Characterisation and Treatment of Patients with Port Wine Stains with Special Reference to the Emotional Impact

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"Nothing has so marked an influence on the direction of man's mind as his appearance, and not his appearance itself as much as his ***conviction*** *that it is attractive or unattractiv".*

~ Tolstoj ~

CONTENTS

LIST OF PUBLICATIONS

The thesis is based on the following papers, which will be referred to by their Roman numerals:

I. Troilius A, Wårdell K, Bornmyr S, Nilsson GE, Ljunggren B. Evaluation of port wine stain perfusion by laser doppler imaging and thermography before and after argon laser treatment. Acta Derm Venereol 1992; 72: 6–10.

II. Troilius A. Ljunggren B. Reflectance spectrophotometry in the objective assessment of dye laser-treated port-wine stains. Br J Dermatol 1995; 132: 245–250.

III. Troilius A. Ljunggren B. Evaluation of port wine stains by laser doppler perfusion imaging and reflectance photometry before and after pulsed dye laser treatment. Acta Derm Venereol 1996; 76: 291–294.

IV. Troilius A. Svendsen G. Ljunggren B. Ultrasound investigation of port wine stains. Acta Derm Venereol. Accepted for publication September 13, 1999.

V. Troilius A. Wrangsjö B. Ljunggren B. Potential psychological benefits from early treatment of port-wine stains in children. Br J Dermatol 1998; 139: 59–65.

VI. Troilius A. Wrangsjö B. Ljunggren B. Patients with port wine stains and their psychosocial reactions after photothermolytic treatment. Submitted for publication August 1999.

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ABBREVIATIONS AND EXPLANATIONS

ALA	Delta amino-levulinic acid
CO_2	Carbon dioxide
CNS	Central nervous system
CVL	Copper vapour laser
CW	Continuous wave
FDA	Food and Drug Administration, USA
Fluence	The amount of energy delivered per unit area (J/cm^2)
Hb	Haemoglobin
He – Ne	Helium – Neon
Irradiance	The rate of energy delivered per amount of skin surface (W/cm^2)
IPL	Intense pulsed light source
J	Joule
LDI	Laser doppler imaging
nm	nano meter, (10^{-9} meter)
Nd: YAG	Neodymium: Yttrium Aluminum Garnet
HbO_2	Oxy-Haemoglobin
PDL	Flashlamp pulsed dye laser
PDT	Photodynamic therapy
PWS	Port wine stain/s
SD	Standard deviation
t_r	Thermal relaxation time (in seconds is about equal to the square of the target dimension in mm)
W	Watt = J/cm^2 = power = the rate at which energy is delivered

BACKGROUND

History of vascular birthmarks

The human mind cannot easily accept random mischance as a cause when a child is born with a birthmark. It is sometimes impossible to regard the imperfection as a mere misadventure. European folklore believed that children so affected were born of some improper behaviour either at the time of conception or during pregnancy *(Mulliken et al, 1988)*. *Maternal impression* means that an influence on a mother's emotions can affect her child's phenotype. In many cultures people believed that certain rituals performed in association with conception could influence either or both parents in a way that would be reflected in the physical characteristics of the offspring. In the Bible *(Genesis, chapter 30)* Jacob increased the number of rare spotted goats and sheep in his herds by standing tree branches, with the bark partly removed so that they too appeared spotted, in the water troughs of the breeding animals. This concept can be traced to antiquity originating independently among peoples of widely separated cultures. There remains an ancient Hebrew legislation prohibiting coitus during or immediately after the period of impurity, because according to folk tradition, PWS are due to conception having taken place during the menstruation *(Rosner, 1983)*. Medieval witch hunters regarded unusual markings on the body, including birth marks as the port wine stains (PWS), as conclusive evidence that the suspect had been branded into servitude by the devil *(Robbins, 1959)*.

Vascular birthmarks were often found on the face and scalp and was attributed to the pregnant woman's tendency to touch these locations in a gesture of fright, and therefore they were warned not to look upon the scene of an accident or slaughter of an animal. The Chaldeans of ancient Babylonia regarded birthmarks and other birth defects as divine omens. In their writings specific congenital disorders were linked to certain predictable outcomes in a dependable "if – then" formulation. For example, a woman gives birth to a child who has "branches of flesh" on its head (probably a hemangioma), "there will be ill-will" and the family will perish. Another theory is that the red birthmark could be a sign of divine preference or blessing; hence the term "angels kiss". This notion *(imaginatio gravidarum)* that mothers imprinted their babies, smouldered along in the Middle Ages and forged into medical doctrine with the revival of learning in western Europe *(Mulliken et al, 1988)*. The 16th century French surgeon Ambroise Paré wrote that some of his contemporaries thought that beyond the 42nd day after conception it was not possible to affect the appearance of a child through the "mother's imagination", as the infant was fully formed. Although for safety's sake women should be protected throughout pregnancy from the sight of deformities. Also, if the pregnant mother was frightened by the sight of her husband with a bloody wound on his face, the baby was certain to be born with a red birthmark on its face. This public scepticism continued and is depicted in art and literature to this day. Finally, a Dr JA Blondel (1666-1734) challenged this concept of maternal impression and wrote a booklet, denying this phenomenon, that had a great effect on medical opinion throughout Europe *(Mulliken et al, 1988)*.

Yet, the doctrine of maternal impressionism flourished in the nineteenth century up until today, although it has slowly decreased with the help of the spreading of knowledge and modern medical literature. The explanations of different cultures vary widely, but all grew out of the same need. The family and the affected persons had to have a way to account for the occurrence of something that marked them so distinctively.

According to Fletcher *(1978)* the name *"port wine stain"* (PWS) arises from English novels and medical writings from the early eighteenth century until the Second World War, when large quantities of their beloved port were consumed in England. In 1687 a ban was placed on French wines, and instead they discovered the sweet, fortified deep red wine "Red Portugal" from Oporto in Portugal. Some PWS look as though the skin had been discoloured by wine and together with the superstition that the mother had a craving for port, the name remains hallowed in our medical lexicon.

In a study of current opinions about the cause of facial deformities, maternal impression was considered an etiological factor only in cases of PWS, in contrast to other facial deformities e.g. cleft lip and prognathism. 50/200 women from Wales believed in an interview that a PWS is related to maternal consumption of strawberries or red cabbage, to an unsatisfied craving for such food, or to contact with blood during pregnancy *(Shaw, 1981)*.

Although the treatment of PWS has improved dramatically with the development of newer techniques and lasers, many patients have been and are denied the opportunity for treatment by the (at least earlier) unfortunate classification of this treatment as a cosmetic procedure.

Classification of vascular birthmarks

The terminology of vascular anomalies has been and still is very confusing for many. This has caused misdiagnosis and mismanagement. In 1976, Mulliken and Young initiated an International Workshop for the Study of Vascular Anomalies. Biennial meetings were held in either a European or an American City. A renaissance began with the "biological" classification proposed by Mulliken & Glowacki in 1982. Now we were able to both accurately diagnose congenital vascular lesions and understand their natural history. In 1992 the organisation was formalised as the International Society for the Study of Vascular Anomalies (ISSVA) and a nosologic consensus was established. The general definition of "anomaly" as any vascular condition that was abnormal was accepted. In the Workshop in Rome, June1996 the ISSVA classification was accepted by the membership (Table I.). Vascular tumours (hemangiomas) and vascular malformations were the two major categories of superficial vascular anomalies. The malformations are classified as simple or combined, where the latter is a combination of the different components (capillary, lymphatic, venous or arterial). They never regress and are comprised of dysplastic vessels, without endothelial proliferation. As an example, CVM

Table I. The ISSVA classification of superficial vascular anomalies. (F = fistula)

Tumours	**Malformations**		
Hemangioma	**Simple**		**Combined**
	Capillary	(C)	AVF, AVM, CVM, CLVM
Others	Lymphatic	(L)	LVM, CAVM, CLAVM
	Venous	(V)	
	Arterial	(A)	

stands for a capillary and venous malformation (Table I.). This was based on clinical and vascular features, natural behaviour, hemodynamic characteristics and biological differences *(Enjolras et al, 1998).*

Classification of capillary malformations—port wine stains (PWS)

PWS are the most common *(Mulliken et al, 1982)* of the capillary malformations.

Waner & Suen *(1999)* classify capillary malformation in accordance with their degree of vascular ectasia because they consider this to be the true cause of variation in clinical appearance. The use of a 6× magnification and transillumination is recommended:

Grade I is the earliest lesions with the smallest vessels (50–80 µm in diameter). Clinically they are light or dark pink macules. (Fig. 1A).

Grade II is clearly distinguishable macules which are more advanced (vessel diameter = 80–120 µm) with individual vessels, which are clearly visible to the naked eye. (Fig. 1B).

Grade III is reddish macules but more ectatic (120–150 µm) with the large end of the vessels visible. (Fig. 1C).

Grade IV is usually thick, purple and palpable and may eventually coalesce to form nodules (cobblestones). The dilated vessels are the most advanced (>150 µm). (Fig. D–E).

This grading system may help us to communicate when we discuss e.g. treatment modalities.

See examples of the grading system Fig. 1.

Waner & Suen *(1999)* consider them to be composed of postcapillary venules within the papillary plexus and therefore they consider the term "venular malformation" more appropriate. However, it would create confusion to change terminology without the consensus of the ISSVA, therefore I will in this thesis refer to capillary malformation (PWS).

Incidence and heredity

PWS are observed in 0.3–0.6 % of all newborn infants, and the male to female ratio is 1:1

(Jacobs et al, 1976. Osburn et al, 1987), but according to a large study of the population of Tokyo, the reported frequency was as high as 2.1% *(Hidano et al, 1986)*. One of the reasons for this higher figure could be that they included PWS smaller than 5 mm in diameter. PWS are found in all races, although they are more visible in individuals of Caucasian and Asian ancestries. Vascular malformations are true developmental abnormalities that are believed to result from a sporadic, non-familial developmental error in the formation of vascular tissue *(Mulliken et al, 1982)*. Psayk et al *(1992)* reported, however, the pedigrees of 2 families with multiple PWS or nevi flammei in various areas of the body. This indicates a possibility of an autosomal dominant inheritance. Also Mills et al *(1997)* demonstrated in a demographic study of 283 patients with PWS a higher prevalence of PWS in relatives than expected in the population.

Clinical appearance and development

PWS are usually present at birth, although they may not always be apparent until a few days later, because of the usual erythema of the neonatal skin. The PWS is a flat macula of different sizes, usually sharply demarcated and grows proportionately with the child. It can be homogenous, but also *geographic* (scattered) with normal skin in between the macules (Fig. 1B–C). The colour is usually pink, but with age it can become deep red to bluish red with sometimes a more hypertrophic surface. A PWS will not involute spontaneously. They occur in 83% of the patients in head and neck area and the V2 (trigeminal nerve) dermatome is the most commonly involved *(Waner et al, 1999)* and according to Barsky et al *(1980)* there are twice as many right-sided (58/100 patients) as left-sided.

Fig. 1A. A child with a PWS Grade I before and after 4 PDL treatments.

Fig. 1B. A girl with a geographic PWS Grade II before and after 5 PDL treatments.

Fig.1C. A woman with a geographic PWS Grade III before and after 2 PDL treatments. The hypopigmentations are caused by earlier treatments.

Fig. 1D. A woman with a PWS Grade IV before and after 9 PDL and 2 IPL treatments and a partial upper lip excision.

Fig. 1E. A woman with a rare cobblestone PWS Grade IV after excisions, 1 PDL treatment, 4 IPL treatments and 1 CO_2 treatment. She will receive treatment with a long-pulse 532 nm laser with a chilled tip.

In a study of 310 PWS (*Tallman et al, 1991*), 68% had more than one dermatome involved; 85% had unilateral and 15% had a bilateral distribution of their PWS. Extensive involvement (trunk, extremities, head and neck) was observed in 12%.

Pyogenic granulomas can develop within a PWS without any known trauma *(Swerlick et al, 1983)* and have the potential to bleed spontaneously. In our experience, the incidence of pyogenic granulomas seems to be lower in those patients who have been treated with lasers.

Pregnancy may be the inciting factor for the development of a vascular tumour arising in a PWS during pregnancy and regress partially following delivery *(Rumelt et al, 1999).*

Histology and innervation

The aetiology of PWS is unknown, but Barsky et al *(1980)* consider them (> 7 years of age) to probably represent progressive ectasia of a once normal vascular plexus and this ectasia would progress with advancing age causing the PWS to darken, became hypertrophic and sometimes even acquire cobblestone appearance. According to Geronemus et al *(1991)* two thirds of the 415 patients with PWS developed nodularity or hypertrophy in the fifth decade of life. This may take place at any point in the development of an individual's lifetime, however the most dramatic changes are noted as the patient becomes older. There is a risk of spontaneous bleeding and haemorrhaging upon injury to the affected area, e.g. men with PWS on bearded areas. In the periorbital area the visual field can be inhibited by a hypertrophic PWS. There are no differences in vessel number, but there is an altered or even absent neural modulation of the vascular plexus *(Smoller et al, 1986)* with a decrease of both sympathetic and sensory innervation of the papillary plexus *(Rydh et al, 1991).* Lesions with a relative deficiency of autonomic innervation will give rise to a slower progress than the lesions with an absolute deficiency that will progress more rapidly with an earlier hypertrophy and even a cobblestone formation.

Histology evaluation has demonstrated the highest amount of vessels in the immediate subepidermal area and then dropping quickly in number as the depth increases *(Barsky et al, 1980).* A mean vessel depth of 0.46 mm (±0.17) has been found.

The mean vessel diameter increases from 16.5 µm in pink lesions to 51.2 µm in purple *(Fiskerstrand et al, 1996).*

Immunhistochemical studies have shown that there are no abnormalities in the PWS vessel wall compared to normal vessels, regarding collagenous basement membrane-type IV collagen, fibronectin and factor VIII *(Finley et al, 1982. Neuman et al, 1994).*

Nevus flammeus

The Latin appellation for PWS is *nevus flammeus* and it connotes the superstition that the mother was frightened by fire during pregnancy *(Mulliken et al, 1988).*

Nevus flammeus (nevus flammeus neonatorum or nevus simplex) has been collectively used to describe both a) midline capillary malformations (salmon patch, stork bite or angel's kiss) and b) often non-midline capillary malformations (port wine stains) although the former often fade within the first year of life. Also the midline capillary malformations (light pink macula often V shaped) almost never progress as common PWS do. Probably, they have ectatic postcapillary venules on the basis of delayed innervation of the plexus by the autonomic nervous system *(Waner et al, 1999).*

Acquired port wine stain

This is a rare vascular lesion that mimics a congenital PWS clinically, but is acquired after birth. The aetiology is unknown, but in a number of cases precipitant factors such as trauma

(Colver et al, 1995) to the perivascular neural elements resulting in ectatic dermal vessels, hormonal changes *(Brinkman et al., 1981)* and medication *(Goldman, 1970)* may contribute to the development.

Psychosocial impact on the patient and his/her family

Until recently, relevant studies on the psychosocial effects of vascular lesions in young children were few. Kalik et al *(1981)* failed to find noteworthy differences between the adult patient sample and normative sample with psychological test instruments, but concluded that among their sample the PWS had been a source of stress and psychological burden. The severity of distress expressed is sometimes out of proportion to the degree of the disfigurement that the patient actually has, but the patient feels "different". Harrison *(1988)* views any birthmark in a child of any age to be able to give significant life stress and have a stage-specific impact on both child and family. Lanigan et al *(1989)* revealed a high level of psychological morbidity from a feeling of stigmatisation although their standard psychological screening tests for psychiatric illness, depression and anxiety reported a similar or less evidence of morbidity than controls. Malm et al *(1988)* demonstrated after interview with 13 patients that those who had a large PWS had a reality problem in common and those with small PWS demonstrated great individual psychological problems. There was a need for a larger study with special questionnaires.

Later Augustin et al *(1998)* found a negative psychosocial influence on the PWS patients and so did van der Horst et al *(1997)*.

In a study of 46 parents of children, with facial PWS receiving PDL treatment, an average range for psychological stress were reported, but some (11%) did not fare as well as others (*Miller et al, 1999*). They recommended health care providers to be prepared to screen for clinical levels of distress and to refer parents for psychological intervention when needed.

Clinical investigation

Pre-treatment consultation

Inspect and palpate the PWS. Ask the patient or the parent whether the red mark was congenital or not. In an infant the differential diagnose is hemangioma, but usually hemangioma is not present at birth and they progress during the first year of life.

The physicians always need to be well aware of and appreciate the psychological and social aspects of body image when they meet their patients and their families. To inform the patient and his/her family about the natural development of a PWS and realistic expectations of the laser treatments is extremely important and this information should be repeated during the treatment sequence, and also be given both orally and in writing. The patients should never be promised a total clearance of their PWS. If patient are old enough to understand the information, they should decide themselves, maybe together with their family, whether they want to be treated or not. The risks considering a possible general anaesthesia should also be discussed and test treatments should be offered. If the patients seems to be emotionally unstable (which is rare), maybe one should consider a psychological consultation. If the PWS are facial, the patients should be informed about the possibilities of camouflage make up, which could be used when needed, during and after the laser treatments.

Medical syndromes connected to port wine stains

No other investigation is needed to diagnose a PWS, except when they are a hallmark of a more complex anomaly. PWS on the bilateral trigeminal area or on both upper and lower eyelids, have a higher risk of eye and/or CNS complications *(Tallman et al, 1991)*.

In **Sturge Weber's syndrome,** PWS is situated on the first branch of trigeminal nerve with choroidal and ipsilateral meningeal involvement *(Paller, 1987. Roach, 1988. Bebin et al, 1988)*. This could cause congenital glaucoma of the ipsilateral eye *(Cibis, 1987)*, calcification and vascular anomalies of the brain, associated seizure disorders, and in some cases mental retardation. MRI is then recommended so that future epileptic seizures can be prevented. There is also 45 % risk of developing glaucoma if the PWS involves both the dermatome V1 and V2 and/or the eyelid *(Barsky et al, 1980. Mulliken, 1988)*. Every child with eyelid involvement should therefore undergo tonometry at 6 month intervals until age 3 years and then yearly.

Other connected syndromes are **Klippel Trenaunay syndrome**, which includes a PWS on a limb with hypertrophy and venous varicosity with sometimes an increased length due to bony growth *(Stern, 1983)*.

If the patient has a PWS within a dermatome of the spine that is affected by an arterio-venous malformation it could be the rare **Cobb's syndrome** *(Jessen et al, 1977. Mercer et al, 1978)*.

Photographs

Photographs provide an inexpensive way of recording PWS before and after treatment, but there are many problems. They are limited by their dependence on inconsistent factors. Even when every attempt is made to standardise photographic settings, such as the same camera, film, lighting and magnification, human colour perception can still be variable and very subjective *(Bjerring et al 1987)*.

Magnetic resonance imaging (MRI)

MRI is the most informative investigation in that it can determine the extent of a vascular lesion with a high degree of accuracy as well as distinguish between the different types of malformation, but it is usually not necessary in the investigation of a PWS. It is indicated only if you suspect e.g. meningeal involvement.

Reflectance spectrophotometry

The destruction of the vessels and the resultant blanching after PDL is a gradual process, which sometimes can be difficult to assess accurately visually. Reflectance photometry is a useful and non-invasive technique that can measure skin redness and pigmentation objectively. It provides a read out of the erythema and melanin figures as a function of the absorbance characteristics of human skin. A portable hand-held reflectance spectrophotometer consists of a light source, a photodetector and a microprocessor. The instrument emits both green and red light (568 and 655 nm) and detects the intensity of the reflected light. When there is increased blood content, resulting in erythema, a greater amount of green light is absorbed and less reflected.

The skin reflectance-determined change in skin redness has been proven to objectively correlate with clinical response in 12 children with PWS after 1 PDL treatment *(Haedersdahl et al, 1998)*.

Laser doppler imaging (LDI)

LDI provides simple, non-invasive means of measuring cutaneous blood flow in the microcirculation *(Nilsson et al, 1989)*, in various dermatologic lesions including PWS *(Serup, 1995)*. (See Fig. 1, Paper I, The principles of LDI). It creates an image of the superficial tissue perfusion distribution. LDI consists of an He –Ne laser scanner, computer system and a code plotter *(Wårdell et al, 1993)*. According to Jiang et al *(1998)* LDI can reflect the degrees of PWS objectively before and after photodynamic therapy (PDT).

Colour measurements

Colorimetry allows for the objective and quantitative measurements of colour. It has been used in e.g. determining skin types *(Elsner, 1995)*, UV-induced erythema *(Westerhof et al, 1986. Pickering et al, 1992. Takiwaki et al, 1994. Elsner, 1995*) as well as measuring PWS response to laser treatment *(Neumann et al, 1991. Pickering et al, 1992, Takiwaki et al, 1994, van der Horst et al, 1998)*. Tristimulus colorimeters (Minolta Chromameter,Minolta,Osaka,Japan) and the Micro Color (Dr.Bruno Lange, Dusseldorf, Germany) *(Elsner, 1995)* generate results similar in efficacy to reflectance spectrophotometers *(Takawaki et al, 1994)*, but also have similar limitations in the test area *(van der Horst et al, 1998, Westerhof et al, 1986)*, cost and blanching with instrument contact *(Pickering et al, 1992)*.

Thermography

Many forms of vascular malformations can dissipate substantial amount of heat. Patrice et al *(1985)* considered it to be useful in the prognosis of the outcome of argon laser therapy of PWS.

Skin ultrasound

Ultrasonography has been shown to provide accurate and reproducible dimensional measurements of structures within dermis and subcutaneous tissue *(Harlan et al,1993, Nielsen et al, 1993,Serup et al,1995, Rippon et al, 1998)*. This technique has also revealed lower dermal echogenicity preoperatively in 12 children with PWS than of postoperatively PDL treated PWS and healthy skin *(Haedersdal et al, 1998)*. An increase in echogenicity reflected a decrease in the dermal water (blood) content. Variations were found in the dermal localisation of the their PWS. There was no correlation between the change in echogenicity and the clinically assessed treatment response and neither could they detect any relation to the initial lesion colour.

Videomicroscopy

Videomicroscopy is a microscope, which is, connected to a video camera making it possible to view the superficial vessels in the skin in a non-invasive way. Computerised set-ups also allow for analysis of capillary morphology and bloodflow. According to Motley et al *(1997)* there are two types of microvascular abnormalities. Type 1 consists of superficial, tortuous, dilated end capillary loops (blobs) which are readily treatable with PDL and type 2 is composed of dilated, ectatic vessels in the superficial horizontal vascular plexus (rings) which are more deeply situated and do not respond as well to the PDL. Videomicroscopy relies on qualitative assessment rather than quantitative, objective measurements. It is useful in characterising PWS in research setting, but is limited in a clinical setting due to its large size and technical difficulty in classifying PWS morphologies.

Treatments of port wine stains

Therapy before the laser era—results and side effects

Until the advent of argon laser the PWS was considered to be essentially untreatable. From the beginning a frequent therapy was **vaccination** in and around the PWS or injection of the **"hospital pus"** *(Goldwyn, 1983).* Treatment techniques have included the most inappropriate applications of radiation, either by **external radiotherapy** or the application of **thorium X** *(Braun-Falco et al, 1975)* or **radioactive phosphorus** *(Roe et al, 1955).* At best this appeared to have had no particular benefits, and at worst these applications may have been responsible for the malignant changes, radiodermatitis and bony hypoplasia which authors have seen in previously radiated PWS *(Hliniak et al, 1966. Li et al, 1974).* Other treatments have included **Bucky (=Grentz) ray, sclerosing agents, cauterisation, cryo therapy, carbon dioxide snow, liquid nitrogen, cortisone, protamine, heparin locally and systemically, obliteration by ligature of vessels, ultraviolet and infra red radiation and dermabrasion** *(Goldwyn, 1983).* Frequently these techniques have replaced the PWS with scarring and pigment changes. In many cases some of the red colour was only replaced by disfiguring scars.

Tattooing the PWS with masking pigment has been tried, but does not seem to have been widely practised or with much success *(Conway, 1965*) and it is not recommended today, when we have the expanding development of vascular lasers.

Even with **surgery** by rotation of flaps, excision and skin grafting, it has been difficult to achieve a natural texture and colour of the skin *(Grabb et al, 1980).* In lesions located in the face, post-surgery scarring is not acceptable.

Cosmetic camouflage

Both men and women with PWS very often have a need to conceal their PWS. Its application is time-consuming and not always successful or appropriate. Nowadays, make up artists are very skilled in covering facial defects in a more natural way and they can teach patients how to do it themselves. In a demographic study of 283 patients with PWS (217 females) cosmetic camouflage was used in 38.5% of patients, who usually had PWS on the face (94%), of whom only 16% had received advice of its use *(Mills et al, 1997).* It has been estimated that only one-third of patients uses special make up and many of those who do use make up are distressed to be seen by others without this protection. Such infrequent use and apparent lack of efficacy of camouflage make up, may be explained by the low number of patients who had received professional advice. Since laser removal of PWS is often prolonged and the results incomplete, patients should be counselled on the availability and use of camouflage, which can then be used during and after treatments.

History of the development of medical lasers

At the turn of the century, scientists were faced with a dilemma related to the electromagnetic energy emitted or absorbed by an object that acts as an absorber *(Itzkan et al, 1997).* In 1905 Max Planck made the assumption that electromagnetic energy could exist in small packets, or "quanta" and these packets of electromagnetic radiation are now known as *"photons".* Niels Bohr proposed that absorption and emission were related to an atomic model in which electrons orbiting the nucleus jumped from one orbit to another within the atom. The various orbits possessed different energies, and the frequency of the light, or photon, multiplied by Plank´s constant was equal to the difference in the energy of the orbits. In 1917 Einstein postulated a third effect, *"the stimulated emission",* whereby an atom in an excited state is forced to emit its energy in the presence of a photon of the correct frequency. Einstein's work is sometimes cited as the birth of the laser, but he did not discuss the nature of the stimulated photon. A fully satisfactory theory of quantum electrodynamics was not available until the 1950s, when Feynman, Schwinger, and Tomonga shared the Nobel prize for this work. Shortly after World War II the sophisticated microwave (developed for wartime radar) was available for scientific research and in 1958 Schawlow and Townes (Nobel laureates) proposed the idea of building an "optical maser" (an acronym standing for *m*icrowave *a*mplification by stimulated *e*mission of *r*adiation) which today is known as the *laser (Itzkan et al, 1997)*. . Laser is an acronym for "***L**ight **A**mplification by the **S**timulated **E**mission of **R**adiation*".

Most of the lasers now used in medicine were first operated in the decade between 1960 –1970. The first ruby laser came in 1960 and a few years after the He-Ne laser. The Nd: YAG laser came in 1964 together with the CO_2 laser and the first organic flashlamp pumped dye laser in 1966 *(Sorokin et al, 1966)*.

In the 1960s Leon Goldman and his colleagues started the era of laser dermatology *(1966)* with preliminary studies of the skin with the help of a CO_2 laser *(1971)*. He was later called "The father of laser medicine in the United States " and in 1979 he became one of the founders of the American Society of Laser in Medicine and Surgery still in existence.

In the early 1980s controlled studies on the use of argon laser to treat port wine stains were conducted by Noe et al *(1980)*. Many therapeutic methods have been used to treat PWS and most of these methods (including older lasers) have been abandoned due to ineffectiveness or adverse effects such as scarring. In 1983 the important work on selective photothermolysis by Andersson and Parrish was published. Since then, rapid development have provided lasers that could be coupled to an optical fiber, efficient detectors and detector arrays and advanced computers for control of medical instrumentation. The medical and surgical applications of lasers and intense pulsed light sources (IPL) have continued to progress along several lines including research, diagnostics and therapeutics.

Basic concepts of laser light and its effect on tissue

Laser technology has now reached a point where we routinely use high-energy lasers to perform treatments that were impossible some years ago. It is very important to have a practical understanding of laser-tissue interaction .

All effects of light begin with the absorption of electromagnetic radiation (EMR), which is a fundamental form of energy that exhibits **wave** properties. This wave is caused by alternating electric and magnetic field. The energy is carried in quanta, known as **photons.** EMR is absorbed by matter through interactions with charged particles such as electrons or the partial separation of charges in molecules called dipoles *(Anderson, 1999)*.

LASER = *L*ight *A*mplification by *S*timulated *E*mission of *R*adiation

Atoms and electrons are normally in a "resting state". If an electron absorbs the energy of a photon of light, the electron is raised to an "excited" state. This "exicted" electron can give up its energy by emitting a photon of light energy identical to the photon that was initially absorbed. If an "excited" electron absorbs a photon of light energy, this electron may emit two photons of light energy while the electron returns to the resting state (=stimulated emission of radiation). Repeating this innumerable times generates a powerful laser beam

(Hruza, 1999). Absorption and excitation are necessary for all photobiological effects and laser tissue interactions.

A lasing medium can be either gaseous, liquid, solid crystal or semiconductor. The external energy source can be electrical, chemical, flashlamp or light from another laser.

Properties of laser light

(Castro, 1992)

I. Monochromaticity: All of the light is of a single wavelength determined solely by the laser medium present in the optical cavity. The wavelength allows for selective absorption of the laser light by specific chromophores such as melanin, haemoglobin or tattoo ink present in the skin.

II. Coherence: The synchronicity in time and space of the photons emitted from lasers is called coherence. It implies that the passing waves have nearly identical and parallel wavelengths with low degree of divergence. Therefore, there is no significant loss of intensity *(Dover, 1990)*.

III. Collimation: This is the same as parallelism of light as a direct result of coherence. It allows the beam to propagate across long distances along optical fibers without beam spreading.

IV. Brightness (intensity)**:** Extremely high power can be generated with lasers due to the tremendous amplification process available in the laser cavity.

