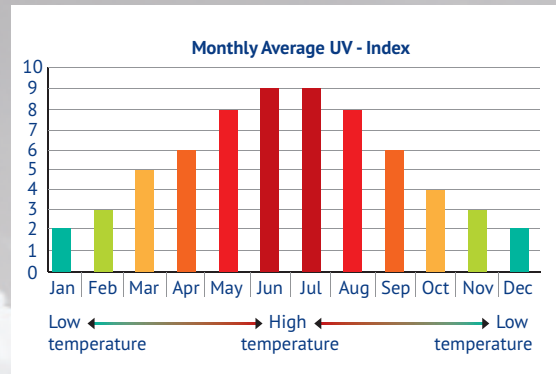


# THE SUN: ITS DANGERS AND HEALING POWER



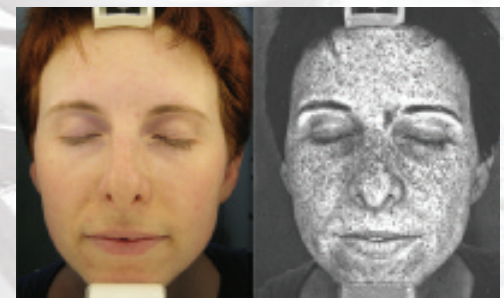


**Few things are more life enhancing than the sight of the sun. We worship it in summer, long for it in winter, and spend large sums of money chasing it round the globe.**

But it is also damaging. Nothing ages the skin faster than the sun. People who spend days exposed to it – from Australian sheep farmers to Californian ladies who lunch – have the prematurely wrinkled faces to prove it.

We all benefit and we are all, to some degree, at risk. But for a few unlucky individuals the sun poses a more serious threat. They come out in lumps and rashes, their skin itches and burns and they may experience screaming pain after even brief exposure. Some will develop skin cancer in early adulthood and die.

Over the last 100 years, doctors have learnt how the sun damages the skin, who is most vulnerable and how best to protect them. In doing so they have also learnt how to use its properties to heal. They have harnessed the power of the sun.



Ultraviolet imaging demonstrates sun damage in a melanoma patient

The sun is life enhancing, but it can also be life changing when it causes disease. Over the last 100 years, doctors have learnt how the sun damages the skin – and also how its power can be used to heal



## History



Nobel prizewinner Niels Finsen, inventor of the first sun lamp

Researchers began investigating sunburn in the mid-19th century. At first it was thought that heat from the sun was responsible until it became clear that, in fact, it was the ultra violet component causing the damage. Ultraviolet radiation (UVR) had previously been identified

from its effect on silver chloride paper, the forerunner of photographic film.

In 1903 **Niels Finsen** of Denmark was awarded the Nobel prize for producing the world's first sun lamp to create UVR which he used to treat *tuberculosis of the skin*. Over the subsequent decades, UVR was used as a therapy for a range of other conditions, including *psoriasis*.

But while UVR therapy developed, the diagnosis and treatment of people with extreme sunlight sensitivity stalled. Although some conditions had been known about for a long time, there was no systematic attempt to investigate them until the development of phototesting at St John's Institute of Dermatology in the 1950s.

