

# Analysis of Tissue Derived from Patients with Vitiligo

Raymond E. Boissy, Ph.D.  
Associate Professor, Department of Dermatology  
University of Cincinnati Medical Center

A current research focus at the University of Cincinnati is aimed at investigating the cause of a distinct form of vitiligo, "occupational" or "contact" vitiligo. This form of vitiligo is unique in that its onset appears to be correlated with exposure to certain chemicals in the workplace or at home. However, eventually, the cutaneous depigmentation extends from the site of chemical contact and develops into progressive, generalized vitiligo well beyond the original site.

There is anecdotal and much experimental evidence demonstrating that certain environmental chemicals may be selectively toxic to melanocytes and thus may be responsible for instigating vitiligo. Specifically, these environmental toxins are aromatic or aliphatic derivatives of phenols and catechols (i.e., hydroquinone, monobenzy ether of hydroquinone, 2, 4-di-tert-butylphenol (DTBP), p-tert-butylphenol (PTBP), p-methyl-catechol, p-isopropylcatechols, p-cholorosorcinol, p-cresol, disopropyl fluorophosphate, and physostingmine). Compounds that contain phenolic/catecholic derivatives are listed in the table. There have been published reports of vitiligo developing in individuals who work with rubber and industrial oils containing phenolic antioxidants or plasticizers, phenolic germicidal detergents, particularly butylphenol containing adhesives and in the general manufacturing of phenolic/catecholic derivatives. Certain phenol and catechols have been shown to be preferentially toxic to melanocytes. In fact, these compounds have been added to bleaching creams, products used to remove hyperpigmented lesions. Interestingly, these creams are not toxic to all individuals. Even at high dosages only a few humans depigment in response to application. In contrast, patients with extensive vitiligo readily depigment in response to application. This observation suggests that these agents are not simple poisons for melanocytes but are injurious to only those people genetically susceptible to the compounds (i.e., vitiligo patients).

Germicidal Detergents	De-emulsifiers for oil field use
Rubber antioxidants	Plasticizers
Varnish and lacquer resins	Insecticides
Motor Oil additives	Printing inks
Synthetic oils	Valve plants
Deodorants	Disinfectants
Soap antioxidants	Adhesives
Latex gloves	

In the research laboratories at the University of Cincinnati College of Medicine we have been investigating the effect of a potent inducer of occupational/contact vitiligo, 4-tert-butylphenol (4-TBP), on the viability of cultured melanocytes. We found that this compound does indeed cause the death of melanocytes in a dose dependent manner. The toxicity of the 4-TBP compound is greater for melanocytes than for the other primary cell type of the skin, the keratinocyte. This data indicates that melanocytes may be preferentially susceptible to damage by phenolic/catecholic compounds. It now needs to be determined if melanocytes of patients with vitiligo are more susceptible to the toxic effects of phenols and catechols than melanocytes of individuals without vitiligo, and if so why. This may provide a key understanding of how the occupational/contact form of vitiligo in specific, and all vitiligo in general, develops.

During this research we have also discovered that the process of melanocyte destruction induced by 4-TBP is a specific programmed cell process called "apoptosis". During destruction by apoptosis the affected melanocyte shrinks, degrades its DNA, and fragments into pieces. This is an important discovery because this process of cell destruction can be regulated and potentially prevented. Therefore, therapeutic approaches to prevent the development of cell damage by apoptosis can eventually be developed in the future.