SIGNIFICANCE OF CUTANEOUS LESIONS IN THE SYMPTOMATOLOGY OF EXPOSURE TO DIOXINS AND OTHER CHLORACNEGENS

K. D. Crow
Princess Margaret Hospital
Swindon
Wiltshire, United Kingdom

ABSTRACT

After a brief review of the subject of chloracnegenic toxicity, this paper examines two proposals. Firstly that the acnegenic potential of all chloroacnegens correlates perfectly with their systemic toxicity and, secondly, that with almost no exceptions chloracne still appears to be the most sensitive marker of poisoning by chloracnegens in the human subject. It is as such a marker that it is of great importance. Various alternative markers are examined and rejected in favor of chloracne. It is, of course, emphasized that the failure of chloracne to appear after apparent poisoning rules out short and medium term effects but cannot entirely preclude the potential existence of long term low dose effects, although none have so far been proven statistically to exist in over 30 years of follow-up.

INTRODUCTION

The cutaneous lesions associated with chloracne may briefly be summarized as follows:

- Chloracne
- Ophthalmic
- Pigmentation
- Porphyric changes
- Palmar and Plantar hyperhidrosis
- Phrynoderma
- Hypertrichosis

In view of the fact that they are non-specific, we can dispose straight away with all these changes except for two. First and foremost there is chloracne, an eruption which is unique in being the skin's only consistent response to poisoning with chloracnegenic...
chemicals; and secondly, there are the peculiar changes which may take place in the meibomian gland of the eyelid. These glands, with the eyelashes, form modified pilosebaceous units in every way analogous to those in the skin. Therefore we might well expect them to react in exactly the same way to chloracnegenic toxins—and so they do, with the formation of keratinous cysts and disappearance of the meibomian gland. Recent work in experimental animals suggests that the cerumen glands in the auditory canal, again modified sebaceous glands, appear to undergo squamous metaplasia in exactly the same way. (McConnell, 1981). This change is so specific to chloracnegenic poisoning that I propose to call these eyelid changes "ophthalmic chloracne" in order to distinguish it from non-specific irritation, conjunctivitis, and other things of that sort.

We can define a dioxin-type chloracnegen very roughly as a molecule with two adjacent aromatic ring structures, which has planarity, symmetry with lateral adjacent halogens, lack of steric hindrance, and the ability to fit into a box-like configuration of some 10 x 3 Å. However, recent work by McKinney suggests that this concept needs modification in order to accommodate toxic and non-toxic halogenated aromatics which do not accord with the above definition (McKinney and McConnell, 1980). For example the 2,3,7,8-isomer of Tetrachloronaphthalene fits the above criteria perfectly but is non-toxic and non-acnegenic, (Crow, 1970) whereas 2,3,7-Tribromonaphthalene, which does not fit, is highly toxic and acnegenic. His theory of electronic polarisation has been described elsewhere, but the importance of this finding as far as I am concerned here, lies in the fact that, despite the changing definition, acnegenicity and toxicity still appear to go hand in hand.

Now, if chloracne is to retain its significance as a vital marker of poisoning by chloracnegens, we must be able to make an unequivocal diagnosis. Clinical features alone, even to an expert, may be insufficient, but, taken in conjunction with other factors such as distribution, age, clustering, and contact with known chloracnegens or other chemicals with the specific molecular characteristics, should be sufficient to make a positive diagnosis. Where there is doubt, and particularly if some hitherto unknown toxin seems responsible, histological examination of the skin is essential. This is because the conversion of the pilo-sebaceous follicle in skin or on the edge of the eyelid, together with an early underlying disappearance of the sebaceous glands, lack of inflammatory cells, and a diminished bacterial flora, (Cunliffe et al, 1975) would seem to be quite specific. Indeed, since the highly typical keratinous cysts are only formed by the squamous metaplasia of infundibular and sebaceous cells, the presence (partial or total) of the one without the absence of the other is an incompatibility. Of all these changes, the squamous metaplasia and thus disappearance of the sebaceous gland, is probably unique to these poisons. It has been shown to occur in human subjects and appropriate experimental animals with every known chloracnegen.