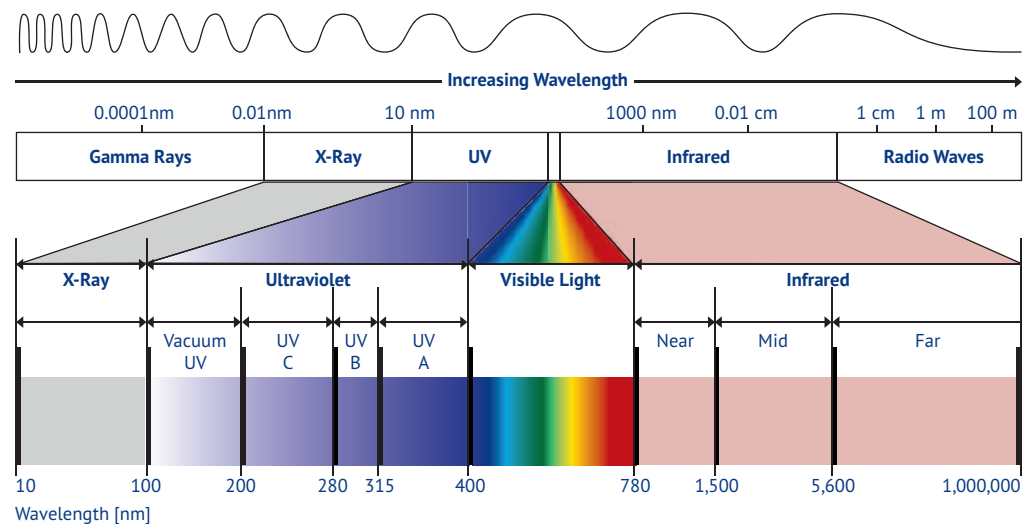


Finsen lamp treatment, London 1925

## Photodermatoses

These are diseases caused by sensitivity to sunlight, which contains two sorts of ultraviolet radiation – UVA and B (a third sort, UVC, is absorbed by the atmosphere and does not reach the Earth). They include the very common *polymorphic light eruption* (prickly heat), characterised by rashes on the skin following sun exposure, affecting one in six people,

mostly women (St John's sees only the severest cases); *chronic actinic dermatitis* (light sensitive eczema), one of the commonest forms of severe eczema, which can be triggered by tiny amounts of sun light; and *actinic prurigo*, which affects children causing itchy rashes that may last for months after a single exposure.



Patient with chronic actinic dermatitis caused by sunlight

In all these cases, the first requirement is an accurate diagnosis. A severe eczema on the face could be caused by a cream, or allergy to sunlight. Phototesting is crucial to determine if sensitivity to sunlight is the cause.

St John's became the first institution in the world to introduce phototesting using a machine designed by **Ian Magnus**, a consultant dermatologist and pioneer in clinical and experimental photobiology who created phototesting at the Institute in 1953.

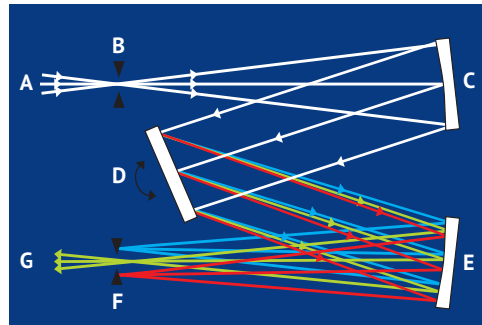
It worked on the same principle as patch testing for allergies. Magnus' machine, called a monochromator, produced UVR of different wavelengths which was focused on a grid placed across the patient's back and delivered at a variety of doses and wavelengths to the skin. The strength of the reaction indicated the sensitivity of the skin to that particular wavelength. Specific patterns of sensitivity were found to correlate with specific clinical diseases, so the approach enabled accurate diagnosis of photosensitive skin diseases for the first time. In addition, phototesting could identify whether UVA or UVB was responsible and thus which sunscreen and other photoprotection to recommend.

Patients were referred to Magnus's clinic from all over South England. The Photobiology unit was established by Magnus and **Arthur Porter** and later developed through the 1980s and 1990s by Professors **John Hawk** and **Anthony Young**. St John's still has the largest clinical service for photosensitivity, and the largest phototesting service in England and one of the largest in the world, and the monochromator remains the key diagnostic tool.

Accurate diagnosis leads to appropriate



Phototesting using the monochromator – St John's was the first institution in the world to introduce phototesting



Ultraviolet radiation is separated into individual wavelengths with the monochromator



Positive phototests in a patient with chronic actinic dermatitis

treatment. Adults and Children with severe and treatment resistant *actinic prurigo* can be treated with thalidomide, the drug that caused a scandal in the 1960s when it was prescribed to pregnant women for morning sickness and led to the birth of thousands of malformed babies. As a treatment for *actinic prurigo* it can be used safely and effectively – the itchy rashes in the skin just melt away.

*Polymorphic light eruption* (prickly heat) can be treated prophylactically with gentle tanning under a UVB lamp in the spring. This hardens the skin and desensitises the immune system so it calms down when exposed to UVR in summer sunshine.

**Phototherapy**

Every time a person goes outside, UVR from the sun is absorbed by their skin causing damage to the cells that make it grow and function correctly. In sensitive people the immune system reacts causing inflammation, leading to the pimples and rashes characteristic of a flare.

But in others, exposure to sunlight can ease skin conditions by calming the immune system down and reducing inflammation. This explains why teenagers with acne often find their skin improves in summer with exposure to the sun.