Laser-tissue interaction

According to Rox Anderson *(1999)*, there are several interactions of light, where two of the most fundamental are absorption and scattering:

I. Absorption occurs when the photon surrenders its energy to an atom or molecule, known as a **chromophore.** The absorption spectra of major skin chromophores dominate most laser-tissue interactions in dermatology. The photon cease to exist and the chromophore become excited and may undergo photochemistry or may dissipate the energy as heat or reemission of light. Blood absorption is dominated by absorption of oxyhemoglobin and reduced Hb, which inhibits strong band in the UV, blue and green and yellow bands, with absorption peaks at 418, 542 and 577 nm (Fig.2). Melanin, in epidermis and in the hair follicles, is the major chromophore and it absorbs broadly across the optical spectrum (320–1200 nm). Therefore the pigmented epidermis could be a barrier to the photons and cause significant epidermal damage leading to non-specific thermal injury *(Anderson, 1999)*.

II. Scattering is when the photons change direction. The light that is returning from the skin is scattered light and a strong scattering contributes towards reducing the optical penetration depth *(Anderson et al, 1981)*. Optical penetration into dermis is largely dominated by the scattering caused by collagen fibers. Because light scattering in the dermis decreases with increasing wavelength, greater light penetration is achieved at longer wavelengths. Back scattering may actually increase the power density of the laser beam. Forward and sideways scattering will attenuate the power density of the incident beam with depth.

III. A **reflection** of 4% of the incident irradiation can be caused by the different refractive indices of stratum corneum and air *(Andersson et al, 1981)* and will give no clinical effect.

IV. Light can be **transmitted** through the target tissue such as the dermis without any clinical effect. In white epidermis the transmission of light increases from about 50% at 400 nm to 90% at 1200 nm *(Andersson, 1999)*. Less than 20% throughout the visible spectrum will be transmitted in black epidermis. For

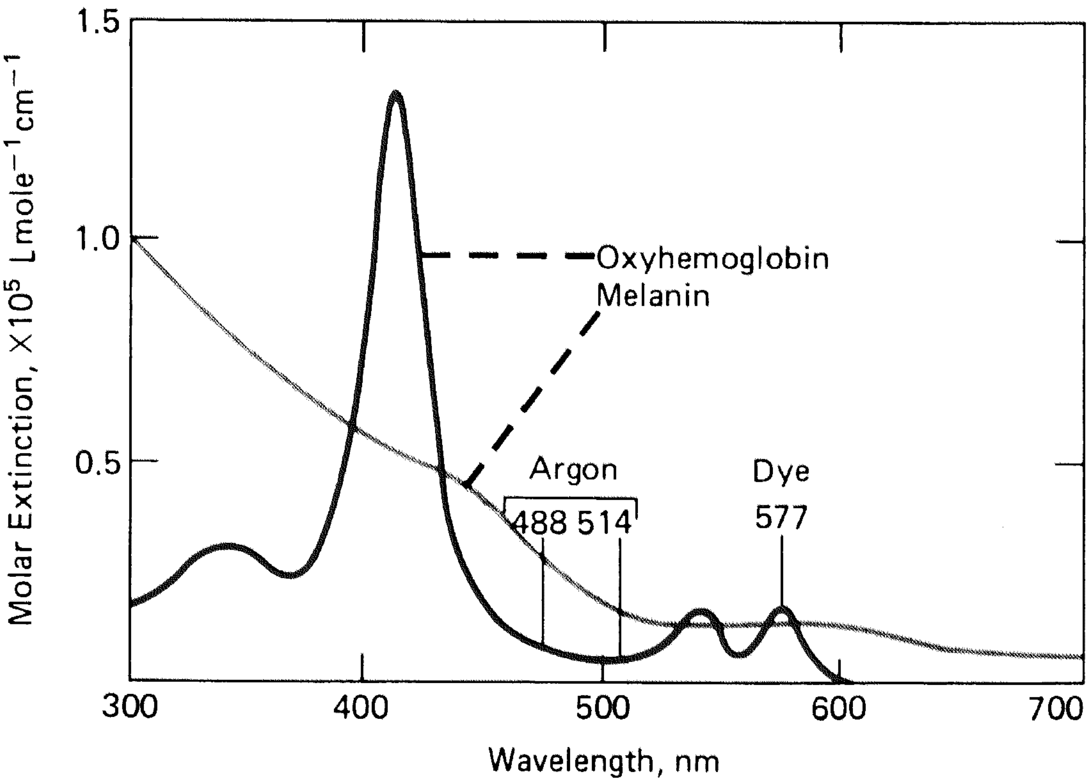

Fig. 2. Absorption spectra of haemoglobin and melanin with the emission spectra of the argon and dye laser superimposed (Wheeland, 1988).

wavelengths <600 nm (with the high absorption of haemoglobin and melanin) there will be hardly any transmission of visible light in dermis.

Cooling devices

Cooling of the epidermis before laser treatment has been shown to enhance the treatment effect of e.g. the PDL, with a decreased incidence of non-specific adverse sequelae, deeper laser penetration and minimised treatment pain *(Nelson et al, 1995)*. Patients with darker skin, type III–IV, experienced less pain when pre-cooling was compared with the PDL alone *(Waldorf et al, 1997)*.

Different cooling devices combined with laser treatment may allow higher energy fluences to treat deeper located vessels while protecting the epidermis and superficial dermis by cooling e.g. variable pulse width frequency doubled Nd: YAG *(Dummer et al, 1998)*. Other therapeutic modalities that have tried epidermal cooling are e.g. intense pulsed light system (IPL), long pulsed ruby systems, alexandrite and diode lasers.

Timing the cooling spray so that the dermal vessels are not cooled as well, has proved to be difficult and if the dermal vessels are cooled, a higher fluence is needed to produce the same clinical effect as that produced without cooling. Improved efficacy has not been clearly established and therefore the cryogen spray-cooling device is only approved by the FDA for pain relief (1998).

Previous and present laser treatments and their results

Decades ago, treatment options for most vascular lesions were either unavailable, ineffective or unacceptable. Laser treatment of PWS began in 1963 *(Solomon et al, 1968)* with the ruby laser, which was the first laser available). Continuous wave lasers were the first and they produced non-selective thermal damage. Because of this, they are associated with a high risk of scarring and therefore treatment success is highly dependent on the surgeon's expertise and judgement of appropriate patient selection. However, recent advances in laser technology have revolutionised the treatment, providing effective and safe treatment. See Table II.

Ruby laser

The majority of the initial laser treatments of PWS were performed with the ruby laser, although the main chromophore at this wavelength (694 nm) is melanin. The insufficient vascular damage that Salomon et al *(1964)* demonstrated in their studies was due to poor absorption in haemoglobin. Ruby laser is no longer suitable in the treatment of PWS.

Carbon dioxide laser (CO_2)

Although it has no specific absorption of blood, the continuous mode of CO_2 laser has been used earlier to seal off vascular network in the superficial dermis in PWS *(Ratz, 1984; Buecker et al, 1984.)* This laser has a wavelength of 10600 nm and the infrared light is absorbed by water and causes a non-specific vaporisation, which is usually only useful in the treatment of nodular PWS. They can be sculpted down to re-establish a normal skin contour with the help of a short pulsed CO_2, then the PDL can lighten the remaining stain *(Fitzpatrick et al, 1994).* The CO_2 lasers are no longer used for macular PWS.

Argon laser

This laser produces blue/green light at 488 nm and 514 nm, which is well absorbed in both haemoglobin and melanin (Fig.2). When the argon laser was developed in the early 1970s it was a major advance in the treatment of PWS and good to excellent results were reported *(Noe et al, 1980, Gilchrest et al, 1982, Lanthaler et al, 1984).* But soon, the severe side effects were discovered with substantial scarring and pigmentary changes, especially in patients younger than 12 years old *(Dixon et*

Table II. Lasers for vascular lesions.

Lasers	Wavelength (nm)	Colour	Type (CW or pulsed)
Argon	488–514	Blue-green	CW
Argon dye	577–630	Yellow-red	CW
KTP (Potassium titanyl phosphate)	532	Green	Pulse train
Q-switched Nd:YAG (frequency doubled)	532	Green	20 ns
Nd:YAG (frequency doubled)	532	Green	1–15 ms
Krypton	521–532–568	Yellow	CW
Cu vapour, Cu bromide	578	Yellow	Pulse train
PDL	577–600	Yellow	450 µs, 1.5 ms

al, 1984). The pigmentary changes are probably caused by the rather high absorption of the 488 nm and 514 nm light in melanin, resulting in a transient temperature rise in the melanin-pigmented epidermis. Histology has demonstrated coagulation necrosis of the entire epidermis and thermal injury to the papillary dermis *(Finley et al, 1984).* Furthermore, the pink PWS, did not respond well to the argon laser, only the dark red-blue lesions. Therefore, today continuous wave lasers as the argon laser, are used for effective shrinking of nodules or smoothing out cobblestone surface in PWS.

Potassium titanyl phosphate laser (KTP)

The KTP laser (a former Nd: YAG laser) with 532 nm has been used in conjunction with a scanner to treat adults with PWS. The best clearing was seen with 3- or 5-ms pulses at 15 or 20 J/cm^2 *(Apfelberg et al, 1976).* Since the pulse duration has been lengthened to 1– 50-msec the KTP lasers are now reported to be equivalent to the CVL or 577 CW dye laser for the treatment of vascular lesions *(Routteleur et al, 1991, Keller 1992).* Histology has demonstrated this laser's capability of selective closure without haemorrhage *(Dierickx et al, 1996).*

Neodymium: yttrium aluminum garnet laser (Nd:YAG laser)

This is a solid state laser with a wavelength of 1064nm, which is in the invisible near infrared light. It is poorly absorbed in water, haemoglobin and melanin and consequently the optical penetration is much deeper (4–6 mm) than other lasers. The vessels are destroyed anyhow because of the non-specific damage of coagulated tissue and therefore the laser has been used to treat thick nodular PWS *(Rosenfeld et al, 1988),* with reported good results, which is remarkable with the relative high risk of scarring there is with this kind of technique.

By passing the Q-switched Nd: YAG laser through a potassium diphospate crystal, its frequency is doubled, and the wavelength is halved from 1064 to 532 nm. This shorter wavelength is well absorbed by red and together with a long pulse and a chill tip to protect epidermis. This laser has been effective in treating even PDL resistant PWS (See Material and Methods). With longer pulse durations, but within the thermal relaxation time of the vessel, purpura is avoided without loss off efficacy. Dummer et al *(1998)* reported significant success already after 1or 2 treatments of 42 PWS, of which 40 had earlier been treated with argon or argon-pumped dye laser. Also, our experience with this modality has been promising.

Krypton laser

The two green bands of 520 and 532 nm are filtered out yielding a beam of 568 nm when treating vascular lesions. The energy can be delivered in a manner identical to the argon dye, cu vapour and Nd:YAG lasers using a tracing technique or a robotic scanner. To my knowledge no reports are published of PWS treatment results with this laser.

Copper vapour laser (CVL)

Although the wavelength of 578 nm is selective for oxygenated and deoxygenated Hb in ectatic blood vessels, significantly epidermal melanin absorption occurs when used at energy fluence necessary to thermocoagulate these vessels. Since each 20-ns pulse is far shorter than the thermal relaxation time of even the smallest vascular ectasia, a single pulse does not deliver enough energy to heat a vascular lesion to the temperature required, producing injury. The microspot tracing technique using the argon pumped tuneable dye laser has also been reported to be a successful technique in the treatment of vascular lesions. However multiple treatments are needed and many lesions do not completely resolve *(Scheibner* *et al, 1989. Waner et al, 1991).* Many have tried to combine CVL with e.g. argon laser, PDL or a scanner, but although successful in some PWS, there is little reproducibility between patients. Also, a high degree of adverse sequelae may occur when treating PWS with CVL, because the long pulse times allow excessive thermal diffusion and may result in tissue damage beyond the targeted vessel *(Goldman et al, 1999).*

Selective photothermolysis—the flashlamp pulsed dye laser (PDL)

The PDL was constructed after the laser light parameters needed for selective destruction of PWS had been determined. Since its approval in 1986 by the FDA, the PDL has gained acceptance due to its efficacy, ease to use with a low risk of complications.

Selective photothermolysis is by far the most precise use of heat in all of medicine. The theory states that selective heating is achieved by preferential laser light absorption and heat production in the target chromophore, when the pulse duration is shorter than the thermal relaxation time of the target *(Anderson et al, 1983).* This theory focused attention not only to the wavelength, but also the pulse duration and the need to limit thermal diffusion by keeping the laser pulse shorter than the time necessary to allow heat to spread from the treated target (for PWS, red blood cells within vessels) to surrounding tissue or t_r = **thermal relaxation time.** t_r is defined as the approximate time for the increase in the vessel core temperature to drop to one half of its peak value *(Anderson et al, 1981).* Larger objects lose heat much slower than small objects. For most chromophores in the skin this time is determined only by the size of the object, e.g. the t_r for PWS vessels that have a 50–100 micrometer diameter is a few milliseconds. The importance of delivering the laser energy within the vessel's thermal relaxation time is extremely important.

Since the late eighties the treatment of choice has been the PDL (see Material & Methods) with its minimal risk of side effects, safetyness and efficacy also in children *(Seukeran et al, 1997).*

Ideal laser parameters are not the only ones that can be used effectively. An experienced laser physician can often achieve good results with a less-than ideal tool, and poor results are possible even with an ideal laser. Still there are some recommendations that can be made.

Ideal wavelength

The ideal wavelength should be near the maximum absorption of target chromophore where minimum competition from other chromophores is present and at a sufficiently long wavelength to penetrate to the depth of the target. Theoretically, this ideal wavelength should be the 577 nm because it maximises the blood absorption with relatively less absorption of melanin (Fig.2), but according to Tan et al *(1989)* the depth of vessel damage at the same fluence was increased when the wavelength was extended from 577 to 585 nm. According to van Gemert et al *(1992)* the maximum depth at which a vessel can be selectively coagulated is dependent on both the wavelength and the dermal blood content, which varies in individual PWS.

Ideal pulse duration

The pulse duration should be long enough to achieve irreversible damage to the vessel and short enough to avoid diffusion of heat out of the vessels into adjacent skin. Probably, it should be sufficiently long to conduct heat from the hot red blood filled lumen to the outer part of the vessel wall *(van Gemert et al, 1992).* Dierickx et al *(1995)* suggest that the pulse durations for ideal laser treatment are in the 1–10 msec region and depend on the vessel diameter. PWS contain vessels with different diameters and to destroy all vessels contributing to the colour of a PWS, the pulse duration must be varied from hundreds of microseconds to hundreds of milliseconds according to the dimensions of the targeted vessels. Some of the modern vascular lasers or IPL has this possibility today. Pulse duration longer than 20–50 μs is recommended to avoid vessel rupture.

Ideal spot size

Due to laser light sideways scattering in the skin, spot size does make a difference. With a small spot size sideways scattering reduces the energy fluence in tissue far more rapidly than is seen in large spot size. According to Tan et al *(1988)* a 5 mm spot coagulated vessels at greater depth than spots with 3 and 1 mm. van Gemert et al *(1995)* reported that the fluence rate distribution at spot diameters larger than 3 mm was about equal to that for an infinitely wider beam diameter.

Ideal fluence

The fluence required to induce permanent vessel damage varies. Therefore, the lowest fluence that produces best lightening after a PDL test is recommended. Subsequent laser pulses delivered to a single skin site can cause widespread dermal injury simply because the target chromophore is no longer confined to blood vessels. According to Anderson *(1999)* multiple lower fluence pulses that do not cause haemorrhage might be used to accumulate selective, gentler, and more complete damage to microvessels.

Depth of penetration

Generally there is a gradual increase of penetration depth and a decreased probability of photochemical reactions with longer wavelength *(Svaasand, 1991)*. However, the absorption of Hb differs at e.g. 532 nm where visible light travels deeper than at 577 nm, due to a lower absorption at the shorter wavelength *(Anderson, 1994)*.

Ideal skin type

The PDL is most effective on skin type I–III where there is less pigment *(Fitzpatrick et al, 1994)*. Skin type IV–VI has too much melanin in epidermis and therefore there will be less laser light accessible to the dermal blood vessels *(Lanigan, 1995)*. Darker skin has a higher risk of post treatment pigmentary changes *(Hohenleutner at al, 1995)*. The patients should be told, prior to, during and after the treatments, to avoid sunbathing.

Different models of PDL

Two manufacturers produce this type of laser. One is the Photogenica manufactured by Cynosure, Inc. (Bedford, MA, USA: Millennium VLS Dual Pulse) (See Material and Methods). Originally a wavelength of 585 nm was emitted with a pulse duration of 450 μsec, but now it can emit wavelengths of 590, 595 and 600 nm with a pulse duration of up to 1500 μsec. The beam profile can be elliptic at 3x5 mm or circular at 2, 3, 5, 7 and 10 mm in diameter. The maximal energy fluence that is available is 10–20 J / cm^2. The other PDL is Candela Corporation (Wayland, MA, USA) with their SPTL line of machines. The one difference between the two lasers is the beam profile and this is because of the gaussian distribution of beam output *(Castor, 1992)*. With the Candela a 10–20 % overlapping spot provides an even distribution of energy fluence *(Dinehart et al, 1980, Jackson et al, 1996)*. Another difference was reported when the 5-mm-diameter spot was compared in these two models. The Candela laser was up to 35 % larger than 5 mm, while the Cynosure laser was up to 8% smaller *(Jackson et al, 1996)*. These are important factors to be aware of before switching from one PDL machine to another.

The procedure of PDL

Multiple treatments (4–7) with at least 6 week intervals, are required to lighten or remove PWS by these lasers. Some PWS require far more than 7 treatments and in some cases as many as 25 have been tried to achieve the best possible clearance *(Kauvar et al, 1995)*. PDL treatment results in a short, mechanical "snap" from the laser pulse together with a sharp pain followed by a heat sensation. This discomfort is only lasting from a few seconds to minutes, but after multiple pulses this sensation is intensified. The following dermal bruise (purpura lasting and average of 5–10 days) and is often likened to the sensation of a mild sunburn. The level of discomfort or pain associated with the treatments is variable and is often tolerated by adults and adolescents in an office setting. Topical anaesthetic (EMLA 5%, lidocaine and prilocaine) under occlusive dressing 1–2 hours prior to treatment is offered and can reduce pain significantly *(Tan et al, 1992)*. However, there is transient paleness after EMLA application caused by vaso-constriction and whether the treatment out-come is affective by this or not, is not known. Office surgery can be performed safely when small lesions are treated, but for infants and children less than 10 years (individual varia-tions) with larger lesions general anaesthesia is recommended. According to Grevelink et al *(1997)* the risk and sequelae of general anaesthesia is minimal in their material (179 patients). Cold packs after the treatment or a group IV of a local steroid cream can relieve some discomfort, but also stop eventual thermal spreading.

Safety

Protective correct eye goggles are very impor-tant to wear during the laser treatments.

EMLA (lidocain, prilocaine and carbopol) cream is widely used as a topical anaesthetic before laser treatment. It should be used with extreme caution around the eye and probably should be avoided when there is a need to insert laser eye shields. Two patients developed corneal abrasion and conjunctivitis, consistent with chemical alkaline burns caused by the sodium hydroxide in the cream *(Eagelstein, 1999)*. EMLA is safe for use in children aged 3 months or older *(Enberg et al, 1987)*, but prolonged application or application over a large area may cause development of methemoglobulinemia. Therefore, EMLA should be used with caution on diseased skin or the mucous membranes of the groin.

There are now several reports of PDL ignitions *(Epstein et al, 1990. Bean et al, 1995)* e.g. if laser energy is absorbed by the melanin in a hair follicle or by other items within the surgical field (cotton fluff, oxygen 5 L/ minute by face mask). PDL induced fires can also occur on non-hair-bearing area and in patients receiving oxygen by nasal cannula *(Fretzin et al, 1996)*.

Recommendations for prevention of PDL induced fires:

- Remove combustible materials from the treatment area or moisten them with either water or saline.
- Shave hairy areas prior to treatment or keep them moist during treatment.
- No alcohol-based solutions should be used.
- During anaesthesia:
  - Oxygen should be used at the lowest possible concentration and never be directed toward the laser field.
  - Laryngeal mask leaks less oxygen than ordinary masks.
  - Endotraceal tubes should be wrapped in aluminium or copper tape and the cuff should be filled with saline instead of air.

Results after pulsed dye laser treatment

Often the standard of clinical evaluation has been highly subjective and semiquantitative. Nevertheless it has been used as the basis for drawing conclusions. According to Alster & Wilson *(1994)* a 79% of clinical improvement was seen after an average of 9 treatments, but treatment results have varied and a significant minority of patients will achieve only a suboptimal response. Katugampola et al *(1997)* reported 38% of excellent (at least 75%) lightening in 160 patients after a median of 8 PDL treatments. 52% of facial lesions of different colours achieved over 75% fading against 18% non-facial PWS. They considered the degree of fading variable and often unpredictable. They were using pre treatment photographic documentation to compare with. Tan et al, *(1996)* found that 78% had better than 50% fading of the PWS in 131 patients and 9% had less than 25% fading. Clinical features are influencing the outcome of treatment with PDL. Face and neck are responding better than e.g. the lower limb *(Renfro et al, 1993. Katugampola et al, 1997)* and the middle of the face and dermatome V2 (Fig. 3) *(Renfro et al, 1993)*. Significantly better results were seen in-patients who commenced treatment before 1 year of age, but also PWS < 20 cm^2 cleared better than > 20 cm^2, irrespective of age *(Morelli et al, 1995)*.

Waner & Suen *(1999)* suggest PDL treatment for PWS grade I–III (see Classification). Grade III–IV may need a copper bromide laser. PWS grade IV with its medium sized vessels can also be treated with a KTP laser with good results *(Waner et al, 1999)*. PDL are easier, faster and less user dependent than the copper vapour lasers and KTP lasers, but both the latter have improved with e.g. robotized scanner and are now easier to use.

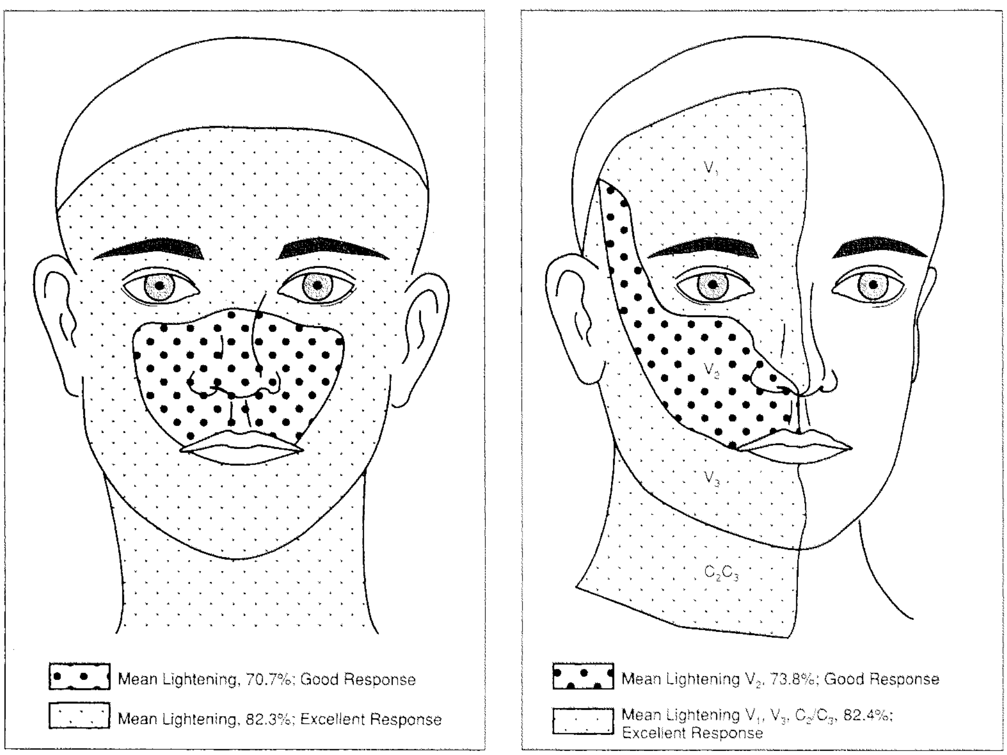

Fig. 3 A. Anatomic subdivisions of therapeutic response of PWS on adults and children after PDL treatment. B. Dermatomal distribution of therapeutic response of PWS on adults and children after PDL treatment. (From Renfro L, Geronemus RG: Arch Dermatol 129;182,1993).

The choice of treatment depends on the degree of ectasia (vessel diameter) and on the colour of the PWS. Fiskerstrand et al *(1996)* concluded that pink (small vessel size) and purple (large vessel size) PWS predict a poor PDL response due the deep locations and to the vessel size. Probably, these are some of the reasons for treatment failure with PDL. With this knowledge it is not surprising that certain PWS fail to respond to the fixed wavelength and pulse duration of the PDL.

In order to be able to compare and generalise the treatment results, similar grouping of patients' age, lesional colour and localisation of the PWS must be standardised.

Early treatment—pros versus cons

It has been hypothesised that children with their thinner skin and smaller sized PWS should need fewer treatments with the PDL than adults *(Morelli et al, 1992)*. The percentage of children achieving complete clearance of their PWS is considerably less than initially reported *(Reyes et al, 1990. Goldman et al, 1993)*.

Better results with early treatment were reported by Tan et al *(1989)* but were not unequivocally confirmed by others *(Garden et al, 1988. Achauer et al, 1990. Onizuka et al, 1995)*. In Alster's study *(1994)* infants and younger children did not need significantly fewer treatment in comparison to older children (>8 years of age) and adults. These studies were all retrospective, and none used objective measurements to assess the results. Van der Horst et al *(1998)* investigated in a prospective study 100 patients with PWS (age of 0–31 years). They were treated with PDL and the treatment result was judged with the help of a colorimeter. They found no evidence that PDL treatment is more effective in early childhood than at later age.

Different wave length

Newer generations of PDL with longer pulse width (1.5 –2.0 msec) and longer wavelength (590–600 nm) result in deeper photocoagulation with encouraging results. There is a higher risk of textural changes consisting of atrophy and hypopigmentation. These lasers are aimed at leg veins and not at deeper vascular malformations *(Hsia et al, 1997)*. A PDL with wavelengths including 600 nm showed superior lightening in 11 out of 22 PWS when wavelengths higher than 585 nm were used *(Wiegleb Edström et al, 1997)*.

Systemic effects

Photothermolysis of blood vessels does result in the release of free Hb into the circulation after PDL therapy. In a study of 15 patients with PWS (age 5 years or younger) serum haptoglobulin immediately before and after PDL was taken *(Barry et al, 1994)*. Also, hemosiderin in urine was collected within 2 hours after PDL. Their results indicated that although haemoglobinemia does occur after PDL treatment of PWS, the level of intravascular hemolysis obtained is not injurious to the infant or child with large cutaneous involvement.

Side effects during and after PDL

The PDL is generally considered to have a very low incidence of clinically visible adverse effects *(Fitzpatrick et al, 1994. Levine et al, 1995)*, but lately more side effects have been reported in larger studies *(Wlotzke et al, 1996. Seukeran et al, 1997. Fiskerstrand et al, 1998)*.

During the treatment a slight pain can be experienced. After the treatment a bluish colour is seen with some oedema and this usually resolves gradually during the week after the treatment. According to a retrospective study of 701 patients, blistering and crusting were seen in 5.9% and 0.7% respectively, but the lesions healed without permanent sequelae *(Seukeran et al, 1997)*. In this study the hyperpigmentation (9.1%) was the most frequently observed adverse effect, but generally showed a gradual resolution over 6–12 months. Fiskerstrand et al *(1998)* noted in a group of 125 Norwegian patients (mainly skin type II–III) 23 % hyperpigmentation with equal frequency during summer and winter. The facial regions did not exhibit higher occurrence than lesions located elsewhere. They suspected that it is not only the epidermal melanin content that is causing this problem, but also a constitutional disposition. The risk of post – treatment pigmentary changes is increased in dark skin *(Fitzpatrick et al, 1994. Aschinoff et al, 1992)*.

Hypopigmentation has been seen in1.0–1.4% and pyogenic granuloma in 1% *(Wlotzke et al, 1996. Seukeran et al, 1997)*.

There is a small risk of atrophic scarring (3–4.3%) with a predisposition for younger patients *(Wlotzke et al, 1996. Seukeran et al, 1997)*.

Hypertrophic scarring can also occur albeit rarely (0.7–1.0%) and there may be a predisposition towards the neck and upper lip, but most side effects were focal and transient *(Wlotzke et al, 1996. Seukeran et al, 1997)*.

Some side effects are caused by too high treatment fluences (6–8 J /cm^2), particularly on the neck, or too much overlapping of the spots. Another reason could be that the patient did not follow the post treatment care instructions. It has been noted with the help of skin reflectance and surface contour analysis that already after one treatment with PDL minor, subclinical adverse reactions (hemosiderin like hyperpigmentation and flattening of the skin structure), could be seen *(Haedersdahl et al, 1998)*. According to our clinical experience hypertrofic skin caused by e.g. radiation, is clearly improved after several PDL treatments.

Intense pulsed light source (IPL)

Technique

This is an intense pulsed light source emitting a continuous light spectrum with most of its energy fluence between 515 and 1000 nm. This non-laser apparatus with incoherent light has cut off filters, that allow selection of appropriate wavelengths of light allowing the fluence to be concentrated up to 1000 nm. This results in deeper penetration of the high intensity light. Single, double or triple pulses can be chosen with different durations (2–25-ms/ pulse) and pulse delays (2–100 ms). All settings are computer controlled to deliver the energy to a flashlamp *(Goldman et al, 1998)*.

Results

According to Goldman *(1998)* it is possible to treat PWS with this device. In a study 6 out of 32 PWS had a better response with this high-energy discharge lamp than with PDL *(Strempel et al, 1996)*. Further work is desired to define more precisely the optimal parameters when treating PWS with this technique.

AIMS OF THE STUDIES —QUESTIONS TO BE ANSWERED

1. How is the blood flow in the PWS in comparison to normal surrounding skin and how is the perfusion effected by argon laser treatment? Is the blood flow a predictive parameter? (Study I).

2. Is a new reflectance spectrophotometry and a more developed LDI, capable of predictive therapeutic outcome and monitoring the treatment? (Study II–III).

3. Can high-resolution skin ultrasound investigate the depth of PWS on different anatomic locations and also the variations within a PWS? Is the depth the cause of the different treatment responses? (Study IV).

