VITILIGO: (1) CAUSES AND TREATMENTS

By Nerys Roberts, MD, FRCP, and Marion Lesage, MA

Vitiligo affects at least one per cent of the population worldwide. The first part of this article looks at the possible causes of and treatments for this skin disease. Part two, to be published next week, will look at sun protection and skin camouflage for people with vitiligo.

Vitiligo is a skin disease that has been known about for at least 5,000 years, but little has been done to understand its causes or to evaluate possible treatments. It is not a painful condition and perhaps that is why it is often trivialised and left untreated. However, vitiligo can have a profound psychological and social impact on the sufferer. Many people with vitiligo feel humiliated and stigmatised, often with no idea of where to turn to for help and information. Research has shown that pharmacists are ideally placed to help both patients and general practitioners by giving specialist advice but, currently, many are not in a position to provide this support because they do not have enough knowledge about vitiligo at their fingertips.

AETIOLOGY AND DIAGNOSIS

Vitiligo is characterised by depigmented areas of skin. The affected areas can be paler than normal skin or completely without pigment. The exact cause of the disease is unknown but there is an association with conditions such as diabetes, thyroid disease, pernicious anaemia and adrenal failure, which are sometimes autoimmune in origin. Epidemiological studies suggest that several genes may be involved, as well as environmental factors. The first locus for vitiligo with a strong autoimmune basis (AIS1) has been mapped, but the exact gene responsible within this locus has yet to be identified. In some families, several members are affected.

The depigmented areas usually appear on both sides of the body equally, and often symmetrically (symmetrical vitiligo). Commonly, the face (especially around the eyes and mouth), hands and body creases (armpits and groins including genitals) are affected but the depigmentation can occur anywhere. Hairs in affected areas can become white. Some patients have vitiligo in white patches on only one side of the body (segmental vitiligo).

There is good evidence that in vitiliginous patches, functional epidermal melanocytes are lost and it has been proposed that mediators released by the nerves in the epidermis may be toxic to melanocytes (neuronal theory), although there is no direct evidence of such an effect.

On the other hand, others have put forward the idea that the pigment cells themselves cause vitiligo and it has been suggested that the melanocytes fail to clear toxic metabolites formed during the production of melanin (self-destructive theory). It has also been suggested that melanocytes are affected by oxidative stress and that there is a breakdown in the antioxidant defence in the epidermis of people with vitiligo, leading to a build up of chemicals that are selectively toxic to melanocytes. It has been proposed that the defence defect is due to a lack of the enzyme catalase in patients with vitiligo, hence the use of a catalase-like compound, pseudocatalase, as a therapeutic agent.

The association of vitiligo with autoimmune diseases led to the search for autoantibodies. Antibodies that have been identified in some patients include ones that target melanocyte specific components. Although it remains to be seen whether these are a cause or consequence of melanocyte damage, this finding strengthens the argument that vitiligo is an autoimmune condition and explains why treatment with corticosteroids, which targets the immune system, can be of benefit.

Vitiligo can be described as generalised (occurring all over the body) or localised (small patches occurring in one area, eg, around the eyes). The condition can be unpredictable and can move between active (spreading) and static phases.

Pharmacists should be aware that many other conditions can present with depigmentation. In vitiligo, the skin texture is normal and there is usually no itching or visible inflammation. Possible diagnoses, other than vitiligo, can include lichen planus, vitiligo-like depigmentation, lichen striatus and guttate hypomelanosis (a condition where small white areas appear, mainly on limbs exposed to the sun). Where the lesions are not clearly segmental or symmetrical or only partially depigmented, a differential diagnosis could be made. Other hypopigmented conditions include:

identify gaps in your knowledge

1. What are the two most common types of vitiligo?
2. Name another patchy white skin disease with which vitiligo might be confused.
3. List two possible treatments for vitiligo.

This article relates to the Royal Pharmaceutical Society’s core competencies of “common disease states and their drug therapies” and “appropriate advice” (see “Medicines, ethics and practice — a guide for pharmacists”, number 26, July 2002, pp105–6). You should consider how it will be of value to your practice.