The first patient to be treated with the UVA1 machine in 2007 (second left) with staff from St John's

The therapeutic effect of UV light, discovered by Nobel prize winning Neils Finsen, is harnessed today by exposing the skin to it in the form of UVB phototherapy or with UVA in combination with psoralens (PUVA), natural compounds known to the ancient Egyptians for sensitising the skin to the sun, whose efficacy was rediscovered in the 1950s.

Ultraviolet radiation from the sun causes damage to skin cells – but it can also ease skin conditions by calming the immune system down and reducing inflammation



PUVA phototherapy involves applying a cream to the skin or taking a tablet containing psoralens and then exposing the skin to UVA. PUVA treatment is especially used at St John's to treat *cutaneous lymphoma*, as well as a variety of other diseases particularly when UVB therapy has not been effective.

*Vitiligo* is a particular problem in black and Asian communities where white patches on the skin are much more noticeable. It is caused by the immune system attacking the skin cells which produce melanin, the pigment that gives the skin its colour. It is often dismissed as a cosmetic problem – but it can be devastating. Steroid creams are often tried and when they fail prolonged courses of UVB phototherapy can be effective in many patients.

The phototherapy unit at St John's is a national centre for phototherapy and acts as the hub for support and training of a network of phototherapy units in hospitals throughout South East England. In addition to the usual range of treatments it is one of only three centres in Britain (the others are in Leeds and Dundee) providing high output UVA1 therapy (shown in photo on previous page). This is a treatment introduced at St John's in 2007 for diseases such as *scleroderma*, which causes fibrosis of the skin, and *graft vs host disease* that can follow bone marrow transplantation making the skin woody and hard.

The long wave UVR is delivered in large doses by a room-sized machine that generates a lot of heat and must be cooled by powerful fans. It is particularly effective against skin diseases where there is extensive scarring, thickening or stiffening of the skin.

One of the dangers of phototherapy is accidental overdose, causing burns and increasing the risk of skin cancer. It is the single largest cause of successful litigation in dermatology. Since 2008, St John's has led a programme in the south east England clinical network to educate nurses in how to give patients phototherapy safely and to monitor treatment in the region. Evidence shows that standards have improved with patients' conditions better managed and a safer and more effective service.



A patient with vitiligo before and after treatment with phototherapy. Vitiligo is caused by the immune system attacking melanin-producing skin cells



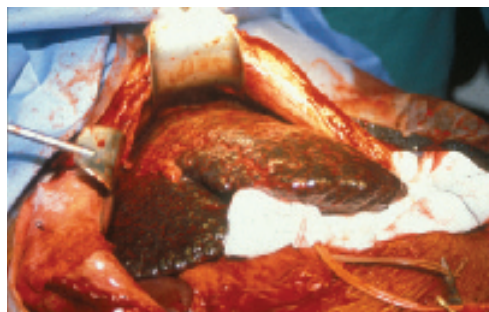
A case of scleroderma: UVA1 phototherapy

## Porphyria

A rare and severe group of skin diseases – the *cutaneous porphyrias*, are caused by the build up of porphyrins in the skin. The name refers to a group of conditions resulting from inherited enzyme disorders.

Porphyria is derived from the Greek meaning "purple pigment" on account of the dark colour of urine and faeces in some affected individuals. Under normal circumstances porphyrins are converted to heme, a precursor of haemoglobin, the constituent of red blood cells that carries oxygen round the body. But when the process breaks down and the porphyrins build up, sufferers become sensitive to sunlight.

In *erythropoietic protoporphyria (EPP)*, patients experience intense burning and swelling of the skin when exposed to the sun, complaining that their hands and face feel on fire with attacks lasting several days. Ian Magnus of St John's played a key role in describing EPP. Although there had