4. How is the PWS influencing the personality and life of the patients and how do their families look upon this influence (Study V)?

5. Does the treatment of the PWS influence the psychosocial impact of the PWS and if so, in what way (Study VI)? Is there any advantage of an early treatment? (Study V–VI).

MATERIALS AND METHODS

Patients

The studies are based on around 470 healthy patients with congenital capillary malformations (PWS), who had been either referred to or found themselves, the Section of Laser Surgery at the Department of Dermatology, University Hospital in Malmö from 1987 until May1999. All the patients came from the southern part of Sweden and they were mainly Caucasian with skin type I–III, from newborn to around 80 years of age. They had been no sun exposure at least 4 weeks before the treatments were performed. Their PWS had been located mainly on the face, but also on other parts of the body. They have varied from macular pale small PWS till big nodular, cobblestone like blue-red PWS. A minority of the patients had been treated before on some part of their PWS with either phosphor radiation, excision, carbondioxide- or argon-laser, but not at the site treated and studied in this thesis.

Laser equipment

1. Argon

An argon laser (Coherent Model 910, Paolo Alto, CA, USA) was used for treatment in Study I. This laser emits light in the spectral range 488–514 nm. The light is guided through an optical fibre from the laser tube to a hand-held treatment head, producing a 1.5 mm wide beam. The parameters that were used were 0.5-sec pulse duration and a mean power of 1.5 W. The average size of the treated areas was 8 cm^2.

2. PDL

A flashlamp PDL (Candela SPTL-1, Candela Corp., Wayland, MA, USA) with a wavelength of 585 nm, pulse duration of 450 µs, spot diameter of 5 mm was used in Study II–III with a fluence of 5.75–7.5 J/cm^2. The treatment intervals were 6–12 weeks (1–9 treatments) during a period of 21 months in Study II.

In Study III the spot diameter was 5 mm and the energy density 6.75 J/cm^2 in general and occasionally it was increased to 7.25 J/cm^2 after the second of 1–3 treatments that were performed during a period of 3 months.

Another type of PDL (Photogenica-V; Cynosure, Inc., Bedford, MA, USA) was used on patients in Study V–VI. This PDL has a slightly different beam profile curve and a spot diameter of 7 mm which made it possible to coagulate slightly larger diameter vessels and to reach slightly deeper down in dermis *(McMeekin et al, 1995)*. We could therefore decrease the fluence to about 0.5–1.0 J/ cm^2 and still get the same treatment result. The fluence of 3.8–6 J/cm^2 was used with at least 6–12 weeks treatment intervals with a break during the summer. The number of treatments depended on clinical results and varied from 4–8 treatments. The treatments were discontinued either when the lesions were totally cleared or when there was no further improvement. The improvement was judged together with the patient and from their photograph.

3. Treatment of PDL resistant PWS

Those of the patients who did not clear completely after PDL treatments (Study VI), were subsequently treated with an intense pulsed light source (Photoderm VL, ESC Medical Systems Ltd, Yokneam, Israel) or a different vascular long pulsed laser with 532 nm and a chilled tip (Versapuls, Coherent, Inc., Santa Clara, CA, USA) which gave a slight additional improvement.

Clinical evaluation (Study I–III)

Photo documentation was made routinely before, during and after the treatments. An overall clinical evaluation, which included photographs was performed at the end of the treatments in Study I–II and also together with the patients appraisal in Study III. The result was rated as excellent (total fading), good (subtotal fading with minimal residual telangiectasia), fair (some fading) and poor (minimal or no fading) response. This has been the unsatisfactory standard of clinical evaluation during the 90s.

Questionnaires (Study V–VI)

Questionnaires were developed in collaboration with the child and adolescent psychiatrist Björn Wrangsjö. They covered subjects that the patients themselves had brought up during their visits to the Laser department during 1987–1994 (Study V) and 1987–1999 (Study VI), but also areas of inquiry from earlier studies *(Wagner et al, 1990. Lanigan et al, 1989)* and from our own experience with this group of patients.

In Study V, there were slightly different versions of the questionnaires, depending on the age of the patient and whether they were on the waiting list for treatment, had started treatment or had completed treatment. Also, their next of kin were given a questionnaire which they answered independently from each other (See Paper V, Table 1–2). The questionnaires in Study VI included 43 questions and they covered the same areas as Study V plus 3 more questions regarding the heredity, recurrence and who had answered the questionnaires, the patient or the relative.

The following areas were covered and the patients were asked to compare with their own age group:

- Self-esteem
- Acceptance of their PWS.
- How their PWS had influenced their lives.
- School problems; e.g. concentration, relationship with friends, teachers and the opposite sex, feeling of getting bullied and the need to avoid sports.
- Social and sexual relationships.
- Difficulties getting a job or problems at work because of their PWS.
- Whether the PWS had prevented them from getting into quarrels and conflicts.
- Whether people in their surroundings were treating them differently because of their PWS.
- If their lives would change if they could have their PWS eliminated without a scar?
- How their relatives behaved towards them.

The relatives' questions covered almost the same areas as above:

- How they experienced the patients' social situation.
- Whether they had feelings of guilt or an existing superstitious feeling of self-blame.

Some questions had a yes or no alternative, others the form of a 5-degree scale.

Example of how a question was formulated:

– *How do you estimate your self-esteem in comparison with your own age group, after the treatment?*

1. *Much better?*
2. *Somewhat better?*
3. *As my age group?*
4. *Somewhat worse?*
5. *Very much worse?*

Reliability test of questionnaire in Study VI

Ninety of our 147 patients had participated in Study V, 4–5 years earlier. Moderate to good reliability (kappa values 0.4–0.8) was recorded in the majority of the parameters. See Study VI.

Non-invasive measuring techniques

Laser doppler imager (LDI), (Study I, n=13. Study III, n=19)

In order to overcome the limitations of laser doppler flowmetry (which only gave information about tissue perfusion in one single point) a new laser doppler imager was developed *(Nilsson et al.1989)*. It created an image of tissue perfusion with the help of a scanning procedure and was better suited for investigation of PWS with their variable vascular architecture (Study I). The method is based on the recording of doppler shifts caused by movements of blood cells in the back scattered light of a laser beam that successively scanned the treated PWS area of 8 cm^2 in average and the surrounding normal skin. A metallic reflector was positioned around the PWS lesion in order to facilitate identification of the boundaries of the lesion on the LDI and thermography.

A colour-coded image showing spatial distribution of the tissue perfusion was generated showing black where perfusion was zero or low and red where perfusion was high. Also normal surrounding skin was measured as a comparison of the perfusion.

LDI measurements were performed immediately before and about 15 min, 24 h, and 48 h and 3 ½ months after one argon laser treatment.

In Study III, a more developed LDI *(Wårdell et al. 1993)* (PIM I Laser Doppler Imager, Lisca Develop AB, Linköping, Sweden) was used on two 4×4 cm well marked areas of lesional and contralateral normal skin respectively, before and directly after each PDL treatment (see Fig.3, Study III).

Photographic documentation and markings on plastic folders made it possible to measure at the same place before each treatment in both Study I – III.

Thermography (Study I, n=13)

Since thermography was considered useful in the prognosis of the outcome of argon laser therapy of PWS *(Patrice et al, 1985)* it was included as a reference method and used before each LDI measurement. Skin temperature was measured in Celsius (°C) using a real time thermal imaging system (Thermovision 870, Agema Infrared systems AB, Stockholm, Sweden). The mean value of the PWS skin temperature was calculated and compared to that of the corresponding reference area on normal skin.

Reflectance spectrophotometry (Study II, n=66. Study III, n=13)

A hand-held microprocessor-controlled reflectance photometer (Dermaspectrometer, Cortex Technology, Hadsund, Denmark) with a digital readout was used in Study II–III in the search for a predictive tool to determine the therapeutic outcome of PDL treatment of PWS. Erythema figures were obtained in triplicate both of PWS and of closely adjacent normal skin immediately before and after each PDL treatment in Study II (See Paper II, Fig.1).

In Study III these measurements were performed only immediately before the PDL treatment of the PWS and on contra lateral skin instead of adjacent skin. The erythema index from the normal skin was subtracted from the erythema index from the PWS area before the relative blanching effect could be calculated. This relative blanching effect ranged from total (100%) blanching, when the treated PWS had returned to the same erythema index as the normal skin, to no blanching (0%) blanching, when no change in redness of the PWS was noted after the treatment.

Skin ultrasound (Study IV, n=55)

A high resolution 20 MHz ultrasound system (DermaScan C Ver.3, Cortex Technology ApS, Hadsund, Denmark) (Fig.4) was used to study the depth of untreated macular PWS on various anatomical locations. One to 8 measurements were performed on each patient depending on the size and location of the PWS. Measurements were also obtained from the normal contralateral side. A PWS appears as a superficial dark band right under the epidermal entrance reflection (Fig. 4).

Statistics

The paired T-test was used for comparison over time in Study I, where p-values <0.01 were set because of the many repetitive measurements. The Spearman rank test correlation test was used for statistical analysis of the data in Study II–VI and to calculate the relationship between age and depth of PWS in Study IV. In Study V statistics were made by comparison of two sample proportions using the normal difference test and the Wilcoxon rank sum test *(Bahn, 1972)*. The latter test was also used in Study III and to compare the retrospectively reported psychosocial parameters before and after PDL treatments in Study VI. The Mann-Whitney U-test was used when comparing depth between groups (Study IV). To study the reliability of the questionnaire used in Study VI with the earlier questionnaire in Study V, the kappa coefficient was used *(Brennan et al, 1992)*.

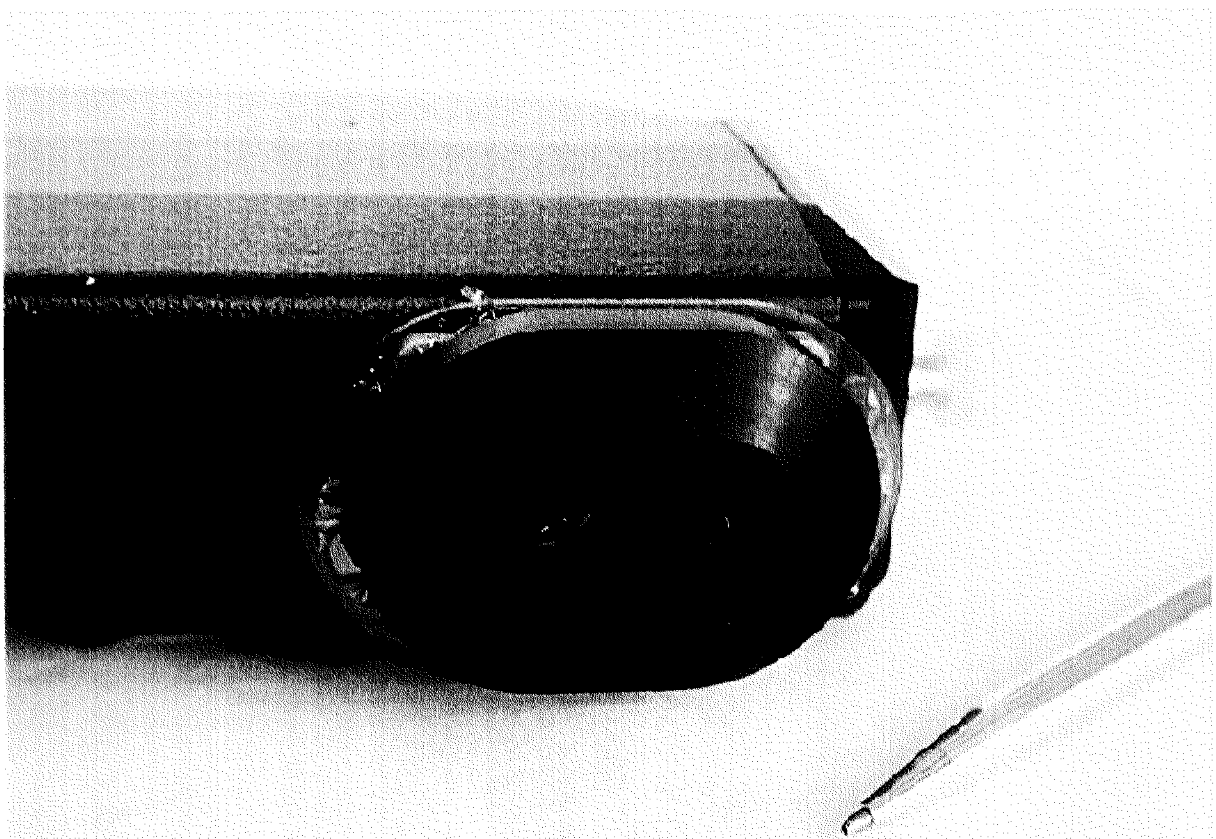

Fig. 4. The B-scanning probe of the ultrasound device

RESULTS

Methods for evaluating therapeutic outcome

LDI and thermography (Study I)

Skin blood perfusion with a Laser Doppler Imager and thermography before and after argon laser treatment.

Thirteen patients aged 17–65 (mean 29 years) with PWS, were measured with LDI and thermography in the PWS and the normal surrounding skin before and about 10–15 min, 24 h, 48 h and 3 ½ month after one argon laser treatment (See Paper I, Table II).

LDI:

Before the treatment: In 9/13 patients there was no difference between perfusion within the PWS and the normal surrounding unaffected skin. In the remaining 4 patients there was a significant ($p<0.01$) elevation of the perfusion within the PWS.

Around 10 minutes after the treatment: The perfusion in the centre of 11 PWS was significantly different from that of normal skin. In 11/13 PWS, elevated perfusion was recorded and in the remaining 2 PWS a reduced perfusion was noted. All patients had increased perfusion (hyperaemia) in the border between the PWS and the healthy skin tissue.

24 and 48 h after the treatment: There was still an elevation of the perfusion in the centre of the PWS in 7 (after 24 h) and 5 (after 48 h) patients respectively. A gradual reduction of the perfusion in the borderline zone between the PWS and the surrounding skin was seen in all patients.

3 ½ month after the treatment: In 5/10 patients a higher perfusion was observed within the treated area in comparison with the surrounding skin. The reactive hyperaemia in the borderline had disappeared.

Thermography

Before the treatments: 2/13 patients had a higher temperature within the PWS compared with the surrounding skin.

Around 15 minutes after the treatment: 10/13 patients had a significantly ($p<0.01$) higher temperature in the PWS than in normal skin.

24 and 48 h after the treatment: The elevated temperatures slowly decreased.

3 ½ months after the treatment: Return to pre-treatment levels of temperature was observed.

Clinical results:

(See Paper I, Table II). When comparing clinical results with the results of LDI and thermography, 2 out of the 3 patients with clinically excellent results, demonstrated high tissue perfusion and elevated temperature in the PWS before the treatment with the argon laser. These 2 patients were older than the others (53 and 67 years, respectively) and their PWS were purple and located on the face.

Neither LDI nor thermography could unambiguously predict the clinical outcome of argon laser treatment of PWS, but both tools may yet be useful in the further understanding of the pathophysiology of PWS.

Prediction and outcome of reflectance spectrophotometry (Study II)

A hand-held reflectance spectrophotometer was used in the search for a predictive and objective tool to determine the therapeutic outcome of PDL.

Sixty-six patients with PWS, mainly on the face, were treated with PDL during a 21 month period. Erythema figures were obtained for the PWS and of closely adjacent normal skin before and after PDL. Based on these indices, a relative blanching effect could be calculated.

There was a good correlation (r =0.844) between the degree of blanching and the therapeutic result. A blanching effect, which averaged 47 %, was already evident after the first treatment in the 'excellent' response group, increasing to between 75 and 100% after successive treatments. In the 'poor' response group, the average blanching after one treatment was 14 %, and did not exceed 40 % after successive treatment sessions. (See Fig 3, Paper II).

Reflectance photometry is a useful objective tool that demonstrated a successive increase in blanching and predicted within 6 weeks after the first treatment the eventual clinical result.

Monitoring and prediction of LDI and reflectance spectrophotometry (Study III)

Trying to define a tool to predict and monitor the PDL treatment we used LDI and reflectance photometry initially, after 1–3 treatments and after 1–6 treatments respectively.

Before the treatments LDI demonstrated that 15 patients (with facial PWS) out of 19 patients had an increased blood flow within the PWS in comparison with normal contra lateral skin. The remaining 4 PWS were situated on breast, neck and thigh. Directly after the treatments 15/18 patients had decreased blood flow within the PWS and all 18 had surrounding hyperaemia.

The blood flow, as measured with LDI, did not correlate well with the photometrically registered erythema, however, indicating that for clinical, predictive purposes, erythema measurements may be more useful than the measurement of blood flow.

Ultrasound to evaluate the depth of the PWS (Study IV)

A high-resolution skin ultrasound device was used to investigate the depth of untreated PWS in 55 patients. The mean depth of all PWS (measured at the deepest point), that were measurable (45/55) was 1.00 mm (±0.50 SD). The variations in depth were from 0.2–3.7 mm and the deepest were seen on the lips, nose and chin.

Lesions on the trunk (0.64 mm, ±0.45 SD) and extremities (0.89 mm, ±0.29 SD) were found to be more superficial than lesions located on the head with a mean maximum depth of 1.08 mm (±0.53 SD). PWS involving areas that have been responding poorly (e.g. medial face, dermatome V1–2) to PDL treatment were on average 0.14 mm deeper than PWS involving good responding areas (e.g. forehead, lateral cheek). Fig. 5.

There was no significant statistical correlation, but a tendency towards deeper PWS with higher age (Fig 2, Paper IV).

In 19 patients 3 measurements were performed on the same PWS. 16/19 patients demonstrated an intra-PWS variability of 0.5 mm or less (See Fig. 3, Paper IV). A variation of only 0.1 mm were seen in 7/19 patients.

We also grouped all 45 patients, with 62 PWS in different anatomical locations into four different anatomical sites to see whether there were any differences in depth:

1. **Head** (face, neck) . This group consisted of 44 PWS. Mean depth was 1.08 mm (range 0.37–3.70) with the largest SD (±0.58) in comparison with the other groups.
2. **Trunk** (chest, shoulder). This group consisted of 6 PWS. Mean depth was 0.64 mm (±0.45 SD, range 0.21–1.30)
3. **Arm** (hand, finger). This group consisted of 4 PWS. Mean depth was 0.90 mm (± 0.30 SD, range 0.57–1.22).

4. **Leg** (femur, calf, thigh, shinbone, knee, buttock). This group consisted of 8 PWS. Mean depth was 0.88 mm, (± 0.29 SD, range 0.28–1.10).

After the study we also measured 7 of our patients with PWS before and after PDL (Fig 6A–B). Six of these experienced a clear clinical improvement, which was also evident on ultrasound and one patient showed normal ultrasound finding after PDL, although clinically there was still some of the PWS left.

Since the PDL, with its superficial penetration, can not reach the deeper vessels of a PWS, the non-invasive skin ultrasound technique could be a good complement to e.g. reflectance spectrophotometry in the prognostic investigation as well as to plan treatment.

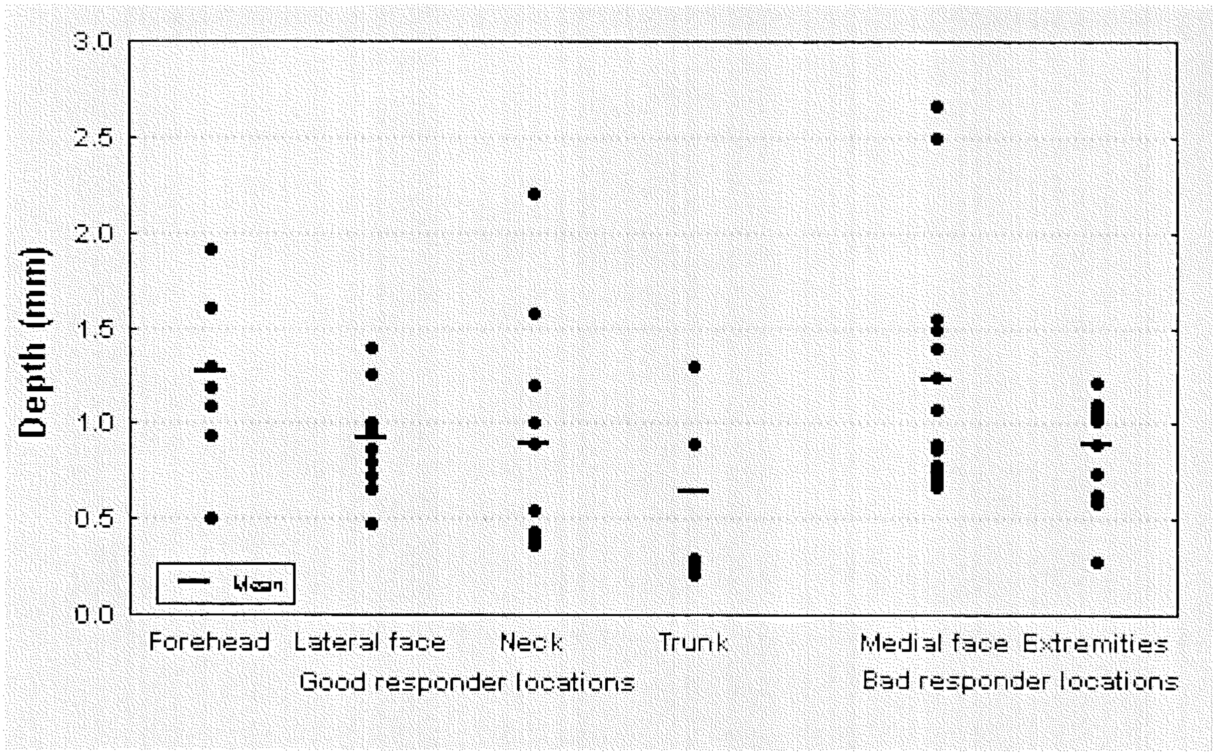

Fig. 5. Ultrasound measurements on PWS on good and bad responding locations. Each point represents one patient with the his/her average measurements on each of his/her anatomical location.

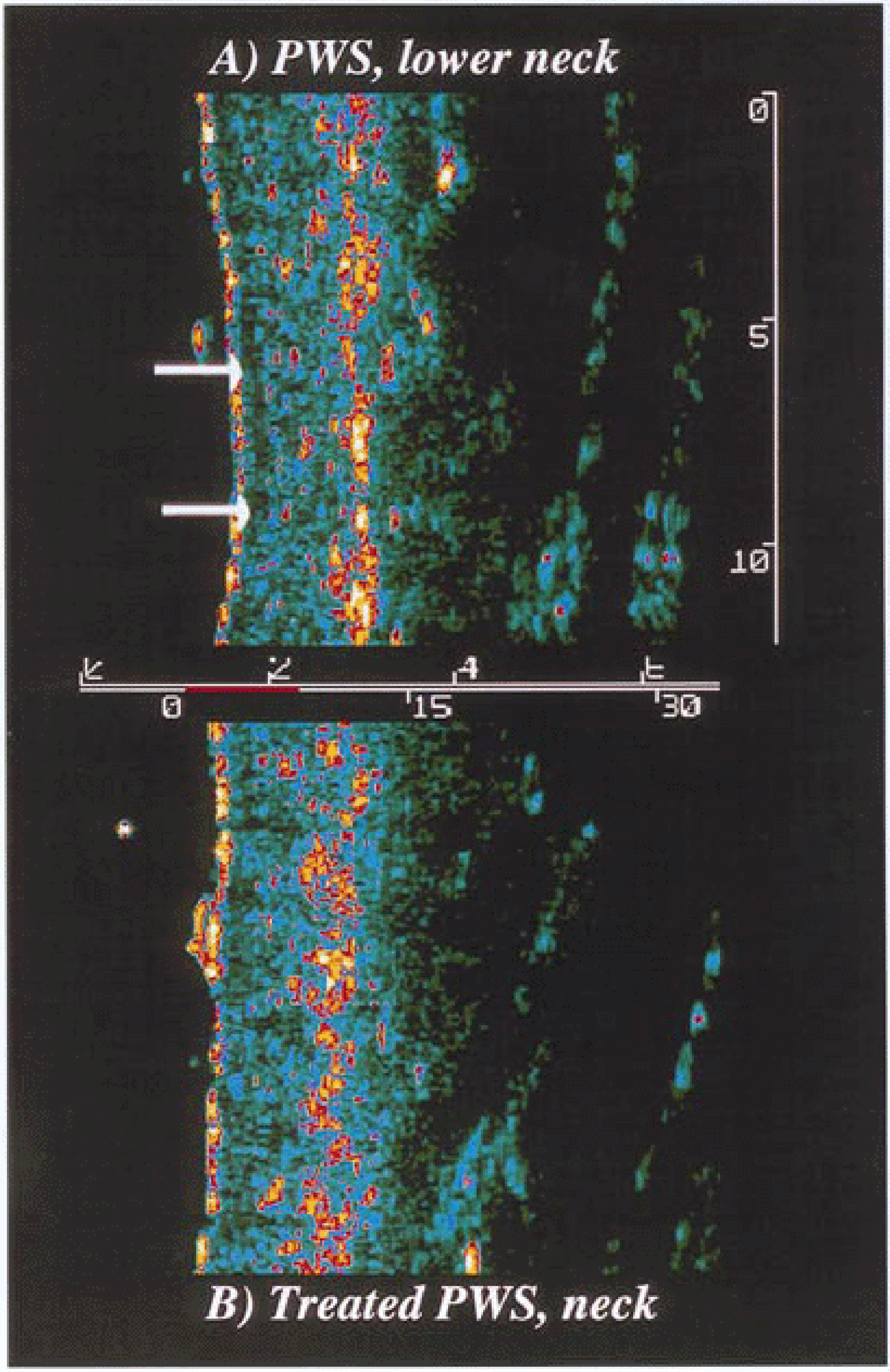

Fig. 6 A. Ultrasound image of PWS lower neck (see arrows) and B. 6 weeks after 1 PDL treatment. (For colour code see text in Paper IV).

Psychological studies (Study V–VI)

Stigmatisation of patients with PWS? (Study V)

231 patients with PWS and their families responded to a specifically designed questionnaire regarding the influence and the eventual stigmatisation that a PWS could cause. The patients were either on a waiting list for PDL, in PDL treatment, or had completed their PDL treatments (smallest group).

During the age period 10–20 years, 73% were most disturbed by their PWS, and 62% were convinced that their lives would change radically if their PWS could be eliminated. Suffering from low self-esteem (when they compared themselves with the same age group) was reported by 47%. The PWS made their school life and education more difficult according to 28 % of the study group.

76% of the relatives considered the patient to be negatively affected in some way by the PWS.

Our result strongly indicates that a high degree of emotional distress is experienced by our patients with PWS. Even birthmarks on other parts of the body than the face can affect the patient negatively.

Improvement of the emotional impact after treatment? (Study VI)

A retrospective psychosocial study of 147 patients with PWS who were treated with the PDL until either total clearing or until there was no further improvement, was performed with the help of questionnaires.

Self-esteem, social relationships, school contacts, the need of covering their PWS with make up or clothes, contact with the opposite sex, conflict avoidance and meeting new people were psychosocial behaviours which were rated more problematic in older age groups, but improved significantly after PDL treatment.

Patients' reports regarding stress, self-esteem and possibilities in making friends in comparison with their own age group:

Age group 2–14 years:
The median age, when the patients reported being most distressed by their PWS was 6 years.

14% considered themselves having a lower self-esteem than their age group.

8% considered that their PWS had prevented them from making friends in some way before and after the treatment (10.5%).

Age group 15–25 years:
The median age of most distress was experienced in the age of 13 years.

42% regarded themselves having a lower self-esteem before treatment and 19% after the treatments.

39% considered that their PWS had prevented them from making friends before the treatment and 28% after the treatment.

Age group > 26 years:
The median age of most distress was 17 years.

58% experienced themselves to have a low self-esteem before the treatments and 12% after the treatments.

32% considered that their PWS had prevented them from making friends before the treatments and 27% after the treatments.

85% considered their PWS to influence their lives in some negative way and 80% experienced that their lives would change to the better, if their PWS could be eliminated. 80% of the patients >7 years of age, had not fully accepted their PWS with higher age.

The older patients had higher negative scores than the younger ones.

Our patients reported a better psychosocial situation after the treatment than before.

Individual comments from patients regarding the emotional impact

For some questions, respondents also had the option to write down their own answers and comments and so they did, especially regarding school life:

"Why me?"

"Low self-esteem... feeling ugly in comparison with other girls... shy...did not want to be seen... did not want any attention..."

"Wanting to hide...avoiding school breaks during the day"

"Did not believe in myself...feeling depressed...did not do well at school"

"Avoiding new acquaintances... fear of changing schoosl... feeling different than others..."

"Being an outsider...always being observed""

"Feeling ashamed of myself...treating myself differently...maltreating myself..."

"Bullied, especially in lower grades... teased...whispering behind my back... stared at...called by different nicknames..."

"Feeling depressed...did not dare to make contact with others..."

"Tired of all the annoying questions from others, especially children...did not want to answer them, but felt I had to..."

"Avoiding sports—because then I had to undress, shower and show my birthmark on my body... was always the last to be chosen for the team"

"Avoiding sports and sweating, because then the covering make up was ruined"

"Avoiding swimming—feeling ashamed of my birthmark on my legs...never learned how to swim"

"Always trying to get a seat close to the wall, so that I could hide my birthmark..."

"Insecure...was I okay or not in other peoples' eyes...?"

"Feeling of that I was pushed aside..."

"All these questions about—'Why do you have it? Is it contagious? Does it go away? Have you been hit? Have you fallen over? Is it dangerous?"

"Tired of always having to explain what I had..."

*"To be called ..—**She** with the birthmark..."*

"Hated school trips.. never went on school trips.. because then I had to take away the make up or show my birthmark"

"Was refused as a model because of my birthmark..."

"Was not allowed to work at hairdresser's, because people would get scared of me..."

"The teachers treated me differently...as if I was not as intelligent as the others"

"Had to be extra clever and intelligent..."

"Had to argue a lot until they accepted me in their different play groups"

"Tired of always being weak and in a disadvantageous position..."

"Always feeling dirty because of the covering make up...still I do not dare to not use the make up".