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Vitiligo should be treated with the same four-week approach and further treatment is reasonable if established patches start to spread.

Oral steroids, intralesional steroids (steroids injected into the patch) and pulsed intravenous methylprednisolone have been reported to induce repigmentation in vitiligo. However, potentially serious side effects can occur and the risks must be weighed against the benefits before any of these interventions can be used.

**Phototherapy**
The relationship between sunlight and vitiligo presents a problem. Because the function of melanocytes is to protect the skin from sunburn by producing melanin, in areas of vitiligo, where the melanocyte population is significantly reduced, the skin is at risk of burning. Conversely any remaining melanocytes will not function and release their pigment to the surrounding skin cells unless they are exposed to ultraviolet (UV) radiation, hence the concept of controlled UV exposure or phototherapy.

Phototherapy is widely used in the treatment of psoriasis. Psoralens and high intensity long-wavelength ultraviolet irradiation (PUVA) is the most established type of phototherapy and involves using a chemical to photosensitise the skin (by bathing in a topical solution of psoralens or taking tablets of psoralens) before exposing it to UVA rays. Twice weekly treatment for about 12 weeks will often clear psoriasis and more prolonged treatment with a similar protocol was found to be of benefit to patients with vitiligo. However a large number of treated patients found that the pigment was lost when treatment was discontinued. Unfortunately, continuous treatment is not an option because it would increase the risk of skin cancer in the same way as an excess of natural sunlight can cause skin cancer.

More recently, narrow band UVB (called TLO-1 phototherapy), has been used. Again, this was initially developed to treat psoriasis. The early results with this form of phototherapy for vitiligo is more promising than PUVA, with greater initial success (both in terms of arresting disease and inducing repigmentation) and lower relapse rates. It is also easier for patients because there is no need to take a bath at the hospital or wear dark glasses for 24 hours after treatment (a side effect of methoxypsoralens tablets is that they photosensitise the eyes as well as the skin).

Patients need to be aware that treatment needs to be regular and prolonged (usually twice a week for 12 to 16 weeks) and repigmentation may be patchy. The most common initial result is small dots of repigmentation around the hair follicles, making the condition appear worse. It is thought that the pigment cells in the hair follicles escape attack in vitiligo and so repigmentation starts at the hair follicle. The most common initial result is small dots of repigmentation around the hair follicles, making the condition appear worse. It is thought that the pigment cells in the hair follicles escape attack in vitiligo and so repigmentation starts at the hair follicle. The most common initial result is small dots of repigmentation around the hair follicles, making the condition appear worse. It is thought that the pigment cells in the hair follicles escape attack in vitiligo and so repigmentation starts at the hair follicle opening and gradually spreads out to join the adjacent area of repigmenting skin. Phototherapy does not work for everyone and the vitiligo can progress after a course of treatment.

**Depigmentation**
Patients with vitiligo often say that being “patchy”, is the worst thing about the condition and they would rather be pigmented or depigmented. In patients with widespread vitiligo, depigmenting agents (as classified in the British National Formulary) need to be used because the melanocytes reside in the basal layer of the epidermis and penetration is less effective with creams and weaker steroids. A small amount of ointment is applied to the patches twice daily so that after each application the treated area appears slightly shiny with the greasy ointment. Treatment is recommended for four weeks only because it is possible to induce skin thinning with longer use of these potent steroids. Often, the first sign of skin atrophy is tiny blood vessels in the dermis becoming visible through the thinned epidermis. If this happens treatment should be discontinued to allow the epidermis to recover.

Weaker steroids are used for more absorptive and sensitive sites such as the face and genital skin. Topical steroids do not induce repigmentation and patients will need to expose themselves to natural sunlight after treatment to try to activate the melanocytes which have survived the inflammatory attack. However, caution is needed to ensure that the person does not suffer from sunburn.