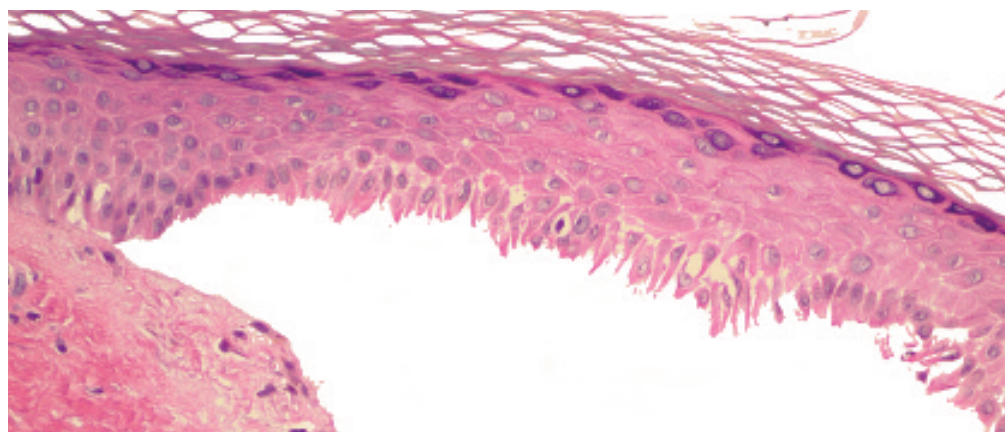
A cirrhotic liver caused by erythropoietic protoporphyria. Sun exposure leads to the build up of toxic porphyrins which can result in liver failure requiring a liver transplant

been a hint that *porphyrins* were involved in the condition he was able to confirm that the pain and swelling sufferers experienced when exposed to the sun was indeed due to the build up of porphyrins to toxic levels in their skin.

As shown in the figure above EPP occasionally also causes liver failure requiring a liver transplant.

The rarest type of *cutaneous porphyria* is *Gunther's disease*, a congenital condition which is very severe, involving extreme photosensitivity, brown teeth that fluoresce in ultraviolet light and purple body fluid. Other effects include severe blistering and scarring of the eyes and fingers, increased hair growth on the forehead, and potentially fatal effects in the blood. Gunther's disease is severe and disabling and some patients who are severely affected may be unable to go outside during the day. It is possible that Gunther's disease has led in primitive societies to various legends involving vampires and werewolves. Such responses illustrate graphically how severe photosensitivity is not only disabling but has the potential to be deeply stigmatising too.

Today St John's is one of the main centres for the treatment of *cutaneous porphyrias*, seeing around 80 of the 230 patients in the country and around half of the 20 patients with Gunther's disease.



Porphyria cutanea tarda: skin histology shows the split in the dermis where the disease has caused blistering

## Xeroderma Pigmentosum

This rare, hereditary disorder, affecting one in 250,000 people, highlights the devastating effect the sun can have. Sufferers are unable to repair the damage caused by UVR present in sunlight, even in winter, putting them at exceptionally high risk of developing skin cancer. Diagnosis often follows severe and exaggerated sunburn when the child is first exposed to sunlight.

St John's provides the largest multidisciplinary clinical service for XP in the world, and the only expert centre in the UK, treating 80 of the 90-100 patients with the condition in the country. It is unique in providing psychological cover – living in fear of the sun creates immense pressure on the whole family – and outreach nurses who visit patients' homes and schools to check on UVR exposure and advise on protective measures.

*XP*, an autosomal recessive gene disorder, is often marked by the development of hundreds of 'freckles' at an early age. Other symptoms include dry skin, blistering on slightest sun exposure, patches of rough skin (solar keratoses) and painfully sun sensitive eyes that may become bloodshot and clouded.

As with *porphyria*, sun avoidance is crucial to maintaining the health of patients with XP. The first inkling of the condition may come when a mother turns up at A&E with a severely sunburnt child, and is often scolded for leaving it in the sun. Yet just five minutes exposure may result in very severe and exaggerated sunburn with blistering.

Sun avoidance involves elaborate protection, with gloves, hats and UVR-protective visors whenever sufferers venture outside. Windows at home, school and in the car must be covered with UVR-filter film





A researcher working on Xeroderma Pigmentosum, which affects one in 250,000 people leaving them unable to repair the skin damage caused by the sun, even in winter



to prevent inadvertent exposure through the glass.

The risk of cancer is ever present. **Robert Sarkany**, head of the photodermatology department, said: “I saw a girl who had her first skin cancer when she was six, despite being dark-skinned. Another patient had had 150 skin cancers cut out by the age of 35. The most common cause of death in these patients is *melanoma* and the mean lifespan is 32. They can also get eye cancer and go blind. On top of that around 30 per cent develop neurological complications. It is a dreadful disease.”

The multiplicity of XP patients’ needs meant they could not be met by dermatologists alone. When Dr Sarkany joined St John’s in 2006 he saw the need for a multidisciplinary service. Drawing on his previous experience with a trial specialist XP service in Worthing, he worked with the patient support group led by **Sandra Webb**, mother of 16 year old Alex, a sufferer, to design a more effective service.