"Although my PWS is almost gone and I do not need make up any more—I still use it. It makes me feel secure"

Along with the questionnaire the patients sometimes wrote a letter or individual notes.

Female 54 years of age with PWS on neck and sternum: *"It would maybe be better to have had the handicap (the PWS) on an open visual place like the face, because during summer season people reacted strongly to my PWS and these reactions and questions were painful to handle. Now when my PWS is eliminated I am so disappointed that my family and relatives do not react and talk positively about it. They are just as quiet as they were before the treatments, when I felt my PWS was a taboo subject".*

Female 68 years of age with PWS on the cheek: *"I felt my mother was worried about something when I was getting close to starting school. Then I suddenly realised that I did not look as everybody else. It was a scary, frightening feeling. I always tried to hide myself, to be quiet and not to talk, because I hoped people would not look at my PWS. During the lessons in school I was terrified to answer questions and to attract attention. Therefore I kept quiet and cried instead. The consequences of this were that I did not learn to read, write or count. My parents did not understand me and thought I was stupid.. The children at school behaved towards me as if I was invisible and that was the way I wanted it. When I discovered covering make up and started to use it I finally realised that I was pretty and that boys liked me. Still, every time I had to go through an operation I panicked, because I had to take away my security – my make up. Once I heard a doctor exclaim during my operation –'Who is that? It is not possible it is she! I thought she was good-looking!'. After the laser treatment I could not believe it was true! It was an enormous relief and happiness, although not all of the PWS was eliminated".*

Individual comments from the relatives

People were insinuating that they had maltreated their child. One family avoided sun and bathing situations because of all the staring at their child who had a PWS on the thorax. Questions were raised like: *"Why did we not get a child that we could show off? Why did we get this punishment?"*

Superstitiousness

Mother (47 years of age) to a 15 year old son: *"There was a fire in our factory and I was watching as it burnt down—I was pregnant—then suddenly I felt something special on my cheek, on the same place where my son had his birthmark. At the same time I felt my son making a quick move inside of me...".*

Mother (around her fifties) to a 20 year old daughter: *"When I was pregnant, I was walking in the dark in the forest, then suddenly a frog jumped up and touched my cheek, exactly at the same place where my daughter received her birthmark..."*

Heredity

In the questionnaires, the patients were asked whether they knew any relative who had a red birthmark like them, and if so, where was it situated. 19.1% (26/136) responded positively and the close family were in majority e.g. sister, father or mother.

All patients with PWS who have come to our Laser department during the last 1 1/2 year, have been asked the same question. In June 1999, 22 % (39/181 patients) reported that they had a relative with a red birthmark like themselves.

Recurrence of PWS

26% (32/122) of our patients reported in a questionnaire that their PWS had become more red, a few months up to 2 years, after the treatments (Study VI). Seven patients reported it to take 2–4 years after the PDL treatments. They pointed out that it was only focally and that a new PDL treatment helped (Fig. 7). They also reported that the redness varied according to different circumstances and that they were not totally cleared of all their red vessels after the treatments. One patient connected the recurrence with a trauma from a glass bottle. Another patient pointed out that it was the untreated part of the PWS that had turned red.

Fig.7. Patient with a geographic PWS Grade III (earlier treated with excision) before and after 4 PDL treatments. Bottom picture is demonstrating some recurrence 6 years after treatment.

DISCUSSION

Since 1986, when the pulsed dye laser (PDL) was introduced with its principle of selective photothermolysis it has been the treatment of choice for PWS. However, varying and conflicting results have been reported *(Tan et al, 1989. Reyes et al, 1990)* and the need to further investigate the PWS and the treatment results increased.

Traditional mechanisms of assessing treatment response have rested mainly on subjective determinations by physician and patient and pre-treatment photographs *(Reyes et al, 1990. Goldman et al, 1993. Onizuka et al, 1995, Perez et al, 1997)*. However, the wide variation in treatment response of laser therapy poses a profound need for development of objective devices to measure and predict treatment outcomes, so that the maximum effectiveness of therapy can be achieved without unnecessary repeat treatments. Visual judgement of PWS may seem inexpensive, but may prove to be financially more costly, if the result is an increased number of treatments with minimal or no improvement, not to mention the psychological pain and discomfort it may cause the patients, when they have to go through all the treatment. In addition to psychological and financial cost the routine use of general anaesthesia for treatment of young children makes the prevention of unnecessary repeat treatments particularly important.

The purpose of Study I–IV in this thesis was to find a non-invasive predictive tool to determine the therapeutic outcome in laser treated PWS and to try to characterise the PWS in the search for better treatment results.

The microvascular blood flow in PWS has been studied by means of several methods over the last decades *(Malm et al, 1988, Apfelberg et al, 1989)*. Many of the earlier techniques influenced the vasculature because they were traumatising to the skin *(Anderson et al, 1994)*. Even slight external stimuli such as pressure or mechanical contact may disturb the flow conditions of the microvascular bed. Therefore, we considered the non-invasive LDI, to be informative in the trial of mapping tissue perfusion. We found that the blood flow within the PWS, was increased in 4 (hand, forehead, 2 neck) out of 13 patients in Study I and in Study III in 15 (all facial) out of 19 patients. It would have been interesting to investigate with skin ultrasound the depth of those PWS that had an increased blood flow, but at the time of these studies, we did not have this facility. We do not consider it surprising that the perfusion varied within a PWS, because it has been reported that the vessels vary in depth around 0.46 mm (±0,17) *(Barsky et al, 1980)* and according to skin ultrasound measurements (Study IV) the mean maximum depth seems to be around 1.00 mm (±0,50 SD) with a range of 0.2–3.7mm. Two out of the 4 patients with increased blood flow in Study I and all 15 patients in Study III, had facial PWS, where the perfusion was known to be high, especially in the medial parts. According to Renfro et al, the centrofacial lesions (including dermatome V2) in adults and children respond less favourably to PDL than lesions elsewhere on the head and neck *(1993)*. Ultrasound measurements of head and neck areas (Study IV) demonstrated a mean depth of 1.08 mm (range 0.2–3.70) (See Results, Study IV), which is far deeper than the LDI is presumed to measure (a few hundred microns). The increased blood flow in the centre of 9/11 PWS directly after argon laser treatment may be explained by the fact that the measuring depth is dependent on the structure of the vessels and the optical parameters of the skin. Although the median measuring depth of LDI was thought to be about 0.2 mm, sensitivity to perfusion throughout a deeper network may still be significant *(Jakobsson et al, 1993).*

Objective characterisation of PWS is an important requirement in therapy, but has been difficult to achieve *(Tang et al, 1983. Malm et al, 1988. Lanigan et al, 1988).* Subjective clinical assessment has thus been the main method of monitoring treatment. Studies have found reflectance spectrophotometry to be more sensitive than the human eye in detecting erythema *(Farr et al, 1984. Diffey et al, 1984),* but the main advantage has been the ability to follow the treatment outcome with the help of objective figures (Study II–III). With the help of reflectance spectrophotometry we found in Study II, that erythema measurements of the PWS correlated well with the clinical results after PDL and that reflectance spectrophotometry could provide an objective estimate of blanching. It can thus be helpful in monitoring and predicting the therapeutic outcome of PDL. Haedersdal et al *(1998)* confirmed this later in their study of 12 children with PWS. However, the device probe needs to have contact with the skin and one needs to ensure there is no pressure and no light escaping when measuring the PWS *(Pickering et al, 1992).* Another disadvantage may be the small test area (12 mm), but this can be compensated for by repetitive measurements on selected parts of the PWS. Studies comparing reflectance spectrophotometers with tristimulus colorimeters have been performed and a colorimeter may be a tool as efficient as reflectance spectrophotometry in measuring clinical response, but it also has the same limitations, e.g. small test size of 8mm *(Westerhof et al, 1986. Takiwaki et al, 1994. van der Horst et al, 1998)* and risk of varying PWS blanching due to instrument contact *(Pickering et al, 1992).* Measurements of cutaneous blood flow, while useful in the research setting, fail to correlate well with clinical response (Study I and III). We found that, the clinical results of PDL therapy on PWS are more strongly correlated with elimination of erythema (Study III), LDI appears limited as a sole means of objective measuring and predicting treatment success. On the other hand, Jiang et al *(1998)* investigated the relationship between the microvascular perfusion changes of 24 patients with PWS (face and neck) and the blanching of the lesions after PDT and compared with normal skin. It was shown that the mean, maximal and minimal values of tissue perfusion in the pretreatment group were significantly higher than those in the control group and after PDT the perfusion had decreased remarkably. The colours of lesions were correlated with decrease of microcirculatory perfusion. They concluded that the microcirculation perfusion can reflect the degrees of PWS objectively.

Erythema can be present without concomitant increase in skin perfusion, probably representing post trauma venous stasis *(Mattsson et al, 1996).* Both Mattsson et al *(1997)* and we (Study III) demonstrated that erythema and perfusion show only weak correlation.

In Study I, performed in spring1990, we used the argon laser, because, this was the laser available at that time. In this study we saw increased blood flow in the majority of the PWS (9/13) immediately after argon laser treatment, but in Study III we saw decreased blood flow in the majority of the PWS (15/18) immediately after PDL treatment. One reason for this finding could be the thermal damage caused by the argon laser. A short time later the PDL was available (Study II–VI) with its very short pulse duration (450µs) and with far better treatment results. Suddenly, we could treat children and pale lesions with a minimal risk of scarring and pigment changes.

Ultrasonography evaluates the echogenecity in the superficial and deep skin layers, whereas clinical evaluation and skin reflectance predominantly determine the superficial skin redness. When we looked at the intra-individual variability of the depth within our 19 PWS there was a variation of 0.5 mm or less in the majority of the PWS, but the variation was from 0.1–2.0 mm (Fig. 3, Paper IV).

The correlation between ultrasound measurement of thickness and presumed outcome of treatment in certain anatomic locations was not that high. The reason for this could be that the thickness of the PWS varied considerably because of the biology itself. Also, Haedersdahl et al *(1998)* indicated in their study of 12 children with facial PWS, with the same ultrasound device, that there was no correlation between change in echogenicity and the clinically assessed treatment response. Their dermal echogenicity was higher in PWS after PDL and they concluded that quantification of treatment result was possible with ultrasound. Perhaps the non-responding vessels had a too small a calibre to be detected by the ultrasound and to be absorbed by the PDL. To our experience pink and purple lesions are poor responders to PDL. Fiskerstrand et al *(1996)* demonstrated that pink lesions have small-diameter vessels (mean 16.5 μm) and that both pink and purple lesions consist of deeply located vessels. Our mean maximum depth of the PWS was 1.00 mm and this was close to the earlier reported median skin thickness of the PWS of 1.00 mm *(Haedersdahl et al, 1998).*

Minor variations in temperature due to normal skin temperature do not seem to have any impact on ultrasound images. As a check up of the reproducibility one of our patients was measured twice on the same untreated PWS location with exactly the same ultrasonical image as 6 weeks earlier.

Patients with PWS (who did not belong to the study), treated earlier with argon laser, had more superficial vessels, which could be explained by the high risk of thermal damage after these treatments and the possibility of developing superficial new vessels after an inflammatory reaction.

We followed 7 of our patients with PWS from Study IV with ultrasound measurements after PDL treatments. One of these patients had no sign of PWS on the ultrasound after the treatment, although clinically there was still some of the PWS left. Ten out of our 55 PWS in Study IV demonstrated no signs of PWS, although clinically they were clearly visible. Probably, this is due to the very superficial location of the vessels or alternatively, too thin a calibre of the vessel.

There was a tendency towards deeper PWS with age and more spreading with age. (See Fig. 2–3, Paper IV,). Many articles have reported "pro or con" early treatment in life (See – Pro versus con early treatment), but probably it is not only the age that is important for the treatment results. The interindividual and intraindividual heterogenicity of the PWS, e.g. the depth, the bloodflow, the vessel diameter, lesion thickness and variation in thickness within the PWS, is perhaps even more important for the treatment outcome.

Emotional impact

The second part of the thesis (Study V) was aimed at investigating whether patients with PWS were stigmatised by their PWS and if so, in what way. The standard tests and questionnaires that we could find, did not stand up to our needs in this case. According to Lanigan et al, *(1989)* and their special questionnaires, patients with PWS had a high level of psychological morbidity resulting from a feeling of stigmatisation that was not apparent in casual social intercourse. However, in their standard psychological screening tests for psychiatric illness, depression and anxiety revealed that these patients had similar or less evidence of morbidity than control subjects or other patient groups *(Lanigan et al, 1989).* Also Kalik et al *(1981)* used standard psychological test instruments, but in their own questionnaire could only find that their patients PWS had been a source of stress and psychological burden. Perhaps the standard tests that are available, are not sensitive enough to detect the emotional reactions that may follow having a PWS.

Society sometimes classifies laser treatment of PWS as a cosmetic procedure that is not medically necessary. Given the psychosocial implications and potential medical complications of this congenital malformation, and the fact that safe, effective, therapy is available, treatment of PWS should be considered medically indicated. We believe there is a potential psychological benefit in starting the treatment of PWS (including non-facial) at as early an age as possible. There is no ideal age when treatment should be started, and therefore it is recommended to decide from case to case. A majority of our patients experienced that their PWS influenced their life negatively and they were convinced that their life would change radically if their PWS could be eliminated (Study V–VI). Our patients reported a better psychosocial situation after the treatment than before. We therefore recommend an early treatment (to be finished before school begins) to try to avoid the negative psychosocial impact a PWS may cause.

Also, all the individual comments and letters that the patients added to the questionnaires were convincing about the negative impact a PWS could cause.

Clifford et al *(1973)* reported in a study that the two most important and usual sources of information about a student, from which a teacher may develop an initial bias are the child's school record and the child's general appearance. In another study from 1975 they concluded that educators and parents alike should be aware of how these variables could unwarrantedly detriment the child's intellectual development *(Clifford et al, 1975)*. Their patients did not have a PWS, but according to our patients and their families in studies V and VI the schooling and educational problems could not be ignored.

The worried parents often express that they consider their child as beautiful and if it were not for the reaction from their surroundings they would not care at all about the birthmark. The pain of being subjected to the frequent insensitivity and intrusion of strangers in public places in response to their child's birthmark is often expressed during the visits to our Laser department. According to Harrison, parents often deny or overlook the birthmark until others call their attention to it *(Harrison et al, 1988)*.

In Study V, only a minority of the patients had completed their treatments. The ideal would have been to have a larger group of these patients. Therefore in Study VI we emphasised the question, whether the laser treatment had improved the negative psychosocial parameters that had been found in Study V–VI or not.

One may object that a retrospective study (Study VI) is less reliable than a prospective study, but according to our test, the reliability was from good to fair in the majority of the parameters (See Paper VI).

We were cautious when we interpreted the answers from our patients, firstly, because it was a retrospective, and not a controlled prospective study, secondly, because the median age was young (22 years of age) and the answers came from a range of very young children up to retired patients (Study V). All of our PWS patients had actively sought our help and it cannot be ruled out that that this resulted in a selection of especially conspicuous patients.

In both studies, the ideal would have been to have control groups of patients of matching age periods. One important aspect in the difficulties of this, is that the PWS would not involute by itself, so we can not find this kind of control group. Another aspect is the difficulty to find the age related groups that directly matches our questionnaires.

At first, we considered it very remarkable that parents still in modern times express feelings of guilt and superstitiousness. Perhaps it is not so surprising that the superstitious belief in maternal marking should persist. Pregnancy taboos exist in slightly different ways in every culture and in every corner of the world and it lingers on to this day, perhaps reinforced by paternal convictions.

Contraindications for treatment must also be discussed, but very little, if any, literature is found in this field. Skin type VI (black) is a contra indication because of the side effects *(Aschinoff et al, 1992).* If patients are old enough to understand the information, they should decide themselves, maybe together with their family, whether they want to be treated or not. They should never be persuaded to go through treatments, if they are not motivated. Also discomfort during the treatment, embarrassment of the purpura during a week after each treatment and risks and side side effects in conjunction with the treatments and eventual general anaesthesia, should be discussed with the patients before the treatment. They should also be allowed to take a break during treatments and be given the opportunity to return for treatments, if they change their minds in the future. The patient's decision should always be respected as in all medical care.

Heredity

Although PWS are not supposed to be inherited *(Mulliken et al, 1982),* many patients still raise this question and during the nineties some interesting studies have been reported *(Pasyk et al, 1992. Mills et al, 1997).* In a prospective study from Wales, 25 % (72/283 patients with PWS) had a positive family history of birthmarks, the majority vascular (20 strawberry hemangiomas and 22 PWS) and this was considered higher than expected for the prevalence of PWS in the population *(Mills et al, 1997).*

We can not draw any conclusions from our figures of reported heredity (19 and 22 % respectively) and perhaps our figures are sporadic as has been reported earlier in literature. Since we have not examined the relatives yet, we do not exactly know how close the relatives were to our patients. Also the terminology has been and still is confusing both for colleagues and patients and it is not rare that e.g. hemangiomas and PWS are mixed up.

The reported frequency for PWS in newborn infants is rather high 0.3–2.1 % *(Jacobs et al, 1976. Hidano et al, 1986, Osborn et al, 1987)* and therefore we will continue our investigation.

Recurrence of PWS

The disturbing finding that 26 % of our patients reported that their PWS had turned more red, at least partially, after the treatments has probably many explanations (Study VI). One could be that the question was misunderstood, because many patients wrote that although their PWS had improved a lot, there was a certain part of their PWS left. Another reason could be that in those PWS that clinically had cleared completely, one could suspect that some ectatic vessels still persisted. In our earlier study with LDI we noticed that 5/19 patients with PWS had before the second treatment no change in their blood flow compared to pre-treatment (Study II). Perhaps there were not enough vessels destroyed to be able to effect the blood flow.

Dixon et al (1986) reported recurrence in 3/37 patients after 1–2 argon and Nd:YAG laser treatments. 36 of these 37 patients had residual colour left in their PWS. Also, Orten et al *(1996)* compared pre- and post-treatment photographs and measured the clinical response also with the help of reflectance spectrophotometry. They noted a gradual 20 % (5/24 patients) return of the vascular lesion 1–2 years after PDL treatments, 40% (4/10) after 2–3 years and 50% (2/4) after > 3 years. Maybe their study included too few patients and maybe the patients that came back, were those that were not satisfied.

We know that with age, some PWS darken and become hypertrophic, probably because of the progressive ectasia *(Barsky et al, 1980).* The reported recurrence of the redness may be caused by the natural progressive ectasia that continues in the persistent vessels. It could also be explained by the fact that the mean maximum depth of the PWS vessels is 1.00

mm (±0.5 SD) with a range of 0.2–3.7 mm according to our ultrasound measurements (Study IV) and the penetration depth of the PDL is probably limited to a depth of maximum 0.65 mm *(Hohenleutner et al, 1995).* Also vessels smaller than 20μm have been shown to be another reason for poor response *(Fiskerstrand et al, 1996).* If these parameters are facts, it is very understandable that some vessels persist deep down in dermis and that some vessels are either too thin or too thick to be destroyed by currently available treatment methods.

We probably need to do "touch up" treatments in the future and this emphasises the importance of a good pre-counselling information to the patients, so that they will have realistic expectations. Reports have suggested that treatment arrests the progression of PWS *(Tan et al, 1989)*, but this has not been confirmed and the contrary may be true. Further investigations are needed.

Future in characterisation, documentation and therapy

Digital photographs incorporate many of the advantages of ordinary photographs, spectrophotometers and tristimulus colorimeters while correcting for their limitations. An entire PWS can be analysed and the cameras are portable and easy to operate *(Mattsson et al, 1997).* Studies of digital photographs for assessing the colour changes after laser treatment of PWS are currently under way.

New techniques with possible applications for PWS measurements are currently under development. Among all, **Infrared tomography** implies a laser source and an infrared camera for imaging blood vessels in the skin *(van Gemert et al, 1997).* This promising technology allows clinicians to know the location and physical dimensions of blood vessels, where choice of optimal wavelength and pulse duration is possible.

Optical reflectance spectroscopy, optical low-coherence reflectometry and optical Doppler tomography are other promising techniques that offer the possibility of greater resolution in imaging of blood vessels and greater precision in determining blood vessel dimensions *(van Gemert et al, 1997. Chen et al, 1997).* These concepts, including infrared tomography, require further investigation and are not commercially available yet.

Photodynamic therapy (PDT) with the wavelength of 630 nm and the photosensitiser 5-aminolevulinic acid (5-ALA) or Photofrin has the capability to destroy human dermal microvascular endothelial cells in vitro and vasculature from a chicken comb in vivo *(Chang et al, 1999).* Promising results have also been shown in the treatment of capillary malformations *(Lin et al, 1997).* According to Jiang et al *(1998)* PDT is one of the most effective modalities for PWS (See Background).

The future of lasers in dermatology continues to be bright with the expansion of therapeutic instrumentation on the skin and with increasing selectivity. Current available laser systems for surgery will continue with miniaturisation, increased flexibility and output, more q-switched models, decrease in the basic cost of the instruments and service contracts. As an example, small inexpensive diode lasers will probably be used at a variety of wavelengths. Another phase of laser development is the further development of multiple frequencies and multiple laser instruments in one or two systems.

CONCLUSION

Reflectance spectrophotometry has been shown to be superior to LDI in the prediction of the outcome of PWS therapy early in the treatment course. It is objective and correlates well with clinical results and is also portable and easy to use.

LDI alone is more useful in the research setting than as a predictive tool in the evaluation of treatment success of PWS.

Ultrasound can help to characterise the PWS in the majority of patients and may help to predict the outcome of PDL treatment before the actual treatment.

Given the big psychosocial impact and the potential medical complications of PWS, and the fact that safe, effective, proven therapy is available since many years, treatment of PWS should be considered as medically indicated and be covered as such by the state health care system. In order to avoid a high emotional impact on the patients' psychological development and school life, we recommend treatment early in life.

Some PWS may fail to respond on the basis of their depth, vessel diameter or the rate of the bloodflow through the lesions or because of other currently unknown factors. Since, medical science still does not have a satisfactory treatment for *all types* of PWS today, we must continue our research for therapeutic alternatives.

Comprehensive summary in English

This thesis covers 12 year of experience in treating patients with congenital capillary malformations, so called port wine stains (PWS). The wide variation in response to laser therapy has developed a profound need for the development of objective devises to measure treatment outcomes, so that the maximum effectiveness of therapy can be achieved without unnecessary treatments.

Study I–IV

The purpose in the first part of the thesis has been to better characterise PWS with the emphasis on blood flow, erythema, the depth in the skin, so that the results of the treatment could be better predicted, followed, documented and improved.

Study I

LDI was more useful in research settings than as a predictive tool.

In 13 PWS patients, we investigated the blood flow in PWS and surrounding normal skin, with the help of a new scanning technique in conjunction with thermography before and after argon laser. We found that 4/13 patients had an increased blood flow in their PWS before laser treatment and that most of the patients had an increased blood flow and raised temperature following treatment. Two of the 3 patients with the best clinical result had higher blood flow and temperature before the treatment.

Study II

Reflectance spectrophotometry gives an objective estimate of blanching after the treatments, correlates well with the clinical results, and is helpful in monitoring and predicting the therapeutic outcome in PDL treated PWS.

Sixty-six patients with PWS mainly on the face, were measured with reflectance spectrophotometry before and after PDL treatments. Erythema figures were obtained for the PWS and the closely adjacent normal skin. A relative blanching effect could be calculated and was correlated with clinical results.

Study III

Reflectance spectrophotometry has been superior to LDI in the prediction of the outcome of PWS therapy. It is objective and correlates well with clinical results and is also portable and easy to use.

Measurements were performed with LDI in 19 patients with PWS, before and after 1–3 treatments and with reflectance spectrophotometry before and after 1–6 treatments. Increased blood flow was seen in 15/19 PWS before the treatment and directly after there was a decrease of the blood flow in almost all patients and surrounding hyperaemia. Reflectance photometry showed a successive increase in blanching and predicted within 6 weeks of the first treatment the eventual clinical result. LDI did not correlate well with the photometrically registered erythema.

Study IV

Skin ultrasound can help to characterise the PWS in the majority of patients and may help to predict the outcome of PDL treatment.

Fifty-five patients with untreated PWS on various locations were measured with a high-resolution ultrasound system. The mean maximal depth of all PWS, that were measurable (45/55), was 1.00 mm (±0.5 SD) Lesions on the trunk and extremities were more superficial than on other locations. PWS on good responding areas had a tendency to be more superficially located than PWS on the poor responding areas, but the depth is not the only and not the main parameter that is responsible for the treatment response.

Study V–VI

The purpose of the second part of the thesis was to investigate the psychological and psychosocial influence a PWS could have on the individual according to their own or that of family members. Another purpose was to see whether these influences were improved after the treatments and if there was any advantage in recommending an early treatment in life.

Study V

We found pronounced psychological and psychosocial negative parameters e.g. self-esteem, school problems and difficulties in social relations such as conflicts and new acquaintances in our patients with PWS.

A special questionnaire, developed in collaboration with a child and adolescent psychiatrist, was distributed to 259 patients with PWS and their families. The response rate was 89%. High emotional stress was encountered especially during the age of 10–20 years. Also, their families considered their family member to be negatively affected by his/her PWS. A smaller group of the patients that had completed their treatments reported improvement after their treatment and they also experienced less need to cover their PWS.

Study VI

There is high risk of developing negative parameters e.g. low self-esteem, school problems and difficulties in social relationships if you have a PWS, but the majority of these negative parameters can improve after the treatments. Therefore we recommend an early treatment in life.

Ninety patients who had completed their treatment received almost the same questionnaire as in Study V. According to the 147 patients that responded, the majority of the earlier reported negative psychological parameters improved significantly. The older the patient, the higher the score of negative experiences in most parameters. They also reported a tendency of recurrence and a preliminary report considering the possibility of heredity in PWS.

Comprehensive summary in Swedish

Populärvetenskaplig sammanfattning

Mellan 0.3 och 2.1 % av alla barn föds med portvins fläckar (PWS). Till skillnad mot vissa andra kärlmissbildningar försvinner inte PWS utan tvärtom blir många mer blåröda och tjockare med åren. Majoriteten av patienterna upplever sig vara negativt psykosocialt påverkade av sitt PWS i jämförelse med jämnåriga. Dessa negativa upplevelser minskar efter behandlingarna.(Se Studie V–VI).

Tidigare har inte denna typ av kärlmissbildning behandlats rutinmässigt på grund av risk för misslyckande. Men i mitten av 1980 talet inleddes behandling av äldre patienter med argon laser. Den medförde dock viss risk för ärrbildning och därför kom behandlingen från 1990 att ske med pulsad färgämnes laser (PDL). PDL hade en kortare pulslängd och dessutom stämde våglängden med blodkärlens upptag av ljuset. Även spädbarn kunde behandlas.

Den nya behandlingen ökade kraftigt i volym. Snart upptäcktes att flera PWS endast blivit partiellt blekta. Det var framför allt de som i utgångsläget var homogent bleka eller kraftigt blåröda och tjocka. Även de PWS som fanns mitt i ansiktet var svårbehandlade.

Många laserkirurger misstänkte att det kunde bero på att PDL inte gick tillräckligt djupt ned i huden och att kärlen antingen var för tunna eller för tjocka.

Om kärlen var för tjocka påverkades bara en liten del av PDL, var de för tunna kunde den uteblivna effekten bero på att laserljuset försvann rätt igenom utan att förstöra kärlen.

Vi studerade därför blodflödet, värmeutstrålningen, djupet av kärlen och reflektionen i PWS. Resultaten redovisas i studierna i I–IV.

Study I–IV

Målet i första delen av avhandlingen var att försöka att bättre karakterisera PWS med betoning på blodflöde, rodnad och djup i huden. Syftet var att behandlingsresultaten skulle vara lättare att förutsäga, följa, dokumentera och förbättra.

Studie I

Laser doppler imager (LDI) är mer användbart i forskningssammanhang än som ett instrument att förutsäga effekten av behandlingen.

Här undersökte vi blodflödet med hjälp av en ny typ av flödesmätning (LDI), som mäter över kärlområdet utan att röra vid huden. Samtidigt mätte vi värmeutstrålningen ifrån PWS och jämförde med normal hud intill PWS före och efter argonlaser behandling. Fyra av våra 13 patienter hade ett ökat blodflöde i sitt PWS före behandlingen jämfört med omgivande hud. Direkt efter behandlingen sågs i regel såväl ett ökat blodflöde som en temperatur stegring. 2 av de 3 patienter, som hade bäst behandlingsresultat hade högt blodflöde, och högre temperatur före behandlingen.

Studie II

Med hjälp av reflektansfotometri går det att objektiv bestämma blekningen efter behandlingarna. Metoden korrelerar väl med behandlingsresultaten och kan väl visa och förutsäga behandlingsresultaten av PWS efter cirka 6 veckor.

En ny typ av reflektansfotometri mätte den röda färgen hos 66 patienter med PWS (huvudsakligen i ansiktet), före och efter pulsad färgämneslaser (PDL). Vi fann en god korrelation mellan mätresultatet och det kliniska resultatet. Denna metod visade sig vara ett värdefullt hjälpmedel för att följa och dokumentera behandlingen av PWS.

Studie III

Reflektansfotometri är överlägset LDI i att förutsäga behandlingsresultaten av PWS. Metoden är objektiv och korrelerar väl med kliniska resultat och är dessutom lätt att använda.

Nitton patienter med PWS mättes med LDI och reflektansfotometri, före och efter 1–6

PDL behandlingar. Vi kunde konstatera ett ökat blodflöde hos 15 av 19 patienter. Direkt efter PDL sågs ett minskat blodflöde i PWS förändringen hos nästan alla patienterna, samt en ökad blodmängd i huden runtom. Reflektansfotometri visade att blekningen ökade successivt och kunde redan efter 6 veckor förutsäga det slutliga behandlingsresultatet. Blodflödet , mätt med LDI, korrelerade mindre väl med hudrodnaden mätt fotometriskt.

Studie IV

Ultraljudmätning kan vara till hjälp med att karakterisera PWS hos majoriteten av patienterna och troligen även bidra till att förutsäga behandlingsresultat eller val av behandling.

