

# Skin Cancer After Transplantation: Where Did We Come From, Where Do We Go?

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When Paul Gerson Unna first described a possible relationship between sunlight and development of cutaneous epithelioma, he would have had no idea of the impending public health epidemic of these tumours to be seen in the 100 years following his publication.

The incidence of sun-related skin tumours, including melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC), has been increasing in virtually every fair-skinned population in which they have been studied throughout the world. Nonmelanoma skin cancers (SCC and BCC) are now the most common cancers in Australia, occurring at least three times more commonly than all other cancers combined. By virtue of their number, they now comprise the biggest burden of all cancers to the health budget in Australia. Variations on this exist in many other countries where there are fair-skinned populations exposing large amounts of their skin to hot sunny climates. In Australia, the latest data suggest that at least two of three people born in the country will eventually develop one of the nonmelanoma skin cancers (NMSCs).

There has been increasing awareness of the public health implications of skin cancer, as was initially reported in the incidence data. The mortality from NMSC has been traditionally very low, with the majority being from SCC. Many organisations have started public health programs on prevention and early detection of skin cancer. Much research is being done into the basic pathogenesis of these tumours, and our knowledge has expanded enormously. There is also much work being done on new forms of treatment, particularly topical treatments, which will gradually replace surgery over time.

In the public health area there have been some remarkable changes in knowledge, attitudes, and behaviours in the sunlight in some countries, Australia in particular. There are early data suggesting a reversal in the increasing incidence and mortality caused by melanoma in younger cohorts in Australia and a similar change in incidence of BCC. But does this mean that we can sit back and relax with the reassurance that it will all be over soon? Of course the answer is no. There is a “new kid

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on the block” – organ transplantation – and this has brought a new dimension to the epidemic of skin cancer.

Whether or not people develop a skin cancer is a combination of their genetic susceptibility and the circumstances in which they have lived their life. Even if they do achieve the right combination to initiate the cellular changes in keratinocytes that we recognise as dysplasia, a variety of mechanisms will act to control further tumour development, immunological mechanisms in particular. A reduction in, or a lack of, these immunological control mechanisms will inevitably lead to an increased ease of induction of what we recognise as invasive cancer. And that is exactly what is being found in patients who have undergone organ transplantation. The immunological surveillance and control currently reduced to prevent transplant rejection is the same as that preventing tumour formation. Thus, predictably, successful organ transplantation is followed by an increased risk of skin cancer, particularly SCC.

Following organ transplantation, it is not just the formation of one or two tumours that is the concern. Very large numbers of tumours, SCCs in particular, develop over time in those at risk. It creates an enormous challenge to everyone involved, both patients and those responsible for their care. So where do we go from here? What can be done?

There are different approaches to disease control. The first and perhaps the most ideal would be to reduce an individual’s genetic susceptibility to develop the disease, in this case skin cancer. Ironically, at the moment this is the most difficult of the approaches, as it is the area in which we have the least knowledge and the least ability to bring about the changes necessary.

Another problem with this simplistic-sounding approach is that by the time many people require their organ transplantation, they have often gone a long way along the pathway that leads to tumour formation. This means, for example, that they may have actinic keratoses already and thus reducing genetic susceptibility would occur too late.

Another approach might be to develop more targeted, or more specific, immunosuppression. Ideally, this would reduce the risk of transplant rejection but would not reduce tumour rejection. There is a promise of this with, for instance, the mTOR inhibitors, but a long-term benefit in skin cancer reduction is not yet proven and must be balanced against other, possibly less favourable, drug characteristics.

The public health approach to skin cancer control would comprise the two classical components. The first component is to deal with the problem people have now, that is, incipient or overt tumours. These must be detected early, either in the “pre-cancerous” stage, or very early in the truly invasive phase, thus allowing an easy cure to be achieved with relatively simple treatment.

The second component of a public health approach is the long-term goal of trying to prevent skin cancer: This is to reduce environmental exposure to the carcinogen that precipitates the tumours in susceptible people: sunlight. The ideal here is to commence photoprotection at a very early pretransplant stage and to continue it to an almost obsessional degree post transplant. Complications of excessive photoprotection, such as vitamin D deficiency, could be easily overcome through dietary vitamin D supplementation.

The final approach is the “when all else fails-approach.” There is the need for better skin cancer treatments that are effective, simple, ideally applied by the patient themselves, and that are not too expensive. As transplant patients frequently have diffuse sun-related changes in their skin, it is necessary to take a broader view of the therapeutic approach. Some people have termed this “treating the field” rather than just treating individual tumours if or when they become clinically apparent.

So, in summary, the need for a book such as this one is a clear indication that the development of skin cancer in patients undergoing organ transplantation is not just a problem now. It also will be an increasing problem in the future, as an increasing number of people are treated with this therapeutic approach to organ failure.

There is no doubt that there have been very many advances over the years in all the components underpinning successful organ transplantation. It is to be hoped that, by exploring all or many of the possibilities to deal with skin cancer outlined here, this side effect of organ transplantation will become less of a problem in the future.