“Our most severely ill patients had needs we were not meeting. There was lots of skin cancer, eye damage, ‘freckling’ that we were not dealing with. The patient support group was pretty angry. We had to do something better,” he said.

In 2008, he started a specialist XP clinic, with ophthalmologists and neurologists, held three times a year. Two years later in 2010 it was launched as a separate national XP service funded by the Department of Health, providing a multidisciplinary clinic fortnightly, headed by consultant dermatologist **Hiva Fassihi**.

The clinic treats adults and children from across the UK working with specialists in photodermatology, dermatological surgery, plastic surgery, genetics, neurology, ophthalmology and



Hiva Fassihi (Clinical Lead of the UK National XP Service) with an XP patient



Patient with multiple scars from skin cancer surgery

psychology. It is the only clinic in the world that looks after patients long term, at the hospital and in their home environment.

Among the specialists it calls on are those in the dermatological surgery department working with the laser scanning confocal microscope, the only one of its kind in the NHS. The microscope allows suspicious skin lesions to be scanned and assessed at a cellular level, thereby avoiding the unnecessary excision of lesions that turn out to be benign (see Chapter 4).

The service’s holistic approach is illustrated by the outreach work of the clinic’s specialist nurses which was recently assessed. The results showed that in over 90 per cent of the 20 schools visited, where advice had been given about improving protection by putting UVR-filter film on windows, UVR levels measured three months later had declined by at least 70 per cent. “We are the only unit to look after our patients in this fashion,” said Dr Sarkany.

## Research breakthrough in X-P

**In addition to running the clinical service, the photodermatology department at St John's is undertaking cutting edge research. In 2013, they made a breakthrough in understanding of XP with the discovery that half of patients with the condition don't get abnormal and exaggerated sunburn from the sun.**

As severe sunburn from minimal sun exposure has traditionally been thought to be a defining symptom of the disease, the discovery is of major clinical significance. The study, led by Hiva Fassihi and published in the British Journal of Dermatology, divided patients into eight groups and found their symptoms varied.

Those that did not suffer sunburn instead developed 'freckles' but were still more likely to develop cancer. The danger from believing that severe sunburn was the defining characteristic of the disease was that these patients (and/or their parents) might not bother with sun protection, exposing them to a higher risk of cancer.

Dr Fassihi said: "If you see a child who is becoming more and more 'freckly' you should think about XP, even if they don't sunburn."

Dr Sarkany said: "We are worried GPs, nurses and A&E staff may not know this. It is an important finding."

In addition to research at the cellular level, identifying which patients burn in the sun, doctors at St John's are also studying the impact of the illness on the psychological well being of the patient and their family. With the help of **John Weinman**, professor of psychology at Kings College, London, researchers are examining what effect having to hide from the sun, put on protective

clothing each time they go out and live behind a visor are having on the individuals and their loved ones.

"If you wear a hood with a visor all the time you lead a very different, more isolated life compared with the rest of us. But if you don't, you get cancer. The question we are trying to answer is: 'What is it like to have this disease'".

A third avenue of research is provided by the overlap between *XP* and *Cockayne syndrome*, which causes premature ageing in children and involves failure in the same DNA repair pathway. Instead of skin cancers, Cockayne patients develop neurological problems as a result of the failed development of the nervous system.

A new national service is being established for Cockayne's patients based in the Clinical Genetics department of Guy's and St Thomas' headed by **Dr Shehla Mohammed**.

"We hope the two national services will provide extra insights working alongside each other," said Dr Sarkany.

## CASE STUDY - EDDISON MILLER

**The first sign that something was wrong with Edison appeared when he was three months old. His parents Andrew, 37, a police officer and Nicola, 36, an architectural technologist, of Ashford, Kent, had taken him for a visit to some neighbours.**

"Afterwards we noticed his face was red. It looked like a chemical burn. He had only been outside for a few minutes and I thought it must be a reaction to the suncream," said Nicola.

They took Edison to the GP who told them it was probably eczema. This was the first of several visits to doctors triggered by Edison's apparently hyper-sensitive reaction to being outside.

"They would say: 'It looks like sunburn.' We would reply: 'But he has hardly been outside.' They would look at us sceptically and say: 'Babies are sensitive.' We would respond: 'We know.'"