Med högfrekvent ultraljud studerades PWS förändringarna hos 55 patienter för att fastställa djup och utbredning av kärlmissbildningen. 45 av de 55 mätbara PWS förändringarna hade ett genomsnittligt maximalt djup på 1.00 mm, men kunde variera från 0.2–3.7 mm. PWS på bålen och extremiteterna var ytligare än i ansikte och på huvud. PWS på kroppsdelar som man vet svarar sämre på behandling låg något djupare än på lokaler som tidigare i regel svarat bra på PDL behandling. Djupen inom ett och samma PWS kunde variera med 0.5 mm eller mindre.

Studie V–VI

Målet med den andra delen av avhandlingen var att undersöka huruvida en patient upplevde sig vara stigmatiserad på grund av sitt PWS och hur patientens familj upplevde sin anhöriges reaktion till sitt PWS. Ett annat mål var att se, om denna eventuella stigmatisering försvann eller minskade efter behandlingarna.

Studie V

Våra patienter med PWS uppgav tydliga psykologiska och psykosociala negativa reaktioner, t.ex. dålig självkänsla, skol- och utbildningsproblem, samt svårigheter med sociala relationer, som att gå in i konflikter eller att träffa nya bekanta.

Vi skickade ut frågeformulär till 259 patienter och deras familjer för att utröna huruvida patienten upplevde sig själv vara stigmatiserad eller psykiskt påverkad av sitt PWS i jämförelse med sin åldersgrupp. Familjen fick i stort sett samma frågor om sin anhörig. Svarsfrekvensen var 89% och vi fann sammanfattningsvis tydliga psykologiska effekter med bland annat försämrad självkänsla, skolproblem och svårigheter i sociala relationer. En mindre grupp färdigbehandlade patienter antydde att dessa problem hade minskat efter behandlingarna.

Studie VI

Det finns en stor risk att patienter med PWS ska utveckla negativa psykosociala reaktioner hos patienter med PWS. Men majoriteten av dessa reaktioner försvinner eller förbättras efter behandlingarna. Vi rekommenderar därför en tidig behandling i livet.

Etthundrasextiotre patienter med PWS som hade avslutat PDL- behandlingarna, antingen på grund av att de var färdigbehandlade eller att man inte fick någon ytterligare förbättring av PDL (eller av intensivt pulsat ljus eller annan typ av laser) besvarade ett frågeformulär liknande det i Studie V. De 147 patienter som svarade ansåg att de flesta av de negativa psykosociala faktorerna de hade uppgivit före behandlingarna förbättrades signifikant efter PDL, t.ex. kontakt med motsatta könet, sociala relationer, skolkontakter, behovet av att täcka sitt PWS, svårigheter att möta nya människor eller att våga gå i konflikt. Äldre patienter hade en mera negativ uppfattning om sitt liv före behandlingen jämfört med de yngre patienterna.

Tjugosex procent av patienterna rapporterade även att delar av deras PWS återkommit efter några månader upp till 2 år efter behandlingen. Det gällde framför allt om behandlingen avslutades innan alla kärlen var borttagna.

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Evaluation of Port Wine Stain Perfusion by Laser Doppler Imaging and Thermography Before and After Argon Laser Treatment*

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Thirteen patients with port wine stains (PWS) were treated with argon laser therapy. Before and at different points in time following treatment, skin blood perfusion and temperature were mapped with laser Doppler imaging and thermography. In nine patients no elevation in blood perfusion was observed in the PWS in comparison with the surrounding normal skin before treatment. In the remaining four patients a significantly ($p < 0.01$) higher blood flow was recorded within the PWS. Immediately after treatment nine patients showed elevated perfusion within the PWS. During the first two days following treatment, all patients showed a gradually decreasing hyperperfusion in the borderline between the PWS lesion and surrounding skin.

Immediately after treatment 10 patients had a significantly ($p < 0.01$) higher temperature in the PWS than in normal skin. During the first 24 h following treatment, an elevated perfusion was in general accompanied by a tissue temperature increase. Three and a half months after argon laser treatment, three patients showed excellent clinical results with no remaining PWS spots or scarring. Two of these patients had had both elevated perfusion and temperature in the PWS prior to treatment. ***Key words: Port wine stain; Argon laser; Laser Doppler imager; Thermography.***

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Port wine stains (PWS) are congenital capillary telangiectasias (1, 2) which were treated with multiple therapeutic modalities including cosmetics, surgery, ultraviolet radiation, dermabrasion and tattooing before argon laser therapy was introduced in the sixties (3). Therapeutic success utilizing argon lasers has, however, varied (4). Best results have been obtained with darker lesions, especially in the face and in elderly patients (4). The treatment is time-consuming and may, unless carefully planned and performed, cause severe scarring. It is therefore of paramount importance to find predictive methods that allow optimal selection of patients for argon laser therapy.

Apfelberg et al. (5) studied blood perfusion in PWS patients with laser Doppler flowmetry, but were unable to predict the outcome of argon laser treatment. The difficulties may be attributed to the fact that the laser Doppler flowmeter gives information about tissue perfusion in only a single point, while the vascular architecture of PWS varies greatly even within the same area (6). In order to overcome this limitation of laser Doppler flowmetry, Nilsson et al. (7) developed a laser Doppler imager that creates an image of tissue perfusion. The method is based on the recording of Doppler shifts caused by movements of blood cells in the backscattered light of a laser beam that successively scans a certain tissue area.

The objective of this study was to investigate the perfusion status of PWS with a laser Doppler imager immediately before and at different points in time after argon laser treatment. Since thermography is considered useful in the prognosis of the outcome of argon laser therapy of PWS, it was included as a reference method (8).

MATERIAL AND METHODS

Patients

Thirteen patients (9 females) with PWS of various extents on different parts of the body were included in the study. All lesions were congenital and only one had been treated before. The age of the patients ranged from 17 to 65 years, with a mean of 29 years. Patient data and PWS sites are listed in Table I.

Argon laser

An argon laser (type Coherent Model 910) was used for treatment of the PWS. This laser emits light in the spectral range 488 to 514 nm. The light is guided through an optical fiber from the laser tube to a hand-held treatment head, producing a 1.5-mm wide beam (9). A 0.5-sec pulse duration was used with a mean power of 1.5W. According to earlier experiences this would give minimal risk of scarring.

In the skin, the light is absorbed mainly by melanin in the epidermal layer and by hemoglobin molecules in the red blood cells. The latter effect generates a certain amount of heat that coagulates and bleaches the tissue (10).

Laser Doppler imager

During the scanning procedure, the patient with PWS tissue is positioned between 12 and 20 cm under the laser Doppler imager (Fig. 1). Light from a 3-mW He-Ne laser is scattered onto the tissue by an optical mirror system. The 0.8-mm diameter light beam is moved step by step over the object, penetrating the tissue to a depth of a few hundred microns (11). In the presence of moving blood cells a fraction of the backscattered and Doppler-broadened light is received by a photodetector and converted into an electrical signal. This signal is further processed to scale linearly with blood flow (11) and eventually used as an estimator of perfusion. The scanning procedure and sampling by the perfusion estimator at each site of measurement is controlled by an AT IBM-compatible personal computer (Copam 386 SXB).

The complete scanning procedure requires about 4 min, during which time the light in the room is switched off in order to eliminate optical interference from the lighting with the Doppler signal. When all data are gathered, a colour-coded image showing spatial distribution of the tissue perfusion is generated on the monitor. Each of the six colours in the image corresponds to a certain interval of perfusion

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Table I. *Patient data*

Pat No	Sex	Age	Site
1	F	23	Back
2	F	67	Forehead
3	F	19	Cheek
4	F	23	Cheek
5	F	20	Thigh
6	M	19	Neck
7	F	22	Shoulder
8	M	20	Cheek
9	M	16	Neck
10	F	18	Thigh
11	F	16	Arm
12	M	53	Cheek
13	F	34	Forehead

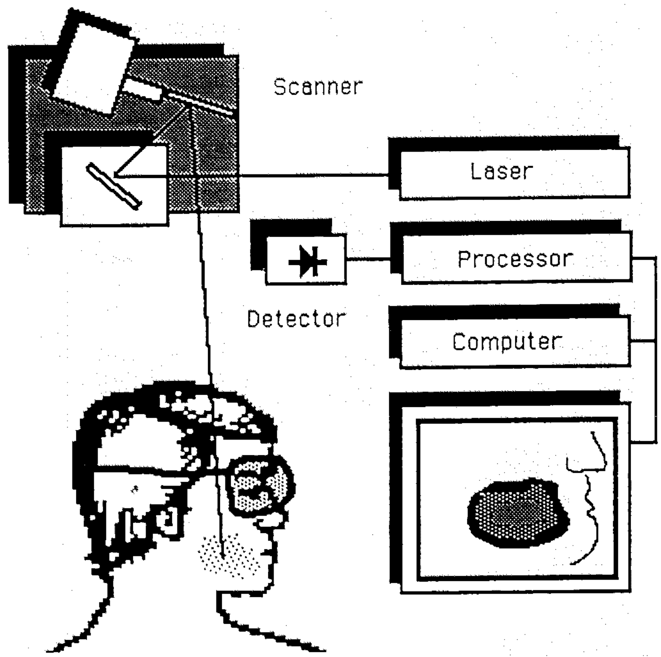

Fig. 1. Block diagram of the laser Doppler imager.

level. Black indicates low or zero perfusion, while highly perfused areas are coded in red. In order to be able to make comparisons between different images, the highest perfusion value in a series of images is used as a reference, and all perfusion values in the whole series are scaled in relation to this reference value. For the record, the images are put into a colour plotter (HP Paint Jet).

To compare the perfusion in normal skin with that in the PWS, the following statistical method was used. Two areas, one on normal skin and one on a PWS, were marked with a cursor. Each of the areas contained between 30 and 70 measurement sites. The samples were considered normally distributed. Mean perfusion and standard deviation were used to test the null hypothesis: the perfusion within the marked areas is identical. The level of significance was two-tailed and set to p-values < 0.01 in all cases.

Thermography

Skin temperature was measured in centigrades (°C) using a realtime thermal imaging system (Thermovision 870, Agema Infrared systems AB, Stockholm, Sweden). The detector is thermo-electrically cooled and the system operates in the short-wave band between 2 and 5.6 μm. Infrared radiation emitted by the object is converted into an electrical video-signal by the scanning unit. The inaccuracy of the system is limited to ± 0.1 °C. A graphic plotter provides colour images showing temperature changes with 16 colours, with black indicating the lowest temperature and white the highest.

The mean value of skin temperature was calculated and compared to that of the corresponding reference area on normal skin. To compare the temperature in normal skin with the temperature in the PWS, the same statistical method was used as for Laser Doppler imaging (LDI).

Procedure

LDI and thermography of the PWS were performed immediately before and about 15 min, 24 h, 48 h and three and a half months after argon laser therapy. Before measuring a metallic reflector was positioned around the PWS lesion in order to facilitate identification of the boundaries of the lesion on the laser Doppler image and thermogram. On each occasion a photographic documentation of the lesion was made and the ambient temperature recorded.

After the first measurements were made, the patient was brought to the treatment room and argon laser therapy initiated. Local anaesthesia was applied (prilocain hydrochloride, 10 mg/ml without epinephrine). The average extension of the treated areas was 8 cm^2. Within 10 min after the treatment a second laser Doppler image followed by a thermogram was recorded in the temperature-controlled room. The

Table II. *Perfusion (Pe) and temperature(T) in PWS compared to surrounding normal skin,before and after treatment*

Pat.	Before		After		24h		48h		3.5mo		Clinical results	
No	Pe	T	Pe	T	Pe	T	Pe	T	Pe	T	3.5 mo	7 mo
1	0	0	+	+	+	+	+	0	0	0	M	M
2	+	+	+	+	+	+	0	+	+	0	E	E
3	0	0	0	+	0	+	0	+	0	0	G	G
4	0	0	–	+	–	+	–	0	+	0	E	E
5	0	0	+	+	+	+	+	+	0	0	U	/
6	+	0	+	0	0	0	0	0	/	/	/	M
7	0	0	+	+	+	0	0	0	/	/	/	G
8	0	0	–	0	blister	blister			0	0	M	G
9	+	0	0	0	0	0	+	0	+	0	U	U
10	0	0	+	+	+	+	+	0	+	0	G	E
11	0	0	+	+	+	+	0	+	0	0	M	M
12	+	+	+	+	+	+	+	+	+	+	E	E
13	0	0	+	+	0	0	0	0	/	/	G	E

0 = no significant difference; + = higher perfusion/temperature in the PWS, $p < 0{,}01$; – = lower perfusion in the PWS, $p < 0{,}01$; / = patient not available for study; E = excellent; G = good; M = moderat; U = unchanged

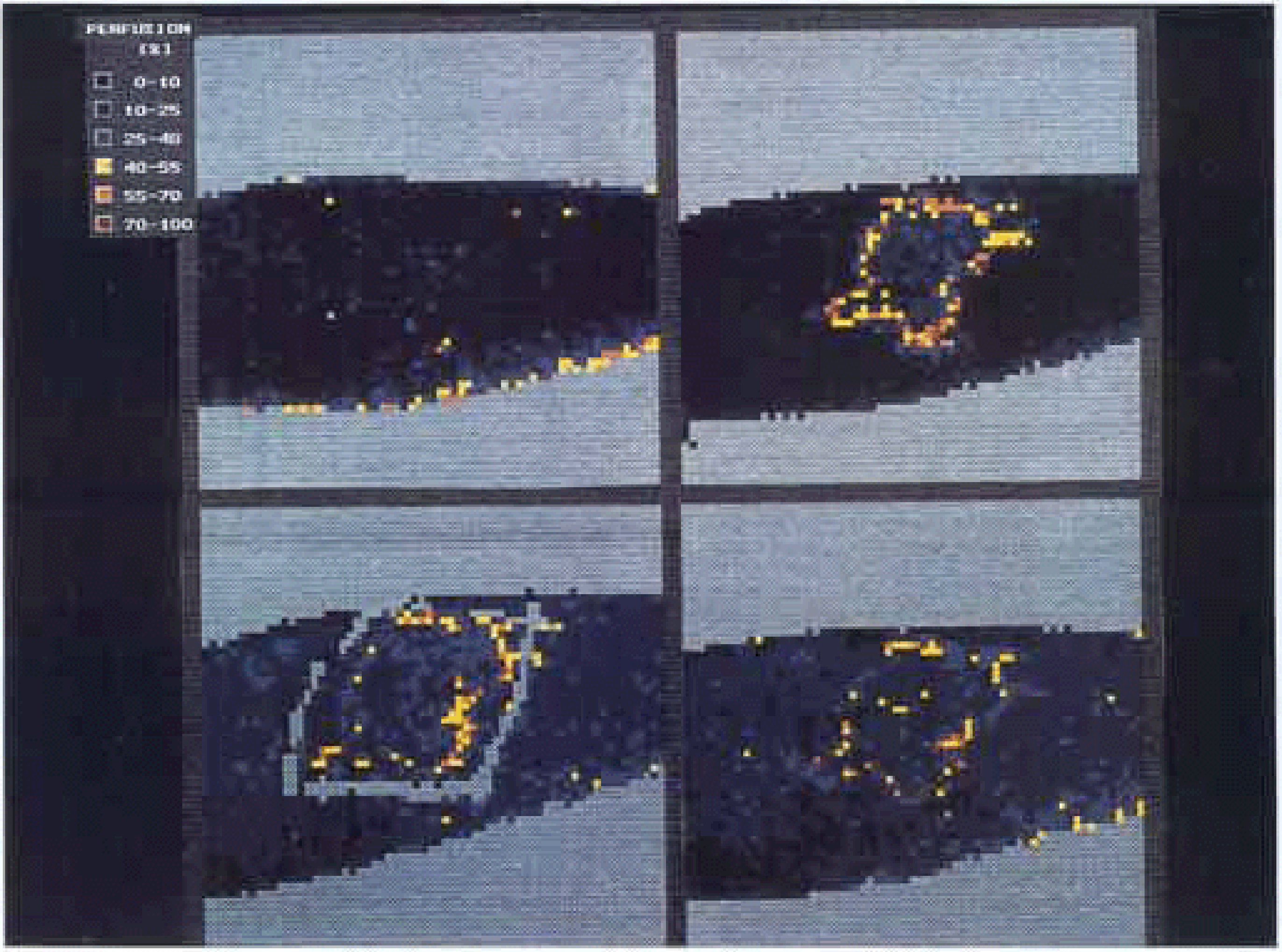

Fig. 2. Perfusion images, from left to right; *a*) before treatment, *b*) directly after treatment, *c*) 24 h after treatment and *d*) 48 h after treatment. The areas marked in green are used for statistics.

ambient temperature was kept within 22.0 ± 1.4°C during all measurement procedures.

In association with the measurements performed three and a half months after treatment, a judgement of the results was made in collaboration with the patient. The results were classified as *excellent, good, moderate* or *unchanged*.

RESULTS

Laser Doppler imaging

Before treatment, LDI did not show any difference between perfusion levels within the PWS and in the surrounding unaffected skin in 9 out of 13 patients (Table II). In the remaining four patients, significantly elevated perfusion was observed within the PWS lesions. In patient No. 12, who was earlier treated with electrocoagulation, high perfusion values were observed in regard to spots within the PWS.

After treatment, all patients showed pronounced hyperemia in the borderline between the PWS and surrounding skin. In 11 patients perfusion in the centre of the PWS was significantly different from that of normal skin. In 2 of these patients (No. 4 and 8) reduced perfusion was observed. In the remaining 9 patients elevated perfusion was recorded.

After 24 and 48 h there was a gradual reduction of perfusion in the borderline between the PWS and surrounding tissue. At these points in time an elevation of perfusion in the centre of the PWS was observed in 7 (after 24 h) and 5 (after 48 h) patients, respectively. One patient (No. 4) still showed significantly lower perfusion in the PWS both 24 and 48 h after treatment.

After three and a half months, reactive hyperemia in the borderline between the PWS and surrounding skin had disappeared, and perfusion returned to baseline levels in all patients. In 5 out 10 patients, however, a blanched PWS and higher perfusion was now observed within the treated area in comparison with the surrounding skin.

Fig. 2 shows examples of perfusion images, before and after treatment for patient No. 11. In the image taken immediately after treatment, the hyperemic zone is clearly seen, as well as higher perfusion in the treated area. The areas used for statistics are marked with a green border.

Thermography

Before treatment only 2 patients (Nos. 2 and 12) showed higher temperature within the PWS as compared to surrounding tissue (Table II). Eight patients showed a measurable rise in PWS temperature after argon laser treatment. The average temperature increase was 1.9 ± 1.6 °C. The PWS that had a higher temperature from the start (Nos. 2 and 12) did show an average temperature increase of 0.7 ± 0.3 °C. Immediately after the treatment all 10 patients had higher temperature in the PWS area than in normal skin. At the 24- and 48-hour measurements the elevated temperature slowly decreased, but a return to pretreatment levels was observed only in measurements made after three and a half months.

Clinical results

Three and a half months after argon laser treatment, three patients (see Table II) showed *excellent* results with no PWS spots left and no scarring. Three patients showed *good*, three patients *moderate* results and two patient were almost *unchanged*. Two patients were not followed up at the three and a half month control. No patient showed scarring in the treated PWS area. After seven months a slight progress in blanching was seen in all patients who were followed up. This was expected according to earlier experiences and literature (3). Two of the patients with excellent results (Nos. 2 and 12) showed high tissue perfusion in the PWS, as manifested with both LDI and thermography prior to treatment.

DISCUSSION

The main abnormalities characterising PWS are vascular ectasia and a substantial increase in the number of vessels.The vessels in mid and deep dermis have a defect innervation which may be of importance for the developement of the disease (12). Mean vessel depth within the PWS is 0.46 ± 0.17 mm and vessel density is highest in the immediate subepidermal area(13). Age correlates well with both progressive vessel ectasia and colour shifts from pink to purple (13). In healthy skin the argon laser beam penetrates the tissue to a depth of about 1 mm (14), while the scanning He-Ne laser beam in the LDI device has a median measuring depth of about 0.2 mm (15). The depth of the argon laser beam is dependent on the amount of melanin in tissue and to some extent on erythrocyte concentration (10). Thus, the majority of ectatic vessels and the thermal energy delivered by the argon laser beam and the peak sensitivity of the laser Doppler imager are all confined to the upper 1 mm layer of the skin.

Thermography (8), transcutaneous microscopy (16), reflectance spectrophotometry (17) and laser Doppler flowmetry (18, 19) are examples of non-invasive methods used earlier in the assessment of argon laser treatment of PWS. Generally, large differences between measurement results obtained from the PWS area in comparison with normal skin correctly predicted a favourable outcome of argon laser therapy (20). This is in accordance with the results obtained in this study, where two (Nos. 2 and 12) out of the four patients with excellent results had both elevated tissue perfusion and temperature within the PWS area. These two patients were older than the others (67 and 53 years, respectively) and their PWS were purple in colour and located on the face. Elevated perfusion prior to treatment was also found in two patients (Nos. 6 and 9) with only moderate and unchanged clinical results. These two patients were, however, younger (19 and 16 years, respectively) and their PWS were not purple colour.

All patients had increased perfusion in the border between the PWS and healthy skin tissue directly after treatment as measured with LDI. The hyperemia, which was interpreted as a normal reaction to heat stimuli in healthy skin, diminished gradually during the following two days and had disappeared completely three and a half months later. The increased blood flow seen in the centre of the lesion in the majority of the patients directly after argon laser treatment was more surprising, because immediate coagulation of the vessels would have been expected. The phenomenon may be explained by the fact that although the median measuring depth of LDI is about 0.2 mm, sensitivity to perfusion throughout a deeper microvascular network is still significant (15). If this deeper network is thermally stimulated rather than coagulated by the argon laser beam, an increase in perfusion, that will give a substantial contribution to the recorded Doppler signal may be expected. In addition, increased perfusion in the deeper dermis could be due to the inflammatory response. In either case the reaction may be the cause of the persistent elevation in PWS area temperature that was frequently observed after treatment. During the first 24 h after treatment elevated perfusion was accompanied by a tissue temperature increase in 14 out of 16 measurements.

In conclusion, this study shows that in only 4 out of 13 patients was the perfusion higher in the PWS than in the surrounding normal skin before treatment. After treatment a parallel elevation of perfusion and temperature within the PWS area was in general observed. The results indicate that neither the LDI technique nor thermography can unambiguously predict the clinical results of argon laser treatment of PWS. Both methods may yet be useful tools in the further understanding of the pathophysiology of PWS.

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II

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Reflectance spectrophotometry in the objective assessment of dye laser-treated port-wine stains

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Summary At present, the treatment of choice for congenital capillary malformations of the port-wine stain type (PWS) is the flashlamp pulsed dye laser. Good results can be obtained in the majority of patients with this technique, but there is a group of poor responders. In the search for predictive tools to determine the therapeutic outcome, we have used a new photoelectric reflectance instrument.

Sixty-six patients with PWS, mainly on the face, were treated with a pulsed dye laser during a 21-month period. Using a hand-held reflectance photometer, erythema indices were obtained for the PWS and normal skin. Based on these indices, a relative blanching effect could be calculated.

The therapeutic result was judged to be excellent in 19, good in 20, fair in 14 and poor in 13 patients. There was a good correlation ($r = 0{\cdot}844$) between the degree of blanching and the therapeutic result. In the 'excellent' category, an average blanching effect of 47% was present after the first treatment, and this increased to between 75 and 100% after successive treatments. In the 'poor' category, the blanching effect after one treatment averaged 14%, increasing to only 40% after up to six treatments.

It thus seems to be possible to predict the outcome of therapy, which is of considerable help in treatment planning. Reflectance measurements, an objective estimate of blanching, correlate well with the clinical results, and are helpful in monitoring and predicting the therapeutic outcome in dye laser-treated PWS.

The treatment of choice for congenital capillary malformations,[1] or port-wine stains (PWS), is the flashlamp pulsed dye laser,[2,3] which produces good cosmetic results, with very few side-effects.

Patients with PWS are stigmatized, especially when the birthmark is situated on the face.[4] The psychological impact of the lesion is already manifest in childhood, and affects not only the patients but also their families.[5] Affected individuals have often been searching for effective treatment all of their lives. They are usually ready to accept treatment risks, and some have already undergone unsuccessful therapy with, for example, phosphor radiation, argon laser or surgery. It is therefore important to be able to predict whether a new therapy, such as the dye laser, is going to be successful or not.

Factors influencing the therapeutic results have not been well characterized. PWS are heterogeneous with regard to the calibre and depth of the vascular malformations,[6] and a poor response to therapy could be due to the presence of larger calibre vessels or because the vascular malformations are situated too deep in the dermis to be reached by this kind of laser radiation, which has a penetration depth of only about 1·2 mm from the dermo-epidermal junction.[7] The anatomical location may also be a factor, as PWS in centrofacial regions, and involving dermatome V2 in both adults and children, showed statistically significantly less lightening following laser treatment than PWS on the other regions of the head and neck.[8]

The destruction of the vessels and the resultant blanching is a gradual process, which can be difficult to assess accurately visually. Techniques used with variable success to monitor treatment effects include photography, laser-Doppler imaging and thermography,[9] colour measurement, and spectrophotometry.[10] We have investigated a new type of reflectance spectrophotometer for the evaluation of PWS, and studied the correlation with the clinical result, as well as its value in predicting the therapeutic outcome.

Methods

Patients

Sixty-six white patients of Scandinavian descent (44 females) with congenital capillary malformations, mainly on the face and neck (58 patients), were studied. Only two had PWS which were blue–red in colour; the others had light-red macular PWS. There were no red-haired Celtic patients; all were of skin types II and III. Only six patients had been treated previously with phosphor radiation, argon laser or carbon dioxide laser. The age range was 4–46 years, with a mean of 24 years, and they were not suntanned.

Pulsed dye laser

We used a flashlamp pumped pulsed dye laser (Candela SPTL-1, Candela Corp., Wayland, MA, U.S.A.), with a wavelength of 585 nm and a pulse duration of 450 μs. The wavelength coincides with the third absorption peak of oxyhaemoglobin. The energy dose used was 5·75–7·5 J/cm^2, and the spot diameter was 5 mm. Local

Figure 1. Measurements with the reflectance spectrophotometer on a pulsed dye laser-treated port-wine stain.

Figure 2. Port-wine stains before (left) and after (right) treatments with the pulsed dye laser. Examples of the clinical evaluation in patients from the different groups: (a) excellent; (b) good; (c) fair; (d) poor.

anaesthesia (EMLA®, Astra, Sweden) was rarely used. Treatment intervals were 6 weeks, but during summer, and if the patient developed reactive hyperaemia, 12-week intervals were used.

Reflectance photometry

A hand-held microprocessor-controlled reflectance photometer with a digital readout was used (Dermaspectrometer, Cortex Technology, Hadsund, Denmark). The instrument, emitting green and red light at 568 and 655 nm, respectively, measures the amount of light reflected by the skin. When there is increased blood content, resulting in erythema, a greater amount of green light is absorbed and less is reflected. The instrument provides a readout of the erythema and melanin indices as a function of the absorbance characteristics of human skin. The measured skin area is a circle with a diameter of 11 mm. The theory behind this instrument has been described previously.[11,12] Only the erythema index was used in the present study. The instrument compensates for ambient temperature and light. Ten repetitive measurements of the same skin area showed a standard deviation of ± 1·4 (mean 24).

Immediately before and after the laser treatment reflectance measurements were performed in triplicate with the photometer (Fig. 1), both of lesional skin and of closely adjacent normal skin.

Evaluation

Treated areas were photographed before and after the treatment sessions. An overall clinical evaluation, which included assessment of the photographic material and

Figure 2. (*Continued*)

the patients' appraisal, was performed at the end of the treatment (but without use of the spectrophotometric results). The result was rated as either excellent, good, fair or poor (Fig. 2). Those with an excellent result had total fading, the good group showed subtotal fading with minimal residual telangiectasia, the fair group had some fading, and the poor group had minimal or no fading. According to the treatment response, from one to nine treatments were given to each patient, at 6–12-week intervals. The measurements were made during a period of 21 months.

Statistics

The Spearman rank correlation test was used for statistical analysis of the data.

Results

Based on the erythema indices of normal and PWS skin a relative blanching effect could be calculated, ranging from total blanching (100%), when the treated PWS had attained the same erythema index as adjacent normal skin, to no blanching (0%), when no change in redness of the PWS was noted after treatment. A blanching effect which averaged 47% was already evident after the first treatment in the 'excellent' response group, increasing to between 75 and 100% after successive treatments. In the 'poor' response group, the average blanching after one treatment was 14%, and did not exceed 40% after successive treatment sessions (Fig. 3; Table 1).

In the overall assessment of the clinical effect, the treatment was judged excellent in 19, good in 20, fair in 14 and poor in 13 patients. There was a very good correlation ($r = 0{\cdot}844$) between the degree of blanching and the clinical evaluation of the therapeutic result (Table 2). None of the patients had scarring or persistent pigmentation.

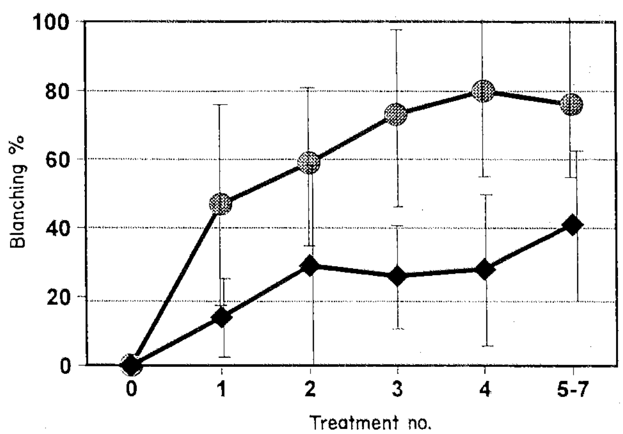

Figure 3. The average percentage of blanching, and the number of treatments, in the 'excellent' and 'poor' groups. Vertical bars indicate standard deviation. ◍, Excellent, ◆, poor.