FACES repigment after steroid treatment and although eyelids also repigment well, caution needs to be exercised when applying a steroid to this area due to the risk of inducing glaucoma. Finger tips are more resistant to repigmentation. New patches of vitiligo should be treated with the same four-week approach and although the patient should avoid re-treating established patches, Potent and very potent topical steroid ointments (as classified in Martindale 33, pp1118–20. Have any of your patients had this treatment? What is their experience of it? and find out how they would deal with a patient suffering from vitiligo.

**Corticosteroids**
Corticosteroids are the safest and most effective therapy for localised vitiligo. The best time to administer treatment is early in the course of the disease, when the patches are spreading. The rationale for the use of topical steroids is to stop lymphocytes attacking melanocytes, thus arresting disease progression.

Age of onset of vitiligo varies, the average being 20 years. Vitiligo occurring at birth is extremely rare and loss of pigment from birth may herald other unrelated diseases such as Waardenburg syndrome (an inherited disorder often involving hearing loss and changes in skin and hair pigmentation) or piebaldism.

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mentation thus appears an attractive solution. Remaining pigment can be “bleached out” by applying hydroquinone, a chemical that increases melanin excretion from melanocytes, twice daily. However the concentration of hydroquinone needed to induce depigmentation, often of the order of 20 per cent monobenzyl ether of hydroquinone, carries a risk of contact eczema, depigmentation at distant sites due to systemic absorption and ochronosis, a yellowing degeneration of the dermal connective tissue leading to paradoxical darkening of the skin in patients of skin types 4 or 5 (Fitzpatrick classification; type 4 skin rarely burns and tans more than average and type 5 skin rarely burns and tans profusely). Therefore the patient needs to be aware of all the potential consequences of treatment.

Skin grafting Rather like hair transplants, skin can be taken from areas where the skin has not lost its pigment and transplanted to the vitiligo-affected area. The rationale is that the melanocytes from the transplanted skin will grow into the vitiliginous skin and cause repigmentation. This is a specialised technique and is only available in a small number of centres.

Pseudocatalase Melanocytes in patients with vitiligo often show vacuolation, which is thought to be due to peroxidative damage. Levels of catalase are low in both normal and depigmented skin of patients with vitiligo and levels of hydrogen peroxide are high in the epidermis. It is postulated that these high levels may be responsible for the imbalance in calcium homeostasis observed in melanocytes and keratinocytes from depigmented sites.

Pseudocatalase can scavenge hydrogen peroxide although it needs UV exposure for full activation of the chemical complex. A research treatment, available only to private patients, involves anointing patients with a pseudocatalase and calcium preparation and then exposing them to UV radiation.

Tacrolimus Theoretically, there are good reasons why tacrolimus, a topical immunosuppressant, may be of benefit in vitiligo, but currently its use in this area is experimental. Although there has been one preliminary report of its use in vitiligo, many more patients need to be treated before any conclusion can be reached about its value. Like topical steroids, tacrolimus is would be expected to arrest disease progression rather than induce repigmentation.

Psychological intervention The effects of skin disease are certainly more than skin deep. It is only in recent years that the possible benefits of psychological intervention have been assessed with regard to dermatological conditions. Research to determine whether the psychological effects of therapy impact on the physical progression of skin conditions, including vitiligo, is now being conducted.

The biopsychosocial model of how psychology can affect the course of skin disease draws a link between stress, the immune system and changing levels of neuropeptides in the brain which affect the skin. Emotional trauma and stressful life events can cause large adrenal secretions and can result in the onset of vitiligo.

It is hoped that the results of new research will help improve the understanding of the role of the mental state in pigmentation disorders and result in more effective treatment for vitiligo that combines counselling with traditional medical treatment.

REFERENCES

Further information about new research and treatments will be given at a forthcoming symposium entitled “Vitiligo from gene to clinic: new insights in research and treatment” to be held at the Royal College of Physicians in London on 16–17 May. For full details of the event visit the Vitiligo Society website at www.vitiligosociety.org.uk