"It got to the point where we were not being listened to. So, on our GP's suggestion, we went private."

The consultant dermatologist they saw could not diagnose Edison's condition, instead referring the family to John's. There a biopsy was taken of Edison's skin and two months later the family was asked back to be given the findings.

"That was when we were told he had *Xeroderma Pigmentosum* – which is incredibly rare. Right up to that point I assumed it was an allergy. The paediatric nurse took Edison off to play while Hiva Fassihi, the consultant, explained what it meant and how we would have to reconfigure our lives. It was a massive shock –



Eddison Miller, age 3, in his UVR- protective clothing and (below) his "indoor garden". Even the 40 watt light bulb was too strong and had to be changed

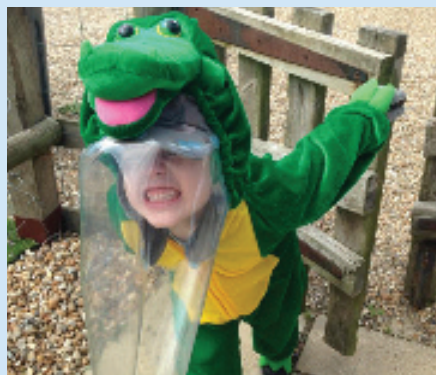


but the care we have had has been absolutely fantastic," said Nicola.

Eddison was then 13 months old. From that day his routine changed. To protect him from UV radiation he has Factor 50 suncream applied every three hours and must wear full body, head and face cover, including gloves. At home all the windows have been covered with a special film that filters out UVA and UVB radiation. Even the light bulbs had to be changed – any over 40 watts had to go and halogen spotlights had to be replaced with LEDs.

Now aged three, going out in his full protective gear is a trial. He gets hot and dehydrated, it is difficult to hear and when windy his visor gets pressed against his face.

On one occasion, the family – there is also a younger brother, Raife, who is unaffected – went for an outing to the beach by moonlight so Eddison could run around without his protective clothing. But the sensation of sand between his toes and wind in his hair was overwhelming. "We underestimated



Eddison will need regular medical checks for the rest of his life

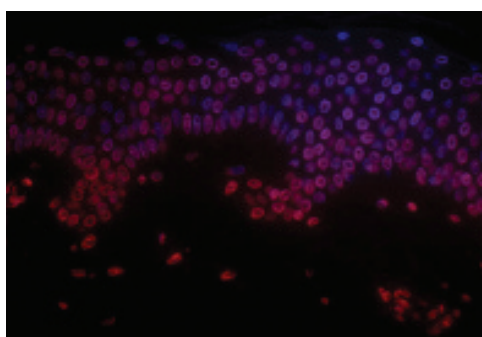
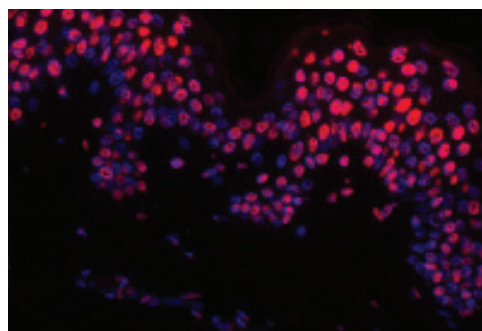
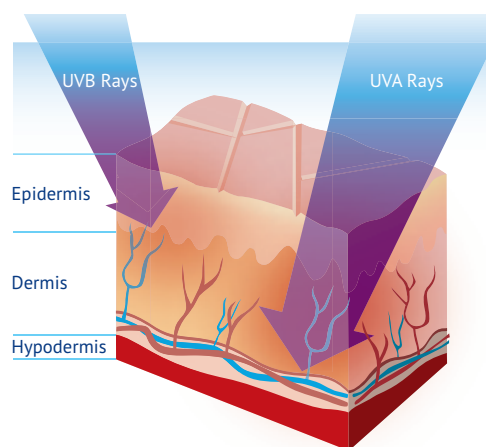
how much of a sensory overload it would be,” said Nicola.

She and Andrew launched an appeal for funds to build an “indoor garden”, which was completed in Autumn 2013, where he can now play with friends.

He will shortly start at nursery school where staff have been specially trained to deal with his particular needs. At St John’s, which he attends regularly for check ups by a multidisciplinary team, doctors are so pleased with his progress they have said he does not need to return for a year.