Table 1. The number of patients still receiving treatment after each treatment session in the 'excellent' and 'poor' groups

Treatment number	Excellent	Poor
1	18	13
2	16	8
3	10	7
4	7	6
5–7	6	6

Discussion

Objective characterization of PWS is an important requirement in therapy, but has been difficult to achieve. PWS contain an increased number of oversized blood vessels, primarily in the papillary dermis. Considerable variation in the structure and size of these vessels is one explanation of why no single type of laser seems ideally suited to treat all PWS. Histological analysis has limited value, because of regional variation, unless a large part of the PWS is studied.[13,14] Subjective clinical assessment has thus been the main method of monitoring treatment.[15]

Several studies have been performed in the search for methods of objective evaluation. Tang *et al.*,[16] using a scanning spectrophotometer in a study on argon laser-treated PWS, obtained reflectance curves after treatment which were identical to pretreatment curves, in young patients. Only in older patients with darker

Table 2. The percentage of blanching at the end of treatment in the four clinical evaluation groups (excellent, good, fair and poor), and the number of patients within each group

	Blanching (%)					Total number
	0–20	20–40	40–60	60–80	80–100	
Poor	62	24	7	7	0	13
Fair	21	14	58	7	0	14
Good	0	10	10	55	25	20
Excellent	0	0	5	5	90	19
Total number	11	7	12	14	22	66

lesions was an increased reflectance seen.[16] Neumann *et al.*[17] determined the lightness of the skin after argon laser treatment in PWS patients, using photoelectric colorimetry. They found a good correlation with the clinical result, but the disadvantage of this technique is its poor capacity to differentiate between melanin and haemoglobin, as an increase of either pigment leads to a decrease in lightness. The reflectance photometer used in our study measures erythema separately. Lanigan and Cotterill,[18] in a comparative study on PWS and normal skin, used a reflectance spectrophotometer with absorption peaks which were slightly different from ours (566 and 640 nm). Local heating or cooling of facial PWS did not induce any significant changes in skin reflectance. Treatment sequences were not monitored in this study. Malm and Tonnquist[10] compared telespectrophotometric reflectance measurements and a natural colour system evaluation in PWS patients after argon laser treatment. The latter system, which is based on psychometric experiments, was claimed to be more suitable for qualitative judgement of the colour change.

We achieved a plateau in laser-induced blanching after three to four treatments in the 'excellent' group. After five treatments, little additional blanching could be achieved. In the 'poor' category, the blanching effect after one treatment averaged 14%, increasing to 40% after successive treatments (Fig. 3). As this low blanching effect corresponded to a poor clinical result, it probably indicates that further laser treatment will not be successful, and should be avoided. It thus appears that the therapeutic outcome is already predictable at the time of the second treatment session, which could be of considerable help in treatment planning.

The number of patients receiving treatment decreased with successive dye laser sessions, either because the results were already excellent after a few treatments, or because of early acknowledgement of treatment failure (Table 2). Our treatment policy has been to continue therapy as long as the patient and the physician notice any additional blanching. This policy can be followed because of the minimal risk of scarring with the dye laser. With other lasers, such as the argon and Nd-Yag, this principle would involve an increased risk of scarring.[19] The clinical results with the dye laser in PWS are generally superior to other lasers.[20]

After the fourth or fifth treatments, we noticed that many patients had a reactive erythema which often persisted for about 2 months. This may have been because the treatments were too frequent. We therefore preferred to postpone further treatments for at least 12 weeks, until this erythema had resolved, as it might have interfered with the evaluation of the clinical effect. Erythema can develop without an increased blood flow, and a stimulus which produces hyperaemia will not necessarily produce erythema.[21] This suggests that erythema may be a more relevant monitoring parameter than blood flow, although we have previously shown that laser-Doppler imaging can also be used as an informative instrument.[9]

To optimize treatment results with the dye laser in PWS we need an objective evaluation technique to define when to continue and when to stop therapy. Reflectance photometry seems to fulfil this requirement well.[22] Reflectance measurements have been shown to provide an objective estimate of blanching, and to correlate well with the clinical assessment of treatment results. They can thus be helpful in monitoring and predicting the therapeutic outcome.

Acknowledgments

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III

Page 291, third session to the right, line 8. 1 and 6 treatments… during a period of nine months. Fifth session, line 6, 568 nm (not 585).

Page 292, Statistics: Wilcoxon rank sum test was also used when comparing smokers with non-smokers.

Acta Derm Venereol (Stockh) 1996; 76: 291–294

Evaluation of Port Wine Stains by Laser Doppler Perfusion Imaging and Reflectance Photometry before and after Pulsed Dye Laser Treatment*

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Treatment of choice for congenital capillary malformations of the port wine stain type is presently the pulsed dye laser. Although treatment results have usually been excellent or good, a few patients respond less well. Looking for a tool to predict and monitor the treatment we used laser Doppler perfusion imaging and reflectance photometry. Measurements with laser Doppler perfusion imaging were performed in 19 patients initially and after 1–3 treatments and with reflectance photometry initially and after 1–6 treatments. Before treatment, 15 of the patients had an increased bloodflow within the port wine stain in comparison with normal contralateral skin. After the laser treatments, 15 of 18 patients had decreased bloodflow within the lesion and all 18 had surrounding hyperemia. Reflectance photometry showed a successive increase in blanching and predicted within 6 weeks of the first treatment the eventual clinical result. The bloodflow, as measured with laser Doppler perfusion imaging, did not correlate well with the photometrically registered erythema. Reflectance photometry is a useful objective tool, which early in the treatment course indicates whether laser therapy will be successful. Laser Doppler perfusion imaging is less helpful in monitoring patients but may be of use in the study of port wine stain pathophysiology.

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Since the late eighties the flashlamp-pumped pulsed dye laser has been the treatment of choice for most congenital capillary malformations of the port wine stain type (PWS) in adults, children and infants (1). Numerous clinical studies have confirmed good to excellent results in most patients, with a very low incidence of scarring or pigmentary loss (2). It has been noted that the degree of response is dependent in some part on the anatomical location of the PWS. The midfacial portion of the cheek, the upper lip and the nose respond more slowly to treatment than other areas (3).

However, there is also a group of patients with congenital capillary malformations without arterio-venous or lymphatic components that are non-responders. These PWS are macular, rather deep pink coloured lesions with no sign of high flow vascularisation. Even after repeated laser treatments with high effect no blanching has been obtained.

Laser Doppler perfusion imaging (LDI), reflecting changes in bloodflow, has been used previously in the study of argon laser treatment of PWS (4). Reflectance photometry is another way of monitoring treatment as a function of erythema following increased erythrocyte content (5). We here compare the results with these two techniques representing different vascular parameters.

MATERIAL AND METHODS

Patients

Nineteen Caucasian patients (11 females and 8 males) with congenital capillary malformations mainly of the face and neck were studied (Table I). Three patients had undergone treatment earlier with either argon laser or phosphor radiation, but not at the site treated in this study. The age of the patients ranged from 12 to 46 years, with a mean of 28 years, and they were not suntanned.

Pulsed dye laser

A flashlamp-pumped pulsed dye laser (Candela SPTL-1, Candela Corp., Wayland, Mass., USA) with a wavelength of 585 nm and a pulse duration of 450 μs was used. This wave-length coincides well with the third absorption peak of oxyhemoglobin. The energy density used was 6.75 J/cm^2 and the spot diameter was 5 mm. No local anaesthesia was used. Occasionally 7.25 J/cm^2 was used at the second treatment session, if the treatment result was not satisfying. Between one and 3 treatments were performed at 6-week intervals during a period of 3 months.

Laser Doppler perfusion imaging (LDI)

Before and directly after each laser treatment two 4 × 4 cm well marked areas, of lesional and contralateral normal skin respectively, were measured with the LDI (PIM Laser Doppler Imager, Lisca Develop AB, Linköping, Sweden). This data acquisition and analysis system generates processes and displays colour-coded images of the tissue perfusion. The optical scanning procedure guides, with the help of mirrors, a low power He-Ne laser beam over the tissue by a maximum of 4.096 measurement sites. This procedure takes about 4.5 min. In the presence of red blood cells, at a depth of a few hundred microns, partially backscattered Doppler-broadened light is detected by a photodetector positioned in the scanner head (Fig. 1). The light intensity transforms through the photodetector into an electrical signal. This electrical signal is fed into a processor which generates an output signal proportional to the perfusion. The computer samples and stores each perfusion for further signal processing and data analysis. A colour-coded perfusion image can be displayed on a monitor (7). The red-orange colour represents a high bloodflow, green a medium bloodflow and the bluish dark colour a low bloodflow. A comparison to the control side was made, where ++ was a much higher bloodflow on the treated side, + a higher and ± no difference. A parenthesis was added when the flow was on the border to the lower sign (Table I).

Reflection photometry

Immediately before the laser treatments triplicate reflectance measurements were performed with the photometer at 23–25°C room temperature, both of lesional and of contralateral normal skin. The instrument used was a handheld microprocessor controlled reflectance photometer with a digital read out (Dermaspectrometer, Cortex Technology, Hadsund, Denmark). Green and red light at 585 nm and 655 nm, respectively, is emitted and the instrument measures the amount of

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Table I. *The results of laser Doppler perfusion imaging (LDI) and reflectance photometry (erythema index) before the first laser treatment*

Treatment results are expressed as % blanching and number of treatment sessions. + + = much higher (bloodflow in comparison to the contralateral normal side), + = higher, + − = no difference, () = on the border to the lower next sign. Clinical outcome after last treatment. E = excellent, G = good, F = fair, P = poor.

Location	LDI	Erythema index	% Blanching	Treatments	Clinical outcome
Cheek	++	13	54	4	F
Cheek	++	19		1	
Cheek	++	15	73	3	E
Upper hip	+(+)	15	7	5	P
Cheek	+	14	100	4	G
Neck	+	11		1	
Cheek	+	15	67	6	P
Cheek	+	10	60	6	G
Forehead	+	7	86	5	G
Neck	+	13	100	3	E
Neck	+	8	100	4	G
Cheek	+	13	62	5	G
Temple	+	5	80	1	E
Arm	(+)	26	46	3	P
Sternum	(+)	28	86	6	F
Thorax	+−	2	100	4	F
Thigh	+−	5	80	6	E
Breast	+−	14	86	5	E
Neck	+−	17	82	3	E

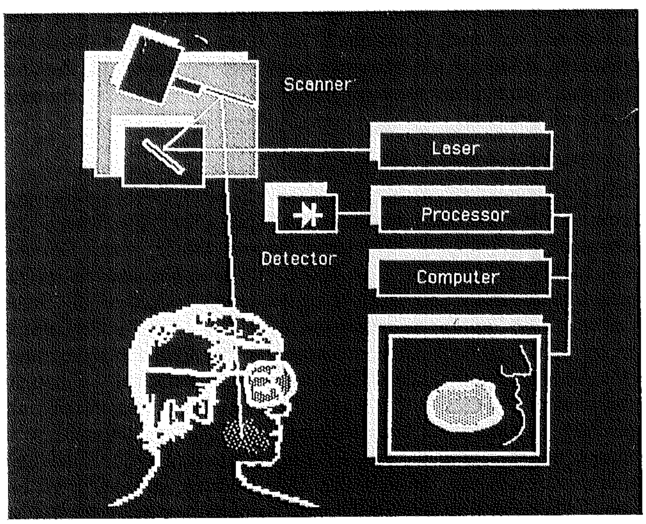

Fig. 1. The principles of laser Doppler perfusion imaging.

light reflected by the skin. The absorbance of the skin is registered as a read out of the erythema indices. For further details please see earlier studies (5, 8, 9).

The erythema index from the contralateral normal skin was subtracted from the erythema index from the PWS area before the relative blanching effect could be calculated. This relative blanching effect ranged from total (100%) blanching, when the treated PWS had returned to the same erythema index as the contralateral normal skin, to no (0%) blanching, when no change at all in redness of the PWS was noted after the treatment.

Statistics

The Spearman rank correlation test was used for the statistical evaluation.

RESULTS

Using the LDI technique, 15 out of 19 patients had higher blood perfusion in the PWS in comparison with normal contralateral skin before treatment. The remaining 4 PWS did not differ from normal skin (Table I and Figs. 2 and 3).

Directly after the first laser treatment 15 out of 18 patients had decreased perfusion, one had no change and 2 had increased bloodflow. All 18 patients showed hyperemia around the treated area, even when the surrounding area consisted of PWS skin. One patient's LDI registration was lost due to a technical error.

Before the second treatment 7 out of 14 patients, who could be measured with LDI, had a decreased perfusion in their PWS compared with the initial value. Five of the remaining 7 PWS had no change in their bloodflow. The last 2 had increased their PWS perfusion.

About 6 weeks after the second laser treatment 10 out of 14 had further decreased their perfusion, 2 had no change and 2 had increased their perfusion. All patients had peripheral hyperemia.

After the fourth or fifth laser treatment many patients had a reactive erythema, which often persisted for several months. Therefore, we preferred to postpone further treatments at least 12 weeks until this erythema was gone.

Reflectance photometry demonstrated a gradually decreasing erythema index along with the treatment sessions. Erythema was measured as the difference in reflectance photometry between the PWS area and the normal contralateral skin initially and before the last treatment (Table I). The average relative blanching effect achieved was 74%. There was no correlation between bloodflow and erythema ($r = 0.16$).

Clinical outcome after the last treatment was evaluated by the physician alone with the help of pretreatment photos. Two

Fig. 2. Port wine stains on right cheek before (*left*) and after (*right*) 4 pulsed dye laser treatments.

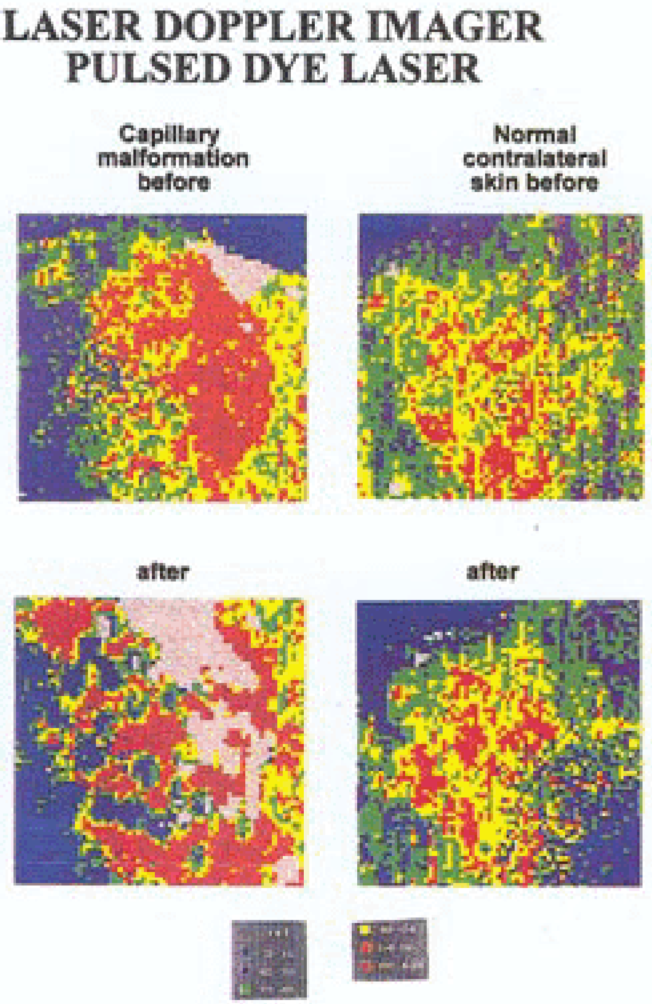

Fig. 3. Laser Doppler perfusion imaging before and directly after pulsed dye laser treatment of the right cheek, in comparison with the left untreated cheek. (Same patient as in Fig. 2). The grey colour is caused by high light absorption of the blue discoloration after the treatment (see Discussion).

patients did not turn up for the second visit for social reasons (Table I).

Seven of the patients were smokers, but there were no significant differences between these and the non-smokers directly after the treatment according to the reflectance photometry measurements.

DISCUSSION

Laser treatment allows a selective photothermolysis, with specific damage to superficial cutaneous blood vessels. The depth of penetration is about 1.2 mm (10). Following treatment superficial blood vessels show agglutinated blood cells, fibrin, and platelet thrombi confined to the papillary and reticular dermis, with little or no damage to the surrounding adnexa. Sequential biopsy specimens have shown destruction of abnormally ectatic vessels with replacement by normal-appearing new vessels with little or no dermal scarring in 1 month (11).

The microvascular blood flow in PWS has been studied by means of several methods over the last decades (4, 12). Many of these techniques influenced the vasculature because they were traumatizing to the skin (13). Even very slight external stimuli such as pressure or mechanical contact may disturb the flow conditions of the microvascular bed under study. It is therefore important to use non-invasive methods. The LDI used in this study is a novel non-invasive method for mapping tissue perfusion. No physical contact between the scanning device and the tissue is necessary, and there is no discomfort for the patient. This device is a modification of an LDI instrument used in an earlier study, where we found that only 4 out of 13 patients with PWS had an increased perfusion compared to surrounding normal skin before treatment (4). This indicated that the red colour of the PWS does not necessarily have to correspond to a high perfusion but could reflect only an increased number of ectatic vessels. In our present study we did not find a correlation between bloodflow and erythema (Table I). A stimulus which produces hyperemia will not necessarily produce erythema, and erythema can develop without an increase of the bloodflow (14).

In the present study we noted that 15 out of 19 patients had increased perfusion in comparison with normal contralateral skin. The remaining 4 patients had almost the same perfusion as in normal skin, and these PWS were situated on the breast, neck and thigh, while all the 15 PWS with increased perfusion were situated in the face. It is technically more difficult with this device to measure the blood perfusion of the thigh than the perfusion of the face. According to earlier studies, the skin microcirculation of the lower extremity decreases after lowering the leg (15), but in our study all the patients were measured in the horizontal position.

After the treatments small islands of either increased or decreased perfusion were often seen with LDI. This could be explained by non-homogenous laser therapy leaving untreated areas, or by the presence of normal vessels within the PWS area. These small areas with normal vessels are not treated and they respond with dilatation and hyperemia. Another point to consider is that PWS vessels in mid- and deep dermis have a defective innervation (16). Two patients had an increased bloodflow directly after the laser treatments. One had a lesion on the thigh and one on the cheek. The latter had earlier been treated with dermabrasion and cryosurgery. Both these patients responded excellently clinically to the treatments.

The blood perfusion of normal skin varies depending on the anatomical location. High perfusion is found e.g. in the face, especially in the medial parts. Centrofacial lesions and lesions involving dermatome V_2 in adults and children respond less favourably than lesions located elsewhere on the head and neck (3).

Before the second treatment, 5 patients had no change in their bloodflow compared to pre-treatment. This could be explained by the fact that vessels deeper than 1.2 mm from the dermo-epidermal junction are probably not reached by the dye laser radiation (10, 17), and vessels wider than 0.2 mm will probably not be effectively coagulated with the characteristics of our laser (18). Revascularisation from deeper vessels could then be a possibility. Two patients had increased their PWS perfusion compared to baseline, and this could be due to revascularisation with normal, not ectatic vessels. Within the lesion, however, the vessels vary in calibre and with age become more ectatic and slightly hypertrophic.

The LDI image registered immediately after laser treatment sometimes showed grey areas due to increased light absorption from the laser-induced bluish coloration of the skin. This could slightly enhance the reduced flow measured directly after laser therapy with the LDI instrument.

The relative blanching percentage in this study is comparable to an earlier report (5). The clinical results correlated well with the reflectance photometry measurements, as was recently shown (5).

LDI is a non-invasive method for mapping tissue perfusion. Bloodflow and erythema do not correlate well, however, indicating that for clinical, predictive purposes, erythema measurements with e.g. spectrophotometry may be more useful than measurements of bloodflow. Reflectance photometry is a sensitive technique for measuring erythema, according to earlier studies (5, 19). The size and the depth of the telangiectasias probably decide the therapeutic outcome with this type of laser.

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IV

Ultrasound Investigation of Port Wine Stains

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Congenital capillary malformation, or port wine stains, have been treated with the pulsed dye laser since the late eighties. Some studies have shown better results when the malformation have been located on the lateral face, forehead, neck, trunk and shoulder and inferior results with more treatments required on the central face area, dermatome V2 and the extremities. The purpose of this investigation was to study the depth of the lesion, in various locations. Fifty-five patients with untreated port wine stains, were investigated with a high resolution 20 MHz ultrasound system.

The mean maximum depth of all PWS, that were measurable (45/55), was 1.00 mm (±0.50 SD) with a rang of 0.2–3.7 mm. Lesions located on the forehead (1.26 mm, 0.44 ± SD) and on the medial face (1.23 mm, 0.65 ± SD), were deeper than lesions on the trunk and extremities, which were found to be more superficial. PWS involving areas that respond poorly to treatment were in average 0.14 mm deeper than PWS involving good responding areas. The depth of the port wine stains, as determined with high resolution ultrasound, seems to correlate only to some degree with the response to pulsed dye laser treatment. Since this treatment, with its superficial penetration, can not reach the deeper vessels of a port wine stain, skin ultrasound could be a good complement in the prognostic investigation as well as to plan treatment. In the presence of deeper vessel, we should probably use a longer wavelength than the 585 nm of the pulsed dye laser or 532 nm with a cooling tip.

Key words: PWS; depth; capillary malformations; good response; bad responder; pulsed dye laser.
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Congenital capillary malformations, commonly known as port wine stains (PWS) are macular reddish lesions, which are characterised by ectatic venular-sized channels within both the papillary and reticular dermis (1). The venules are normal in numbers (2), but immunohistochemistry demonstrates a decrease or absence of perivascular nerve fibers within the papillary and reticular dermis, highly suggestive of a lack of autonomic innervation of this vascular plexus (3). A relative or absolute deficiency of autonomic innervation may result in decreased tonus of the vessels and/or loss of neuronal trophic factors (4). Therefore with age, PWS become hypertrophic and darken (purple) in colour. In the presence of an absolute deficiency, the rate of progression or hypertrophy will be more rapid, whereas with a relative deficiency, this will be much slower (5). According to laser doppler perfusion imaging studies a high proportion of the PWS have an increased bloodflow in comparison with normal contralateral skin (6). After the pulsed dye laser (PDL) treatment most of the PWS showed a decreased perfusion (6). Thermography on the other hand, demonstrated a higher temperature with respect to surrounding skin in only 2 out of 12 patients with PWS (7).

Since the late eighties the treatment of choice for PWS has been the PDL with 585 nm wavelength and 450 microseconds pulse duration. More recently, modifications in the form of a longer wavelength and a longer pulsewidth have been introduced. Renfro & Geronemus found significantly different treatment responses in PWS of different anatomical locations (8). In addition to this, the age of the patient, the maturation (colour, thickness and degree of hypertrophy) and the size of the PWS and scarring from prior treatments affect the result. Fewer treatments were required for forehead, temple, lateral aspects of the face, neck and chest and shoulder lesions. Facial dermatome V2, medial and central aspects of the face and the extremities required more treatments (5). Non-responding PWS are usually confluent i.e. the whole dermatome is affected. On the other hand geographic PWS usually respond well and many of these have disappeared completely. Many investigators have addressed the question of these treatment failures (5,8,9). The penetration depth of the PDL is approximately 1,2 mm according to Tan et al (10) but limited to a maximum of 0.65 mm (mean 0.37 mm) according to Hohenleutner et al (11). Because of the limited penetration of the PDL the depth of the PWS may be one of the main causes of failure (9). Fiskerstrand et al studying punch biopsies, postulated that PWS with good blanching after PDL had significantly more superficially located vessels than the PWS of the moderate and poor responders (12), Vessels of a small calibre, around 20 µm, has also been shown to be another reason for poor response (12). Presently, there is no laser or intense pulsed light source, that can treat every type of vascular lesions successfully.

Haedersdahl et al (13) have demonstrated with ultrasonography, lower dermal echogenicity in PWS before pulsed dye laser treatment than after. According to our knowledge, no previous study has measured PWS with ultrasound, with the attempt to correlate the depth of the PWS vessels with various anatomical locations.

MATERIAL AND METHOD

Patients

Fifty-five patients (37 females) with untreated PWS were studied with skin ultrasound . All had macular PWS. The mean age of the patients was 18.9 years with a range of 3 months – 69 years. The median age was 15 years. The anatomic location of the PWS varied. One to 8 ultrasound measurements were made on each patient depending on the size and location of the PWS. In 19 of the 55 patients we performed 3 measurements on the same PWS macula, i.e. anatomical unit. Skin ultrasound was also always measured on the normal contralateral side of the site of the PWS.

Skin ultrasound

Throughout this study the depth of the lesions was evaluated using a high resolution ultrasound system dedicated to skin applications (13). A DermaScan C Ver. 3 (Cortex Technology ApS, Hadsund, Denmark) was used. The system configuration for this study operated at 20 MHz and provided a resolution of 60 × 130 microns (axial × lateral) with 10 mm penetration.

The system consists of a main unit accommodating the signal processing and computing components, a colour monitor to display the two-dimensional recordings and a handheld B-scanning ultrasound probe. The size of the probe is 19 × 33 mm and the scan-length 12.1 mm.

The principle of ultrasound imaging is based on the ultrasonic wave being partly reflected at the boundary of adjacent structures when travelling through tissue. The strength of this reflection depends on differences in density of such structures, which leads to an amplitude variation of the reflected signal. Finally, processing of the signal received from multiple ultrasound pulses over an area of the skin forms a two-dimensional image—a so-called B-scan.

The system calculates distance (a) using the equation:

$$a = \frac{1}{2}\ c\ t$$

where c is the average velocity of sound in the tissue and t is the time required for the ultrasound pulse to travel from the transducer into the tissue and back to the transducer. c was set to 1580 m/sec as an average speed of sound.

Depth measurements were based on A-scans, i.e. individual point to point measurements perpendicular to the skin surface, which were then averaged. All images were stored on disk for later analysis and printing.

The DermaScan C Ver. 3 was set up to use a colour coded greyscale, which displays less reflective tissue as dark/dark green colour and highly reflective tissue as yellow/white colour.

In order to compare with later recordings the lesion was carefully mapped on a transparent plastic overlay film and the scan position marked. The same interpreter (G.S.) evaluated all ultrasound images.

Ultrasound image

The visual appearance of an ultrasound image depends on the body site from which it originates. Homogeneous components (fat, water blood) show less internal reflections than non-homogeneous tissue (dermis). For this reason, blood in the dermis can be clearly distinguished from surrounding structures. A PWS appears as a superficial dark band right under the epidermal entrance reflection (Fig.1). Our measurements have been taken from the deepest part of each PWS image.

Statistics

In the calculations, the means within patients and localisation was used. Mann-Whitney U-test was used when comparing depth between groups. Spearman rank correlation coefficient was calculated for studying relationship between age and depth.

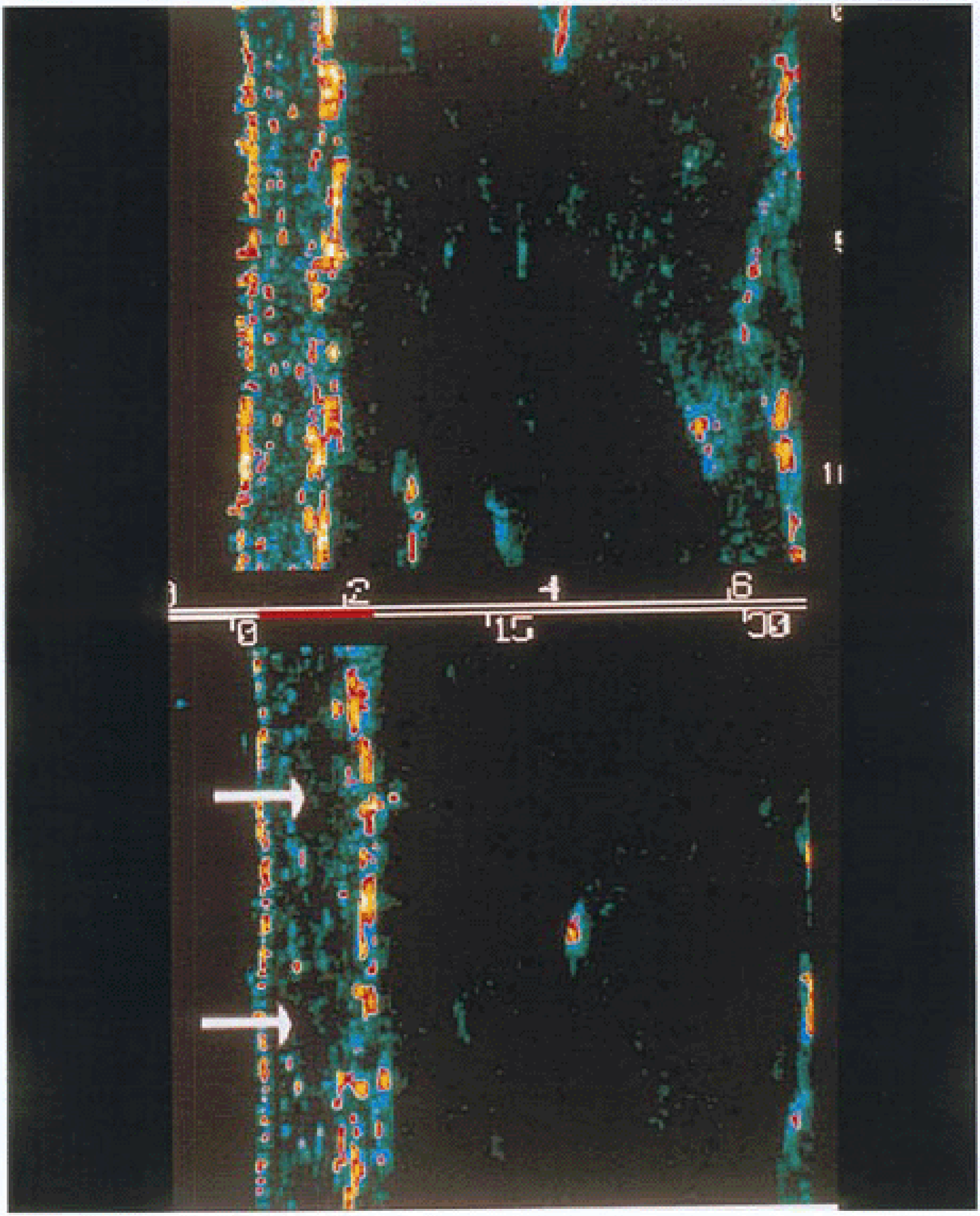

Fig.1. *Ultrasound images of normal skin upper arm (upper image) and PWS upper arm (lower image) (see arrows). (For explanation of colour code see text).*

RESULTS

In 10 of 55 (18 %) of the patients there were no clear indication of a PWS on the ultrasound image and therefore no possibility to measure the depth. Clinically these PWS were clearly visible. In the 45 patients (82 %) with PWS, that could be evaluated ultrasonically, the variations in depth was from 0.2 to 3.7 mm. The mean maximum depth of all PWS was 1.00 mm (± 0.50 SD). The deepest PWS were seen on the lips, nose and chin. Eight measurements were made on 7 upper lips with a mean depth of 1.21 mm (±0.37 SD, range 0.78 – 1.8).

