious difference between atrophic and hyperplastic blood supply is the distance the vessels are to be found away from the epidermis (Fig. 11). There are reports on changes in the composition of glycoaminoglycans with ageing so that their binding to elastin is impaired (Bernstein and Uitto, 1996); an
impairment of the interstitial pathway into the lymphatic could be one consequence (Ryan and De Berker, 1995) with a consequent accumulation of agents promoting fibrosis.

1.10. The skin as a surveillance organ

One affect of ageing, that is partly the consequence of impaired vascular function, is that the skin at the interface with the environment is less able to recognise threats, destroy them if they penetrate its barrier and repair that barrier when breached. The epidermis is largely anaerobic and its blood supply at rest is not rich but in youth after injury, it can increase blood flow some 200-fold through local axon reflex neural stimulus. If as in many wounds a sustained increase in blood supply is required then a new organ, granulation tissue, must be formed. It must also be removed before the functions of the skin can be fully resumed. The recognition and effective elimination of foreign agents followed by repair, requires recruitment of white cells and consequent control of their passage out of the blood vessel and in the case of the T cell into the lymphatic. Within the epidermis, supporting its barrier function, there are in addition melanocytes and Langerhans cells. The necessary recruitment of inflammatory cells and the significance of leukocyte adhesion during inflammation or the role of endothelium in cell-mediated immunity have been extensively reviewed. It is only relatively recently that the richness of epidermal production of cytokines for the control of all this has been identified. Also to be taken into account is the fact that this behaviour is clearly modified in certain diseases such as psoriasis and atopic eczema. Even in extreme old age, the high rate of epidermal cell turnover in psoriasis demands angiogenesis (Ryan, 1980; Creamer and Barker, 1995; Bhushan et al., 2002). On the other hand the wound healing needs of a scratch in atopic dermatitis is poorly served by the characteristic pallor such a scratch induces in that condition, although this is less a feature in old age (Ryan, 1991).

1.11. Antigen presentation, memory and dermal microvascular endothelial cells

White cell traffic into the lymphatic and from thence to the lymph node requires preferential route taking from the epidermis by the Langerhans cell. Relative to the size of the cell this is a long way to travel and in sun damaged elastotic dermis, this is not straightforward. It also requires the usual stimuli for flow such as movement of the tissues. Impediments of these are featured in lymphoedema and in conditions such as leprosy (Ryan, 2002). On the other hand, evidence of greater utilisation of the system is seen in the lymphadenopathy of the eczematous child or in the high frequency of multiple allergies in those ulcers of the leg due to venous hypertension. The poverty of the immune system in old age may be in part due to atrophy of its largest organ the skin and loss of low resistance pathways into the lymphatic system such as along the elastin fibre. Not surprisingly elastosis is correlated with a greater propensity to develop epidermal malignancy and a lower propensity to develop contact dermatitis. Grewe (2001) reviews the ageing of the immune system and like most authors sees the atrophy of the dendritic cell as its most significant feature; a failure of migration to the lymph node is suggested. Most authors blame the cell itself for this rather than the poor state of the pathway favoured by this reviewer (Ryan, 2000).

In old age the loss of the papillary loop and the increased distance of the blood vessel from the epidermis must be an impediment to such reactivity. Functionally the lymphatic pathway may be supposed to be similarly less easily accessed. The widely dilated vessels lying deep to a flattened epidermis show little white cell reactivity compared to the outpourings of white cells from the peaks of the papillary vessels once termed ‘the squirting papilla’ (Pinkus and Mehregan, 1966).

Most attention has been given to cell traffic function rather than to pathways, but the anatomy of the skin points to the importance of the preferential channel or open doorway for white cells from the vascular lumen to the epidermis, as well as, more problematically, how cells carrying information acquired in the epidermis find there way to the lymph node as quickly as possible without getting hung up or lost on the way.

Diminished immunity may be due to a poverty of cell reaction or due to reduction in the numbers of cells carrying out the following functions. As a response to foreign antigen dermal microvascular endothelial cells upgrade their surface proteins to encourage the adhesion and hence recruitment of circulating T cells. Poher et al. (2001) emphasise that this is rapid and effected by the presence of high levels of class I and class II MHC molecules, as well as the narrow lumen of the upper dermal postcapillary venule ensuring contact with T cells. Further more it is clear that the production and release into the upper dermis of several cytokines such as INFγ determines such behaviour. Some of the co-stimulating systems are better developed in the human. Thus, the LFA-3 (CD58) signal used in humans is lacked by rodents. It is also of relevance to human skin function that the production of IL-12 and IL-4 by damaged epidermis helps to differentiate specialised TH-1 or TH-2 function in T cells brought to the skin by endothelial cells. Poher et al. (2001) review also the role of the Mast cell which is so significant a player in the vascular response to injury immediately the skin is injured. Thus histamine enhances blood flow and speeds the arrival of the leucocyte and then hastens the process of adhesion and passage into the tissues, all of this being further enhanced and prolonged by the addition of TNF and IL-1 richly provided by a damaged epidermis. T cell responses of the skin are dominated by TH-1 responses explained by a cutaneous lymphocyte antigen-1 (CLA-1) that binds to E-selectin VCAM-1 and ICAM-1 present on dermal endothelial cells. This process is absent on umbilical endothelium but otherwise little is known about different age groups. The focus of certain diseases affecting the epidermis depends in part on the phenomenon of epidermotropism whereby cells are delivered direct to the epidermis from a closely applied and activated endothelium.
1.12. Oxidant stress

One of the strongest influences on ageing is deemed to be damage from free radicals. In the vascular system, much has been written about ischaemia and reperfusion for internal organs such as the kidney but later its importance for skin survival and its possible role in vasculitis was emphasised (Cherry and Ryan, 1976). Damage from ischaemia destroys some free radical inhibitory and quenching systems making tissue susceptible to further damage from oxygen free radicals on reperfusion. At the capillary level in the skin, blood flow is characterised by frequent stops and starts. The phenomenon of vasomotion, that characterises blood flow in disease, exaggerates this. It is postulated that factors impairing blood flow such as venous hypertension inflame partly through free radical formation. In the skin, melanin is one significant quencher often present in cells exposed to free radicals. In some skin conditions melanin deposition and changes in the vascular bed are seen together as in poikiloderma.

Age related chronic diseases, such as diabetes mellitus, arthritis and neurodegenerative diseases show accumulation of advanced glycation end-products that are one consequence of free radical damage. As a consequence there are deleterious changes in the charge, hydrophobicity, turnover and elasticity of collagen and the above mentioned properties of endothelium with respect to permeability and white cell adhesion (Baynes, 2001). Much of the age related changes occur in the larger blood vessels but cross linking of collagen and thickening of the basement membrane is seen in the small vessels of the dermis. Elastin fibres are fragmented by the age related process. In diabetes, glucose mediated cross-links decrease the flexibility and permeability of the tissues. Thus chemical reactions are mediated in part through mechanical influences on the vascular system.

A review of the vasculature of the skin that focuses on ageing must bring together the interests of the skin specialist and of the angiologist and record the state of their ‘art’ not just as of now, but where still relevant, what has been recorded over previous decades. Neither the state of the art nor the skin itself is ever completely static. Both shifts in emphasis under pinning dogma, and in the amount of movement experienced by the skin, are worthy of long term study.

References