Nicola said: “Developmentally and mentally he is doing really well. If anything he is ahead of his peers. His stamina has improved enormously since he had the indoor garden.”

The future is uncertain and he will need regular medical checks for the rest of his life to detect any sign of cancer or neurological problems. But for now things are looking rosy for the boy who is one in a quarter million.



## Climate change and the sun

**St John’s works closely with Professor Anthony Young, head of photobiology at Kings College, London, who has recently completed a three year, 3.5 million euro project studying the impact of climate change on exposure to ultraviolet radiation.**

The project brought together photobiologists, dermatologists, immunologists, epidemiologists and climatologists from six European countries and involved measuring personal exposure to UV by individuals wearing dosimeters. The researchers are analysing the findings in relation to meteorological, environmental and behavioural factors and their impact on health.

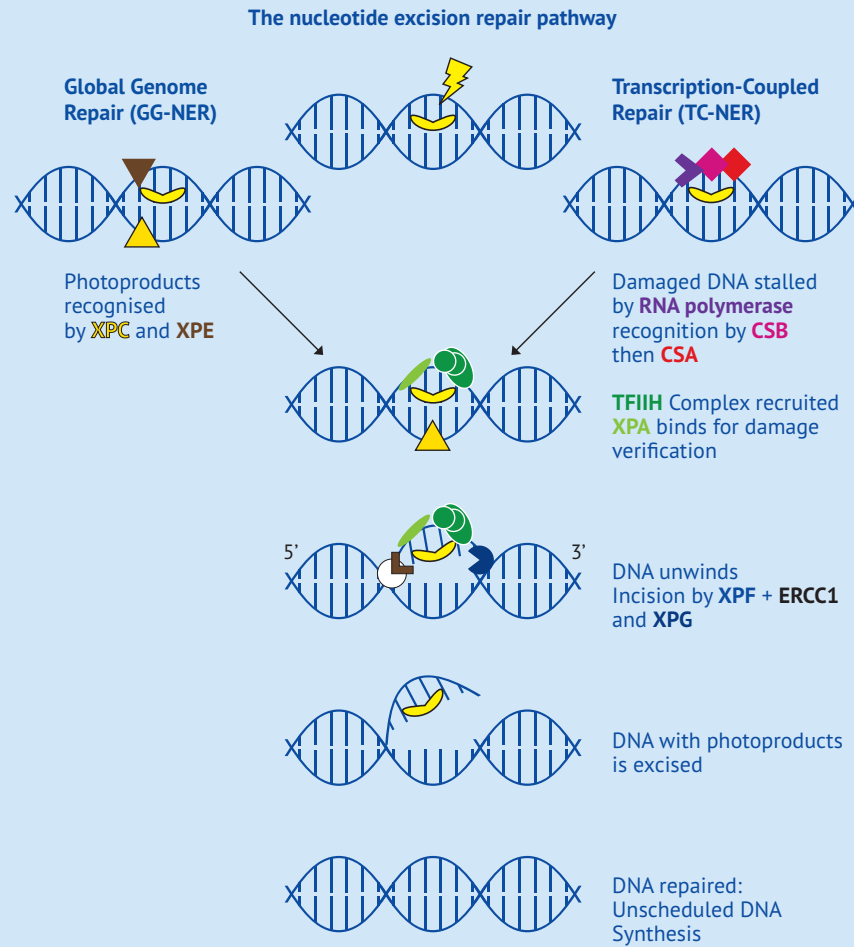
Research led by Professor Young, published in 2011, revealed that UVA caused similar damage to the DNA in skin cells as UVB and could put individuals at risk of cancer. Previously UVB was thought to be the cause of skin cancer.

The research showed that UVA, previously thought to cause wrinkles and premature ageing but not cancer, could be more damaging than UVB because the rays penetrated to deeper layers of the skin.

The finding has implications for sun protection because many sunscreens do not contain enough UVA protection. Most people do not put on nearly enough lotion, he said.

Sunlight causes damage to the skin at different depths (top). Fluorescence microscopy shows damage to DNA caused by Ultraviolet B (middle) and also by the deeper penetrating Ultraviolet A, which was unexpected (bottom)





The Nucleotide Excision Repair Pathway: a key mechanism that removes DNA damaged by ultraviolet light. When it fails owing to in-born genetic errors, severe human disease such as Xeroderma Pigmentosum results