Although there was not a significant statistical correlation, a tendency towards deeper PWS with increasing age was seen (Fig. 2).

When we looked after differences between the anatomical locations there were no significant differences when comparing with e.g. medial face (Table I). Only the forehead demonstrated some significant changes in comparison with the other locations.

We divided all of our PWS into two groups, in order to determine whether or not there was a correlation with previously published data on the response to PDL treatment on certain anatomic locations (5, 8):

I. Good responding locations: forehead (incl. temple), lateral face, neck, trunk had a mean depth of 0.94 mm (range 0.21–2.2, ±0.47 SD).

II. Bad responding locations: medial face (incl. nose, lip, chin, dermatome V2, extremities (incl. buttocks) had a mean depth of 1.08 mm (range 0.28 – 2.67, ±0.53 SD).

The mean value of group II were 0.14 mm deeper than of group I, but the difference was not significant.

In order to study the intra-PWS variability, nineteen patients in this study had 3 measurements performed within one confluent capillary macula (Fig. 3). All except 3 PWS showed a variation of 0.5 mm or less within different parts of the lesion. A variation of only around 0.1 mm were seen in 7/19. There was a tendency towards more spreading of the depths within the PWS with age. The younger patients were around the depth of 0.6 mm – 1.0 mm.

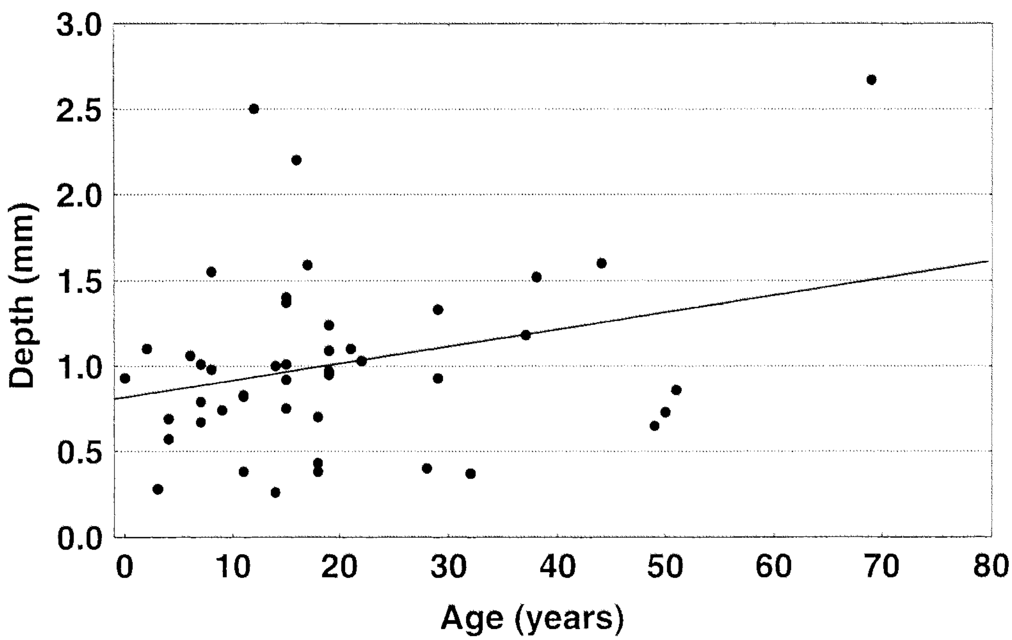

Fig. 2 *Mean depth of each PWS on 45 patients with correlation to their age. Each point represent one patient with the average of their measurements within their PWS.* $r_S = 0{,}19$. *NS.*

Table I. Anatomical locations of PWS and their depths. p* versus forehead. ($p < 0.05$, ns = not significant).

Location	N PWS	Mean (mm)	SD±	p*
Forehead	8	1.26	0.44	
Medial face	14	1.23	0.65	ns
Lateral face	12	0.92	0.25	ns
Neck	10	0.90	0.62	ns
Extremities	12	0.89	0.28	0.045
Trunk	6	0.64	0.45	0.023

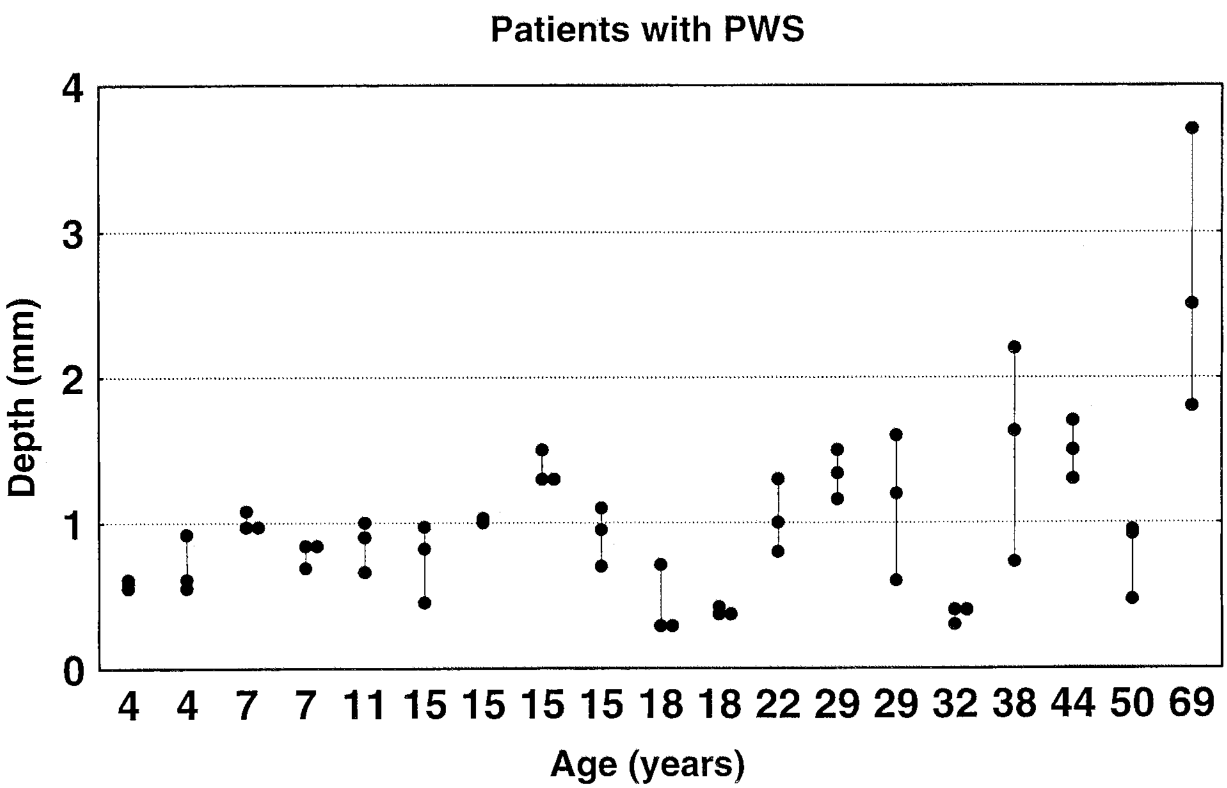

Fig. 3. *Nineteen patients (arranged in order of increasing age) with 3 ultrasound measurements of the same port wine stain in order to study the intra-individual variation.*

DISCUSSION

High resolution ultrasound is an objective and non-invasive technique which provides valuable information about the depth of the majority of PWS prior to treatment and during follow-up with no discomfort to the patient. This technique has been shown to provide accurate and reproducible dimensional measurements of structures within the dermis and subcutaneous tissue (13–17). The probe is easy to handle and its relatively small dimensions provides access to most body regions although scanning around the nose, the eyes and the ears may prove difficult. This would have been even more difficult if we would have used a C-probe, that is available on the market. A C-probe can scan a bigger area (22.4 × 22.4 mm) than the B-probe, but according to our knowledge the B-probe is better to use in the investigation of PWS, because of its smaller size and shorter scanning time. Many of our PWS are situated in the face, where it can be difficult to fit in with a large probe. Also many of our patients are children and sometimes it can be difficult for them to sit still during the investigation.

It is important to hold the B-probe floating on a thin layer of gel to avoid compression of the vessels.

Attenuation of the ultrasound signal varies due to body composition, measurement site, depth, frequency etc. and, accordingly, the gain setting may need to be individually adjusted to obtain the very best image quality. No other set-up parameters need attention during scanning.

Horizontal shadows in the image caused by tiny air bubbles trapped in the coupling gel are frequently seen. This is a well known artefact in high frequency ultrasound imaging, which is easily identified and corrected for simply by wiping off the membrane and skin surface prior to applying fresh gel.

One must pay attention to other skin conditions capable of causing subepidermal dark bands in the image. Particularly in sun exposed areas solar elastosis may provide similarly looking ultrasonic patterns. Consequently, it is important to perform a reference scan of normal skin adjacent to the lesion for comparison.

Histological evaluation of the depth of a PWS has earlier been used as the standard method of depth determination. The fixation of the tissue sometimes causes an artefact effect. Punch biopsies are of limited value for comparative study since they undergo retraction and change of dimension on cutting (14). Moreover, punch biopsies cause scarring. When we studied the intra-PWS variability we noted that there was some variation and that this variation ha a tendency to increase with age (Fig.3). Therefore, we took several measurements within each PWS, especially if they varied in colour and surface. Earlier histology studies of PWS have demonstrated a mean vessel depth of 0,46 mm (2) which is less than half the depth we have found . There are structural changes that are better visualised by ultrasound than histology, e.g. the age band of papillary dermis and vice versa (18). The major advantage of ultrasound lies in the fact that it is a non-invasive procedure, it provides an immediate result, and a large in situ tissue block can be examined easily with a good presentation of the tissue microanatomy and with free choice of body region. Ultrasound is thus akin to a "living biopsy".

The penetration depth of the 20 mHz ultrasound is 10 mm which is adequate to be able to register all PWS. The penetration depth of the PDL is according to earlier punsch biopsy studies on albino pigs a maximum of 0.65 mm with a mean depth of 0.37 mm (11) down to 1.2 mm measured on patients (10). It is obvious that many of the deeper PWS, e.g. of the medial face, might not respond well to PDL. Deeper vessels may not be coagulated because of shadow effects by superficial vessel layers (11). According to Motley et al there are two types of microvascular abnormalities (19). Type 1 consists of superficial, tortuous, dilated end capillary loops (blobs) which are readily treated with PDL and type 2 is composed of dilated, ectatic vessels in the superficial horizontal vascular plexus (rings) which are more deeply situated and do not respond as well to the PDL.

Ultrasonography seems to evaluate parameters different than skin redness (13). Ten out of 55 PWS were not visible on the ultrasound image. This was probably due to the very superficial location of the vessels or alternatively, too thin a calibre of the vessel. All of these 10 were pale in colour and 9 were geographic in pattern and not confluent. The patient with a confluent PWS was less than 1 year old. These lesions involved the lateral cheek (5 lesions), the neck and forehead (2 lesions) and one each the eyebrow, chest and buttock. PWS involving these anatomical locations (except the forehead) are more superficial according to our measurements. Seven of these PWS were at good and 2 at bad responding locations. One PWS covered both types of locations.

Two previous studies have also suggested that there is a correlation between the depth of the vessels, as determined histologically, and the response to treatment (9, 20). The level of the vessels of lesions in the bad responding areas, was only 0.14 mm deeper than the vessels of the good responding areas, a difference not statistically significant. Interestingly, the forehead, which according to earlier experience is a good responding location (Table I), had almost the same maximum mean depth as the medial face, which has been shown to be difficult to treat. Both locations should theoretically be too deep to be reached by the PDL. Also, the depth of our PWS on the extremities, were the most superficial ones, although they are considered to be a poor responding area. One reason for poor response on a superficial area could be the small calibre of the vessels (12). Maybe we had too few PWS on different locations to be able to draw any conclusions.

Our earlier studies have shown that there are potential psychological benefits from early treatment of port wine stains in children (21). Some studies have found that younger patients with PWS respond better than the older patients (22, 23). It has been postulated that PWS in adults need more treatments because the vessels are significantly wider than in children (23). Our study however, could not show a significant increase of the depth of the PWS with increasing age, but our material represents several anatomical locations and may have been too small from some of the locations. Tang et al suggested that with advancing age, both normal skin and PWS have a greater total haemoglobin content and an increased proportion of deoxyhaemoglobin, consistent with increasing vascular dilatation and tortuosity; and that the age-associated changes in PWS are an exaggeration of those in normal skin (24). The prominent ectasia is characteristic of the adult PWS but there are variations in between patients. The reason for this is unknown, but one explanation might be that the collagen degeneration that accompanies age may weaken the supporting dermal structures and allow the abnormal vessels to dilate. Barsky et al demonstrated that mean vessel area correlates with elastosis, but since both these parameters increase with age, this relationship is less helpful (2). Orten et al on the other hand, felt that there is a relative or absolute deficiency in autonomic innervation of the papillary plexus and that this may well offer an explanation for the variation in maturation (5). An absolute deficiency is associated with a more rapid ageing process of the PWS whereas a relative deficiency would tend to slow this process.

Haedersdahl et al (13) scanned 12 children with facial PWS (with the same device as ours), before and after one PDL treatment. There was no correlation between the change in echogenicity and the clinically assessed treatment response, but lower dermal echogenicity of preoperative PWS than of postoperative PWS and healthy skin were revealed. Their median values of skin thickness were 1.00 mm (0.92–1.13 mm) before PDL treatment. This figure correlates well with our findings of the mean maximum depth of 1.00 mm in our untreated PWS. They concluded that lesional thickness correlated inversely with the ultrasound-assessed treatment response

We can not conclude that the depth of the vessels is the only prognostic factor, but should be taken into consideration, as well as e.g. the rate of blood flow, which is higher in some PWS in comparison to contralateral side (25), and the vessel diameter (12), when considering treatment of a PWS. It is not surprising that some lesions fail to respond to the fixed wavelength and pulse duration of the PDL. Awareness of these inter- and intra- individual PWS variations may lead to continued improvement of predictive tools and of treatment modalities.

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Page 60, line 33, Patients and methods: We had 28 drop outs (not 26) 10.82 % of our patients.

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Potential psychological benefits from early treatment of port-wine stains in children

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Summary There is a commonly held conception among referring doctors that very small children with congenital capillary malformations, so-called port-wine stains (PWS), should not be treated until they are older. Our experience leads us to believe that the flashlamp pulsed dye laser is a safe and effective treatment even for infants. We have not encountered any persistent pigmentation changes, post-treatment scarring or other adverse effects. It is important to quantify the psychological disabilities associated with this disorder to assess the need for and the benefits of treatment. Questionnaires were distributed to 259 patients and their families who visited our clinic because of their PWS. Patients who were on the waiting list for laser treatment, undergoing treatment or had completed their treatment received different questionnaires. The response rate was 89%. High emotional distress was encountered. During the age period 10–20 years, 73% (125 patients) were most disturbed by their PWS. That the PWS influenced their life negatively was experienced by 75% (171 patients), and 62% (106 patients) were convinced that their life would change radically if their PWS could be eliminated. Suffering from low self-esteem (in comparison with the same age group) was reported by 47% (87 patients). The PWS made their school life and education more difficult according to 28% (51 patients) of the sample. Of the families of patients, 76% (106 relatives) considered the patient to be negatively affected in some way by the PWS. After the laser treatment, all of these distress parameters were significantly relieved, together with a need to cover their PWS, their fear of going into conflict or quarrels, their social relationships, problems with the opposite sex, rage attacks, depressions and abnormal reactions from their peers. We believe there is potential psychological benefit in starting the treatments of PWS (including non-facial) at as early an age as possible.

Congenital capillary malformations, so-called port-wine stains (PWS), are not rare birthmarks. The incidence figures vary because of the confusing terminology but, according to Mulliken,[1] 3·8% of newborn children have a vascular birthmark, and about 0·3–0·5% have a PWS located somewhere on the body.[2] About two-thirds of the PWS may develop hypertrophy with nodular elements that may bleed either spontaneously or after trauma. The vessels become more ectatic with age, making the bluish colour stand out more. Pyogenic granulomas can also develop.[3] There is no spontaneous regression of PWS.[1]

The emotional impact of having a PWS has been discussed in earlier reports,[4,5] and it has been pointed out that it appears that patients with PWS suffer a considerable degree of psychological morbidity, which they suppress. The standard psychological screening tests for psychiatric illness, depression or anxiety revealed that these patients had similar or less evidence of morbidity than control subjects or other patient groups.[6] Also, patients with large PWS were shown to have reality problems in common.[7]

The treatment of choice today is recognized to be the flashlamp pulsed dye laser (PDL), and many studies have shown its effectiveness both in the treatment of grown-ups[8] and in the treatment of children.[9] Several PDL studies have been carried out with infants and children, and their results have been effective and the procedures safe. Laser treatment improves the appearance of the PWS and is regarded favourably by patients. Patient assessments of treatment outcomes correlate well with the clinical results obtained.[10] The purpose of this study was to evaluate the degree of stigmatization among these patients and their families and to assess if patients on the waiting list for treatment differed in some way from the patients who were in treatment or had completed their treatment.

Patients and methods

Patients

Special questionnaires were developed in collaboration with the child psychiatrist (B.W.). The ethics committee of Lund University reviewed and accepted the study protocol. The following areas were covered: questions considering their self-esteem in comparison with the same age group, their acceptance of the PWS and how the PWS had influenced their lives; questions about school problems especially in consideration of concentration problems in school, relationships with friends and teachers; other school-related areas covered the feeling of being mobbed or the need to avoid different sports; questions about social and sexual relationships were always compared with the same age group. Those patients who were working were asked about difficulties at work caused by their PWS. They were asked whether their PWS had prevented them from going into quarrels and discussions with their colleagues at work. The patients were also asked about their relatives' behaviour towards them and how their relatives experienced the patients' psychosocial situation. The relatives were asked whether they had a feeling of guilt or an existing superstitious feeling of self-blame. The patients were asked if their life would change if they could get rid of their birthmark without a scar. These areas of enquiry were chosen from earlier studies[6,7] and from our experience with this group of patients.

Questionnaires were given to 259 patients. There were 26 drop-outs equally distributed among the groups. The completed questionnaires were returned by 231 patients and, of these, 185 were on the waiting list or in treatment and 46 had completed treatment. The latter group filled in the questionnaire in two parts. One part focused on how they experienced their situation after treatment and the other on how they remembered their situation before treatment. Their answers were compared with the 185 patients who were on the waiting list or still undergoing treatment. As there were no significant differences, the 185 answers before treatment were compared with the 46 answers after treatment to obtain a measure of the treatment effects.

The questionnaires were distributed during a period of 1 year (November 1994–November 1995) to all patients who attended the department for evaluation or treatment of PWS. Each patient and their next of kin received questionnaires, which they answered independently from each other. There were different versions of the questionnaire depending on the age of the patient and whether they were on the waiting list for treatment, had started treatment or had completed treatment. The parents were asked to answer for their children under the age of 9 years. The other age intervals were 9–15 years and 15 years and above (Tables 1 and 2). Many standard questions were the same in all questionnaires, and most of the questions were graded in five steps from 'big problem', 'evident problem', 'rather evident problem', 'in some way a problem' to 'hardly any problem at all'. For some questions, respondents also had the option to write down their own answers or comments. The group that had completed their treatment had the largest number of questions. Care was taken to avoid leading questions. The answers were computerized anonymously.

Statistics were made by comparison of two sample proportions using the normal difference test and the Wilcoxon rank sum test.[11]

The response rate was 89% with 231 patients of 259 returning the completed questionnaires. Sixty-six per cent were female and 34% were male. The age interval was from 1 to 80 years (see Fig. 1). Seventy-three per cent of the PWS were on exposed areas difficult to hide with make-up or clothes, e.g. face, neck and hands.

Table 1. Frequency distribution of patients within the three groups: waiting list for laser, during laser and completed laser treatment

	Age (years)			
	<9	9–15	>15	Total
Waiting list	16	5	68	89
During treatment	25	9	62	96
Completed treatment	3	4	39	46

Table 2. Frequency distribution among relatives within the three groups: waiting list for laser, during laser and completed laser treatment

	Age of family member (years)			
	<9	9–15	>15	Total
Waiting list	16	5	63	84
During treatment	25	9	59	93
Completed treatment	3	4	31	38

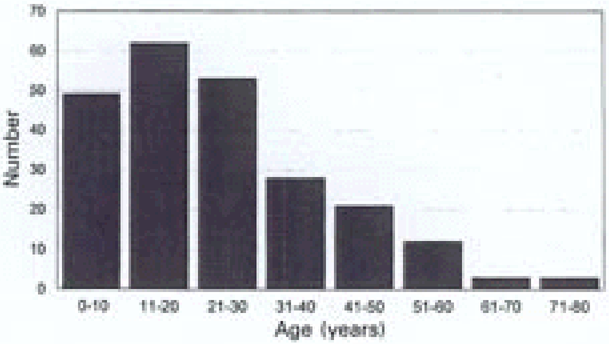

Figure 1. Age distribution of the patients.

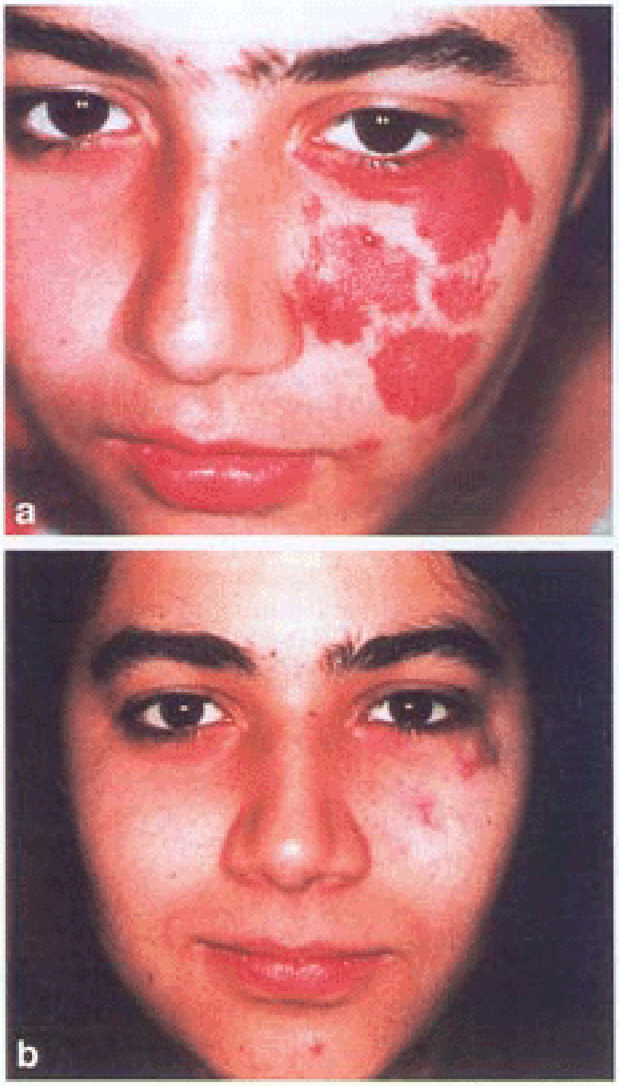

Figure 2. A patient before (a) and after (b) pulsed dye laser treatments.

Most (34%) of the PWS were situated on the cheek, and 55% were on the face in general. Thirty-nine per cent of the patients were living with both of their parents. Twelve per cent were living with one of their parents. Thirty-nine per cent of PWS patients were married or living together with someone. The remainder lived alone. Eighty-nine per cent came from Swedish families and 9% from families that had immigrated from countries outside Scandinavia. The remainder came from Scandinavian countries. The mothers constituted the majority (70%) of the relatives responding to the questionnaires. Twelve per cent of the patients were adopted. Eight per cent of the responders were either the biological father or husband/wife.

Pulsed dye laser

The laser used was a PDL (PhotoGenica-V; Cynosure, Inc., Bedford, MA, U.S.A.) emitting yellow light at 585 nm wavelength with a pulse duration of 450 µs. The spot diameter was 7 mm and the fluence was 3·8–6 J/cm^2. Treatment intervals were at least 6 weeks. The number of treatments depended on clinical results and varied from four to eight treatments. Photodocumentation was made before and after treatment (Fig. 2). We discontinued the treatment either when the lesion was totally cleared or when there was no further progress. The progress was judged together with the patient and from their photograph. When there was uncertainty considering the treatment effects, measurements were made with reflectance spectrophotometry.[12]

Results

Responses common to all patient groups

Seventy-three per cent of all patients were most disturbed by their PWS in the age group 9–20 years (majority 14–16 years) and 18% between 0 and 10 years (majority 6–8 years). The PWS influenced their lives negatively according to 75%. Their lives would change radically if their PWS could be eliminated according to 61%. Forty-eight per cent considered themselves as being treated in a different way (in comparison with the others) by persons in their surroundings before treatment. Those who were treating them differently were the opposite sex (60%), friends (47%), workmates (34%), their mother (32%), their father (31%), their siblings (27%) or others than those mentioned (60%).

Forty per cent felt that it was 'something wrong' with their PWS that led to them being treated differently. Twenty-eight per cent had not been able to accept their

PWS as they got older. There were 18 questions that all patients were asked to answer covering their psychosocial life before the treatment. There was no significant difference (Wilcoxon rank sum test)[11] in all aspects between the answers from the patients who were waiting for and those who were undergoing treatment in comparison with the patients who had completed their treatment. We could therefore go on to compare the answers of the patients on the waiting list with the patients who had completed the treatment.

There were highly significant differences ($P<0 \cdot 001$) in the answers to questions considering problems in their contact with the opposite sex, where 48% had problems before the treatment and only 10% after. Before the treatment, 47% considered themselves as having lower self-esteem in comparison with the same age group, but after the treatment only 8% experienced this. Difficulties in school life and education had been experienced by 28% of the patients before the treatment and no-one afterwards.

There was a significant difference ($P<0 \cdot 01$) before and after treatment in the answers to the following questions. Before treatment, 55% of the patients were covering their PWS sometimes or almost always, and afterwards it was 30%. The PWS prevented 29% of the patients from going into conflict or into quarrels with their peers before the treatment, and afterwards only 6% experienced this problem. Twenty-three per cent of the patients had fewer social relations in comparison with the same age group before and 11% after the treatment ($P<0 \cdot 05$). After completing the treatment, 40% of the patients experienced persons in their everyday lives changing their behaviour towards them.

Responses from relatives of patients aged 9 years or older

The relatives' opinion of their family member's reactions towards their PWS was as follows: 83% considered the patients had very good to rather good self-esteem; 61% of the relatives claimed that their family member was most negatively affected by their PWS during the first 10 years of life.

Comparing the group before the treatment with the group after treatment, there was a significant difference ($P<0 \cdot 001$). Seventy-six per cent of the patients were negatively affected in some way because of their PWS before and 35% after the treatment. Fifty-one per cent of the patients had school problems before the treatment and 3% after the treatment.

Thirty-five per cent of the patients considered themselves as having social problems with friends before the treatment and 8% after the treatment ($P<0 \cdot 01$). Thirty-eight per cent had problems with their relations with the opposite sex before the treatment and 9% after the treatment ($P<0 \cdot 01$). Twenty-seven per cent of the patients were having different kinds of rage attacks caused by their PWS before the treatment and 0% experienced these afterwards ($P<0 \cdot 05$). Twenty-nine per cent of the patients were reserved or feeling depressed because of their PWS before the treatment and 0% afterwards. Sixteen per cent had low self-esteem before the treatment and 3% after the treatment ($P<0 \cdot 05$). Twenty-nine per cent of the relatives considered themselves as treating the patients differently and in a more overprotective manner before treatment than after treatment, and only 8% continued with this behaviour ($P<0 \cdot 05\%$). Thirty-five per cent of the patients had learning problems before the treatment, and 3% experienced these afterwards ($P<0 \cdot 05$). Twenty-five per cent of the patients experienced abnormal reactions from people they came into contact with before the treatment, and 7% experienced this after the treatment ($P<0 \cdot 05$).

Fifty-three per cent of the patients experienced new acquaintances often staring at them before laser treatment, but only 11% of the patients experienced the same behaviour after treatment ($P<0 \cdot 01$). Twenty-three per cent often experienced people looking right through them without seeing them before the laser treatment, and no patients had this feeling after the treatment ($P<0 \cdot 05$).

Responses from patients who dropped out

The patients and their relatives did not always respond to all the questions, sometimes because it was too painful or personal. Most of the 10% of the patients who did not respond at all told us that the procedure was too painful for them to go through. Some did not have contact with their parents and therefore would not give the questionnaires to them. The response rate to the sensitive questions was therefore lower than for the questions of fact. Some relatives with younger children remarked that some of the questions were more directed towards schoolchildren or teenagers and therefore they had difficulties in answering these questions.

Individual comments

Patients aged over 9 years who were on the waiting list or undergoing treatment said that lesions on the body caused embarrassment when they had to change clothes for athletic activities, which they therefore avoided. Some experienced mobbing, especially at new schools and with new acquaintances. They had feelings of being different. Accusations of having suction marks on their neck and other insinuating remarks from teachers or classmates, as if they had been maltreated (especially up to the age of 9 years) or were less intelligent, were reported. They were disturbed by all questions, remarks and teasing, and this resulted in the avoidance of school breaks during the day. Concentration difficulties were reported by several patients. They avoided being at the centre of attention because of the uncomfortable feeling of being stared at.

The relatives of patients aged under 9 years who were on the waiting list or undergoing treatment made spontaneous comments. The families were clearly disturbed by all the curious comments and questions from passers-by, especially from people they did not know. People were insinuating that they had maltreated their child, and people treated their child as if it were less intelligent than normal children. They would stare and loiter around the family. Other children would also make annoying comments. The relatives were worried about the PWS not going away before school and if their child would be mobbed because of the lesion.

Usually, the child disliked their lesion and did not like to look into the mirror when they noticed that they were different from the rest of the family. One family spontaneously avoided sun and bathing situations because of all the staring at their child who had a PWS on the thorax. All relatives were tired of questions and comments from unknown people. Questions such as 'Why did we not get a child that we could show off?' or 'Why did we have this punishment?' arose. After treatment, there were fewer individual comments in the questionnaires.

Discussion

According to our knowledge, there is an equal sex distribution among patients with PWS.[1] In our study, 66% were female and 34% male, and this is rather natural because one expects females to seek treatment more than males. The adoption rate in our study was 12%. This number is higher than in the normal population. Maybe parents who have adopted children are seeking treatment more actively for their children, or maybe adopted children have a higher frequency of birthmarks than non-adopted children. Our data correspond well with the results indicated by earlier studies, showing a considerable emotional impact of a PWS.[6,7,13] Data from patients in 71 questionnaires emphasized that over 50% of the patients felt embarrassed and depressed because of their birthmark. Forty-one per cent felt that people avoided looking at them.[6] These results are strongly supported by our material. Body images of oneself and others are of fundamental importance in the development of personality and interpersonal relationships.[14]

In a study of psychological distress in 247 patients with PWS attending a laser clinic for the first time, the highest psychological distress was in the statement 'I feel the need to hide my birthmark', and the highest score was seen in non-facial PWS.[15] The second highest distress was 'My birthmark affects my self-confidence'. Females had a significantly higher psychological distress than males. In our study, we found that 55% of the patients covered their birthmark sometimes or almost always before the treatments, and after the treatments only 30% covered it. The patients who used make-up to cover their birthmark had difficulty stopping using it after treatment, as it made them feel safe and secure, even if most of the lesion was gone. Also, we have to bear in mind that deeper smaller vessels can persist after the laser treatment.[16]

It is a well-known fact that not all PWS respond equally well to the PDL because of the limited depth of penetration of the laser and the anatomical differences in the PWS.[17] Pink lesions predict poor blanching as a result of deeply located small vessels, while red lesions predict a good therapeutic result because of more superficially located vessels. Hence, an increasing vessel diameter reduces the negative outcome of increasing depth.[16]

Not all the patients in the group that had completed their treatment had their PWS totally cleared, but we stopped the treatment when we did not expect more clearing with this laser. In reality, this procedure takes a couple of years, because there is at least a 6-week interval between the four to eight treatments. The patients whose lesions had not cleared completely often had difficulty in accepting the decision to stop treatment with this laser. The measurements with the reflectance spectrophotometry were a good help in these cases.[12,18] When our patients compared their self-esteem with other people's self-esteem in the same age group, 47% of our patients rated their self-esteem as lower. After the treatment, only 8% had this problem. Only 55% of the PWS were situated on the face, but still the non-facial PWS disturbed the patients as much as the facial ones, but in other ways.

It is important to keep in mind that the patient group which answered our questionnaires (e.g. about the feelings) before their laser treatment is different from the group which answered the other questionnaires. Each patient has only answered one questionnaire in our study. This can be corrected by a follow-up after they have completed their treatment. The conclusions about treatment effects with respect to psychological aspects should be confirmed in a prospective study. When we compared the 18 common answers relating to their psychosocial life before the treatment, there were no significant differences between the groups.[11] Therefore, we were able to compare the answers from the patients on the waiting list before treatment with those from the patients who had completed the treatment. We found several significant and, for the patient, positive changes after the treatment, e.g. school problems disappeared. Children with normal looks are judged more positively by their school-age peers than children who differ from others. Lanigan and Cotterill[6] found that 23% of 75 patients avoided sexual contact because of their birthmark. It is known that the expectations of teachers can be dependent on how attractive a child is.

We do not know the long-term psychological effect of laser treatment on children aged under 2 years. Although it seems that children can cope very well with repeated general anaesthesia, we do not know whether health and psychological risks can develop. During our laser treatments of children aged under 8 years, we always had a qualified anaesthetist who specialized in work with children. They always recommended that the child should be more than 3 months old and, according to them, there was no morbidity or mortality risk if we were following their rules and also had proper postlaser surveillance. The cognitive phase of self-consciousness develops in the period 1·5–2 years of age and therefore we assume it must be important to treat children before that stage. Tolstoy once wrote that 'Nothing has so marked an influence on the direction of man's mind as his appearance, and not his appearance itself so much as his conviction that it is attractive or unattractive'. The feeling of being attractive is important for the development of both psychological and social relations. The body image of yourself and others is fundamentally important in the development of your personality and interpersonal relations.

It is a selective group of patients with PWS that has come to us, and it is a small group in comparison with the number of people with a PWS who do not seek help for it. One of the reasons why they do not seek help is probably because they do not know that there now exists an effective treatment with a very low risk of side-effects. The older treatment modalities (e.g. phosphor radiation, surgery and argon laser) involved a risk of scarring and pigment changes. It is less necessary to accept a PWS now when the PDL is available and when there is such a low, if any, risk of complications.

Children with PWS sometimes have a problem in developing a positive relationship with their parents. According to our study, the relatives thought the birthmark affected the whole family and made them treat their child differently and often in an overprotective manner. They also thought that their child had some problems at school, problems with learning, problems with relations with friends and with the opposite sex. These parameters improved significantly after the treatment.

The impact of a birthmark is sometimes at a subconscious level and can appear later in life. A woman in her fifties (in this study) discovered when she finally had her PWS treated that she had projected all her life problems on to her birthmark. After the treatment, she had to deal with her problems in a more realistic way, and she felt relieved when she could talk to her parents about their silence and guilt about the birthmark. Sixty-one per cent of our patients thought that their life would change in many ways if their birthmark was eliminated. They hoped that it would create new possibilities in their lives. The feeling of guilt in the relatives (34% before the treatment and 19% after) is often irrational[19] and therefore not affected so much after the treatment, as noticed in our study. This guilt is a mirror of their feelings about their relations. Our observations concerning personal, professional and social disadvantages resulting from the PWS are similar to those reported by Dixon *et al.*[20] Patients really hope for complete removal without any imperfection according to Kalick *et al.*[21,22] who considered them as sometimes having unrealistic expectations of their argon laser treatment.

We have a slight imbalance in the number of patients in the different groups. The ideal would have been to have more patients with completed treatment, but treatment usually takes a couple of years, and some patients are lost to follow-up. We consider that our results are interesting and strongly indicate a high degree of emotional distress. In conclusion, it is important to treat patients with PWS as early in life as possible in order to avoid a high emotional impact on the patients' psychosocial development and school life. Even birthmarks on the body can affect the patient negatively, and we recommend that these also be treated early.

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VI

Patients with Port Wine Stains and Their Psychosocial Reactions after Photothermolytic Treatment

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Background. Since the pulsed dye laser (PDL) was introduced in the late eighties the question has been raised whether one should treat congenital capillary malformations, commonly called Port Wine Stains (PWS), early or not. Also the psychosocial importance of an early treatment needs to be clarified.

Methods. This retrospective study includes 163 patients with PWS treated with the PDL until either total clearing or until there were no further improvement. When a period from a few months up to 8 years had elapsed after the treatments, the patients were given a questionnaire, which had been developed in co-operation with a psychiatrist, in order to evaluate the psychosocial implications of the PWS and the consequences of treatment.

Results. 80% of the patients >7 years of age had not fully accepted their PWS with increasing age and 80% experienced that their life would change to the better, if their PWS could be eliminated. 85% considered their PWS to influence their life in some negative way. 45% of the patients considered themselves to have a lower self-esteem than their own age group. The majority of the patients considered themselves negatively influenced by their PWS. Most psychosocial parameters improved significantly after PDL treatment, such as self-esteem, contact with the opposite sex, social relationships, school contacts, the need of covering their PWS with make up or clothes, the difficulties to get into conflicts and meeting new people. The older patients had higher negative scores than the younger ones indicating the advantage of an early treatment. Patients who had been treated earlier with other methods with less good results scored unfavorably compared to previously untreated patients.

Conclusion. Patients with PWS treated at our clinic consider their psychosocial status to be improved after treatment. An early treatment seems to be favorable for these patients.

Keywords: capillary malformation; port wine stains; emotional impact; psychosocial behavior; pulsed dye laser; recurrence; heredity.

Acta Derm Venereol (Stockh).

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Port wine stains (PWS) are congenital capillary malformations that can be disfiguring and may lead to psychosocial as well as medical complications. They are reported to occur in 0.3–0.6 % of the population, but according to a Japanese study the incidence is as high as 2,1%.[3] The male to female ratio is 1:1.[1, 2] The usual presentation is that of a flat, pink macula, and most (83%) occur in the head and neck area.[4] Because of altered or absent neural modulation of the vascular plexus there is a progressive ectasia, which with age can cause darkening in color, hypertrophy and eventual "cobblestone" formation.[5] PWS in all ages can, since the late eighties, be safely and successfully treated with the pulsed dye laser (PDL) in most cases.[6] The incidence of adverse effects has been very low, although hypertrophic and atrophic scarring can occur, albeit rarely.[7] Office surgery can be performed safely when small lesions are treated but for larger lesions treated in children the use of general anesthesia does not appear to be accompanied by increased risk.[8]

Whether one should treat PWS early in age or not has been a subject for discussion and there has been pros [9, 10] and cons[11, 12], but these studies have mainly emphasized the clinical treatment results. The stigmatization of patients with PWS has been shown by us in an earlier study in 231 patients, but only a minority of these patients had completed their treatment with PDL at the time of the study.[13] Therefore, we considered it to be of interest to study a larger group of patients with completed treatment and to evaluate how the patients retrospectively rated their psychosocial behavior before and after treatment.

Materials and methods

Patients and treatments

This retrospective study included 163 patients from the Section of Laser Surgery at the Department of Dermatology in Malmö, with congenital PWS. Patients were treated 4–9 times with PDL (Photogenica VL, Cynosure, Inc., Bedford, MA, USA) until the PWS had cleared or until there was no further improvement (Figure 1). All patients responded as expected from earlier experiences.[14]

Those who did not clear totally were subsequently treated with an intense pulsed light source (Photoderm VL, ESC Medical Systems Ltd, Yokneam, Israel) or a different vascular laser (Versapuls, Coherent, Inc., Santa Clara, CA, USA) which gave some slight additional improvement. The treatment intervals were at least 6–12 weeks, with breaks for the summer season and therefore the whole treatment sequence took a few years until finished.

A questionnaire was given to the 163 patients in spring 1999, when a time period from a few months up to 8 years after the treatments had elapsed. This questionnaire was developed in co-operation with a child and adolescent psychiatrist (BW) and slightly modified with the experience from our earlier study on stigmatization caused by PWS.[15] These modifications were caused by questions that had been raised by the patients since 1987, when we started treatment of PWS at our clinic. One was about heredity and the other was covering the risk of recurrence. After the treatment the patients were asked to rate their psychosocial behavior and reactions after treatment and as they remembered them before treatment. The questionnaires were anonymously computerized.

The 147 (90% response rate) responding patients (62% female) were from 2 to 74 years of age (median age 22) (Fig. 2). One patient did not answer the question regarding age, but responded to all other questions. Since all questions were not relevant in each individual, the response rate for specific questions may be lower. Patients below 15 years of age (20%) received a slightly different version of the questionnaire and 21 (15%) of these youngest patients needed some help from their parents to answer the questions. Ten (7%) of the patients were too young to be able to answer the questionnaires themselves. Seventy-three percent of the PWS were localized on the head and neck area with the majority on the cheeks (47%) (Table1). Fifty percent (70/140) of the patients had undergone treatment before with either phosphor radiation, surgery or argon laser and the median age of the patients at the time of treatment had been 12 years (range 1–45). 73% were unhappy with the result of their earlier treatment. Ninety of these 147 patients had participated in our earlier study of psychosocial stigmatization.

Fig 1. Patients with PWS before and after pulsed dye laser treatments.
(See in the thesis page 46, Figure 7).

Statistics

Wilcoxon´s paired rank sum test was used to compare the retrospectively reported psychosocial parameters before and after PDL treatments. To analyze relationship between variables the Spearman rank correlation coefficient was calculated. To study the reliability of the questionnaire used in this study with the earlier questionnaire study, the kappa coefficient was used. The following cut off values for kappa were accepted: <0.20 poor, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good and 0.81–1.00 very good reliability.[16]

Table 1. Anatomical locations and frequencies of the PWS. (3 locations are missing).

Location	No
Forehead	17
Cheek	67
Chin	4
Neck	16
Hands	2
Thorax	3
Other	17
Multiple	18

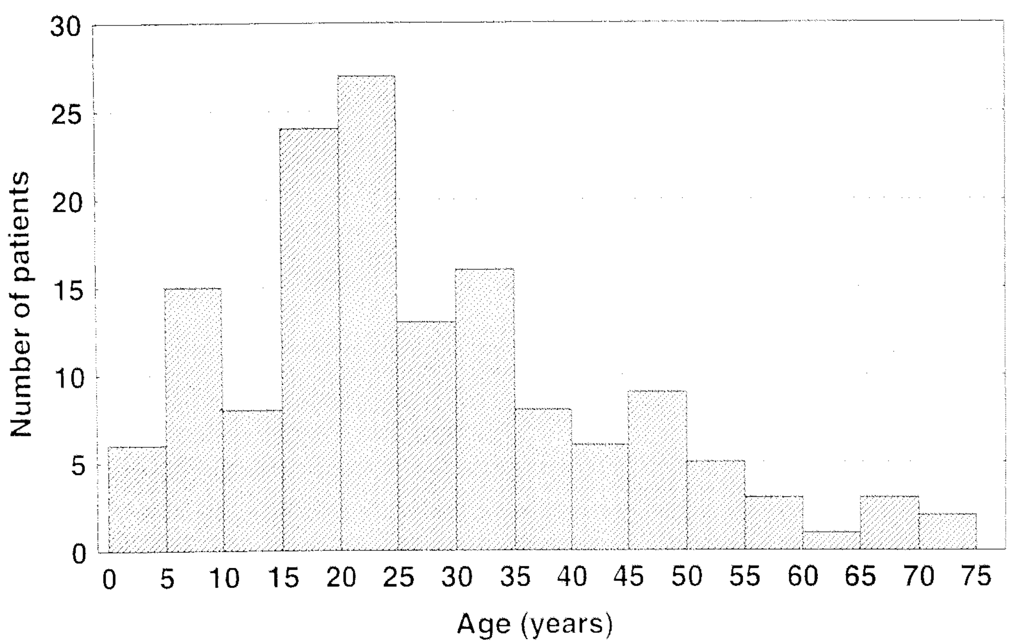

Figure 2. Age distribution of our responding patients with PWS.

Results

Ninety percent of the patients had grown up in Sweden or in Scandinavia and therefore we concluded that the Swedish and Scandinavian society and culture had influenced the majority of them. The majority had skin type I–III. Fifty-three percent of the patients, younger than 30 years of age and 67% below 22 years of age, were living with both of their biological parents and 54% of the patients, over the age of 18, were either married or living together with their partner. Seventeen percent were living alone. The remaining 12% lived either with one parent alone or together with a stepparent or in some other combination. The majority (88%) of the patients had 1–3 brothers and sisters and only 5% had no siblings. At the median age of 2 (range 0–15) years the patients reported that they became aware of their PWS. Eighty-five percent (121/143) of the patients considered their PWS to influence their life in some negative way.

Age when the patients with PWS experienced most stress

In the age group 2–14 years the median age, when the patients reported being most distressed by their PWS was 6 years. In the older group of 15–25 years the median age of most stress was 13 years and among the patients who were 26 years or older the median age was 17 years.

Acceptance of their PWS

Eighty percent (104/129) of the patients, over 7 years of age, had not fully accepted their PWS with higher age. Eighty percent experienced that their life would change if their PWS could be eliminated without scarring.

Self-esteem

Forty-five percent (61/135) of the patients considered themselves having a lower self esteem than their age group, the older the patient the more negative was the grading of their self-esteem ($p<0.001$). After the treatments their self-esteem had improved significantly ($p <0.001$) more so in older patients ($p=0.001$).

When we subdivided the patients, we found that in the age group of 2–14 years, 14% (3/22) considered themselves having a lower self-esteem than their own age group before the treatments and after the treatment none of the 19 patients who responded to this question, had this problem. In the age group of 15–25 years we found 42% (22/52) of the patients with the same thoughts before the treatments and 19% (9/47) after the treatments. In the age group of 26 years or older the respective figures were 58% (35/60) before the treatments and 12% (7/57) after the treatments. From the age of 15 a significant improvement ($p<0.001$) of the self-esteem after the treatments was demonstrated.

The need of covering the PWS with make up or clothing after the age of 12 years

Sixty-four percent (73/114) of the patients were covering their PWS with either make up or clothing and the need for this covering was significantly increasing with age ($p <0.001$), e.g. the older the patient the greater the need for covering. After the treatments this need for covering had significantly diminished ($p <0.001$). The younger the patients were the less need for covering after the treatments ($p = 0.046$).

Social behavior from others

Fifty-eight percent (80/139) of the patients experienced that they were treated differently by people in some way because of their PWS. Friends or the opposite sex and "others" (excluding the parents, the class—or work—mates and teachers) were those who treated the patients differently. After the treatments there was a significant reduction of this feeling ($p = 0.006$) and it was mainly (49%) the friends and the opposite sex who still treated them differently according to the patients experiences.

Possibilities to make friendship

Thirty percent (41/137) of the patients considered before the treatment that their PWS had in some ways prevented them from getting friends. After the treatment 25% (29/118) of the patients had the same opinion. There was no significant improvement of this parameter after the treatments. Nineteen percent (22/119) of the patients considered themselves to have less contact with friends after the treatment than they thought their friends had.

When we subdivided our patients into different age groups, we found that 8% (2/25) of the patients in the age of 2–14 years considered their PWS had prevented them from making friends in some way before the treatment and after the treatment 10.5 % (2/19). In the age group 15–25 years we found the figure being 39% (20/52) before the treatment and 28% (13/47) after the treatments. In the age group >26 years we found almost the same figures e.g. 32% (19/59) before the treatment and 27% (14/52) after the treatments. No statistically significant changes were seen in either group.

Social relationships

Thirty-six percent (47/130) of the patients estimated that they had less social relationships in comparison with the same age group, and relations became more difficult to establish with age ($p < 0.001$). After the treatments there was a significant improvement ($p = 0.001$) and the younger the patients were the greater the improvement ($p = 0.011$).

School and education experiences after the age of 7 years

Thirty-three percent (40/123) of the patients experienced that their PWS made their schooling and education more difficult in some way and this problem was considered bigger in older age groups ($p = 0.008$). After the treatments this was significantly improved ($p = 0.016$). The younger the patients were when the treatment was given, the less difficulties with schooling and education ($p = 0.005$).

Conflicts and arguments

Thirty-two percent (41/130) of the patients reported that their PWS prevented them from getting into conflicts or arguments with persons in their surrounding and this was increasing with age ($p = 0.017$). After the treatments it was easier for the patients to handle conflicts and arguments ($p < 0.001$).

Contact with the opposite sex after the age of 12 years

Fifty-three percent (61/115) of the patients noted that their PWS made it more difficult for them to have contact with the opposite sex. With age this was more difficult for them ($p = 0.027$). After the treatments there was an improvement ($p < 0.001$) and the younger the patient the more positive the effect after the treatments ($p < 0.001$).

Possibilities of getting a job after the age of 16 years

The majority of the patients (83%) did not have any problem in getting a job. Seventeen percent (17/98) of the patients had the opinion that their PWS reduced their possibilities of getting a job. After the treatments there was no significant improvement. The age had no importance for the patients experiences of how the PWS prevented them from getting a job, neither before nor after the treatments.

Making new acquaintances

At least 74% (106/144) of the patients had their PWS at locations where it was difficult to hide with clothes. Eighty-one percent (107/132) of the patients experienced that when they met new people, these had a tendency of looking at the PWS instead of looking into the patient's eyes. This impression was significantly improved ($p < 0.001$) after the treatments.

Patients treated earlier

Fifty percent (70/140) of our patients had earlier been given older forms of treatment. The earlier treated patients reported higher negative scores in more of the psychosocial parameters than the previously untreated patients e.g.: People treated them differently because of their PWS ($p = 0.023$) and new acquaintances looked at their PWS instead of into their eyes ($p = 0.019$). The PWS caused problems in the contact with the opposite sex ($p = 0.002$). They had lower self-esteem in comparison with the same age group ($p = 0.007$). Make up and covering clothes were used more often than in the untreated patients with PWS ($p = 0.002$). Their PWS prevented them from getting into conflicts and arguments ($p = 0.009$). Their lives would change positively if they could have their PWS eliminated without scarring ($p = 0.001$).

There were no differences between the earlier treated and the untreated patients considering if the PWS had influenced their life negatively or in the possibilities of making friends. Nor was there any difference in possibilities to get work, social relationships, schooling and education, age of most stress or acceptance with age of their PWS.

Reliability of questionnaires

Ninety of the 147 patients had also participated in our earlier study[13]. We compared 12 of these patients' answers to the same questions about their situation before and after PDL treatment. Anatomic locations of their PWS showed very good reliability (kappa 1,0) and so did their opinion of possibilities to get a job before the treatments. Moderate to good reliability (kappa values 0.4–0.8) was recorded in the following parameters e.g.:

Good reliability was seen in making friends and contact with the opposite sex before the treatment and in the possibilities of getting a job after the treatments. Moderate reliability was noted in how the PWS prevented them before the treatments from social contacts, getting into conflicts and in problems in school before and after the treatments. Their feeling of self-esteem in comparison with their age group before the treatments and the experience that new acquaintances did not look them into their eyes before the treatment had also a kappa >0.4. Some other parameters had only fair reliability e.g. how the PWS influenced their life, if people were treating them differently because of their PWS and even poor reliability e.g. if their life would change if they could eliminate their PWS without scarring.

Recurrence after treatment

Twenty-six percent (32/122) of the patients reported that their PWS had to some extent recurred since the treatments were stopped from a few months up to 8 years ago.

Heredity

Nineteen percent (26/136) of the patients reported that they had a relative with a red birthmark like themselves.

Discussion

To what extent and in which proportion different factors influence the overall perceived PWS disfigurement is incompletely understood. According to Lanigan et al, patients with PWS had a high level of psychological morbidity resulting from a feeling of stigmatization that was not apparent in casual social intercourse.[17] But, their standard psychological screening tests for psychiatric illness, depression and anxiety revealed that these patients had similar or less evidence of morbidity than control subjects or other patient groups.[17] Also patients with large PWS were shown to have reality problems in common.[18]

Koster et al studied 7 PWS patients with the help of questionnaires, one professional panel and one panel of lay persons.[19] The following PWS characteristics were rated: color, patchiness, boundary, size, shape, surface structure and hypertrophy of the underlying tissue. The size turned out to be the most important characteristic and the 2 following were color and boundary. Their conclusion was that reducing the size and fading out the boundary of the stain probably reduce overall PWS disfigurement more effectively than primarily trying to lighten the often persistent center of the stain.[19] Augustin et al in a questionnaire study in 76 PWS patients also found a significantly higher emotional stress than in healthy controls.[20] Patients with high emotional stress placed high hopes on laser therapy with regards to chances of employment and social contacts.[20] They also found that the patient's quality of life was impaired with respect to their social life and that they felt less attractive than a healthy control group.[20]

Acquired PWS are uncommon vascular lesions with the appearance of a congenital PWS, but the onset is after birth and can be associated with preceding trauma. Lanigan found that also adult acquired PWS showed similar psychological morbidity to that seen in patients with congenital PWS[17] although the age of onset varied from 2 years of age up till 43 years of age in his study of 19 patients.[21] This morbidity was also, as in this study, successfully improved after PDL treatment, although the PWS only cleared completely in 6/13 patients.

The patients in our study experienced significant improvement in many of the psychosocial parameters after the treatment although we had not succeeded in obtaining a total clearance of their PWS. In our experience, a realistic pre-treatment information to the patients is extremely important[22] and the patients are never promised a total clearance of their PWS. Maybe psychological consultation for emotional labile PWS patients should be considered.

Fifty percent of our patients had been treated before with older therapies and this group reported higher negative scores than our previously untreated patients. The reason for this could be that this group of patients and/or their parents had been more motivated for treatments and the often poor treatment results had made them disappointed.

We found our results in this study to be rather convincing concerning the question whether one should treat PWS early or not. Eighty percent of the patients over 7 years of age had not accepted their PWS with age and they experienced that their life would change positively if it could be eliminated. Many of the negative psychosocial factors scored significantly higher in older age groups e.g. low self-esteem, the need of covering their PWS, the difficulties in social relationships (e.g. contact with the opposite sex), difficulties in school/education, getting into conflict and discussions.

Most of these parameters were significantly improved after the treatments except the patient's opinion that the PWS prevented them from making friends or getting a job. When we subdivided our patients in different age groups we found that the older the patient the more difficult it was experienced to make friends because of their PWS. After the treatment there was a tendency to improvement. Maybe this is such an important early knowledge in life and although the PWS is gone or improved the "imprint" or self-image is hard to change later on in life. A good early attachment in life and a good self-esteem will probably make it possible to make friends with or without a PWS. Only a minority of the patients (17%) experienced that they had difficulties in getting a job and this was rather surprising. May be the low median age contributed to this. Interestingly, we found that making friends and getting a job before the treatment had a good to very good reliability respectively (kappa 0.7–1.0). The patients also pointed out that it was mainly the friends and the opposite sex that treated them differently because of their PWS both before and after the treatment. However they considered that after the treatment there was a significant improvement of their possibilities to get in contact with the opposite sex, especially for the younger patients.

In our earlier study assessing the extent of psychosocial stigmatization in-patients with PWS we used a similar questionnaire, but the majority of the patients were on the waiting list for PDL or in treatment.[22] Only 46/231 patients had completed their treatment. Therefore, we considered it to be of interest to look specifically at how treatment is experienced to affect the psychosocial behavior. We consider the reliability of our questionnaire to be good to moderate, when we looked at how the weighted kappa figures from e.g. the anatomical locations as a reference and which had kappa = 1 (which is considered a very good reliability) and many other psychosocial parameters with kappa >0.4. That some questions had a fair and poor reliability might be explained by the fact that 4–5 years had passed since they answered the first questionnaire and their life situation could have changed during this time.

When we compared our result from the present study with our earlier one regarding stigmatization, we found that there were many similarities:

The response rate was 90% and 89% (231/259) respectively, obviously the patients were well motivated. During the age period of 10–20 years 73% of the patients were most disturbed by their PWS in our earlier study and in our present study one could find a similar distribution. In the present study our patients in the three different age groups, expressed that they were most distressed by their PWS at the median age of 6, 13 and 17 respectively. That the PWS influenced their life negatively was experienced by 85% of the patients and in the earlier study 75%. The feeling that their life would change radically if their PWS were eliminated reported 80% of the patients and in the earlier study 62%. Suffering from low self-esteem in comparison with the same age group was reported by 45% and 47% of the patients respectively. The PWS made their school life and education more difficult according to 32% of the sample compared to 28% in the earlier study.

An interesting finding was that 26% of the patients reported that their PWS had become more red since the treatment had stopped (a few months till up to 8 years). This might be due to the fact that a certain fraction of the PWS was not fully eliminated and the patients therefore were on the waiting list for a better vascular treatment system than PDL, or maybe some ectatic vessels still persisted although the PWS cleared completely visually. Also Orten et al reported that 40% of patients whose last treatment was between 2 and 3 years prior, recurred, and 50% recurred after 4–5 years, but only a small number of their patients were followed for that long.[4] We know that with age, some PWS get darken and hypertrophic, probably because of the progressive ectasia.[5] Maybe the reported recurrence of the redness is caused by the natural progressive ectasia that continues in the persistent vessels.

Vascular malformations are true developmental abnormalities that are believed to result from a sporadic, non familial developmental error in the formation of vascular tissue.[23] PWS are probably due to a relative or absolute deficiency in autonomic innervation of the postcapillary venular plexus.[5] A demographic study of 283 patients with PWS reported a family history of PWS being higher than expected for the prevalence of this naevus in the population.[24] The 2 and 3 generations' pedigrees of 2 families with multiple PWS (or naevi flammei) in various areas of the body indicate autosomal dominant inheritance.[25] However in the present study 19% of the patients reported that they had a relative with a similar red birthmark. We are planning to examine these relatives and we have an ongoing study where we question all our patients with PWS about their relatives. As our figure is quiete high compared to the earlier reported incidence of 0.3–2.1% [1,2,3], we will continue our investigation.

We have to keep in mind that our patients were a selection from a group of patients seeking help for their PWS and that this group may differ from patients not seeking medical attention. Parents wanted their child with PWS to be treated, because they were bothered about comments from the surrounding. To select a representative group from all patients with PWS is difficult, also since the terminology of vascular malformations and tumors has been confusing.

According to a study of PWS patients undergoing PDL treatment there is a correlation between lightening of the PWS and reduction of emotional distress[26]. Since the treatments can be performed safely with low incidence of side effects[8] we recommend selective photo-thermolytic therapy not only as an effective treatment to eliminate the PWS, but also in order to prevent the negative psychosocial reactions that may follow having a PWS.

We can conclude that in this retrospective study patients with PWS seeking medical help, report a better psychosocial situation after treatment than before. One also has to keep in mind that it takes at least 1–3 years until the treatments are completed and therefore it could be advisable to try to finish the treatment sequence at least before school begins. We would recommend an early treatment to try to avoid the negative psychosocial impact a PWS can cause.

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As the sceptical essayist Montaigne (1533–1592)
expressed the eternal question

"Que sais-je?"

("What do I know?")