Occupational chloracne

Report by the Industrial Injuries Advisory Council in accordance with Section 171 of the Social Security Administration Act 1992 considering prescription for occupational chloracne

Presented to Parliament by the Secretary of State for Work and Pensions by Command of Her Majesty
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Dear Secretary of State

REVIEW OF OCCUPATIONAL CHLORACNE

We present our report, which considers prescription for chloracne arising from exposure to halogenated hydrocarbons.

The Industrial Injuries Advisory Council (IIAC) has conducted a horizon scanning exercise to compare diseases listed as occupational by the European Union (EU) and the International Labour Organisation (ILO) with those scheduled in the UK’s Industrial Injuries Scheme. One finding is that the disease chloracne, while not currently recognised under the Industrial Injuries Scheme, appears on both of these alternative lists.

In reviewing this matter we have since considered published research on chloracne and consulted with experts in the field.

Chloracne is a variant of acne caused by exposure to certain halogenated aromatic hydrocarbons called ‘chloracnegens’. It is a disease which may result in severe disfigurement of the skin. Clinical symptoms often continue for 2 to 3 years following exposure and sometimes may still persist for up to 30 years. Exposure to halogenated hydrocarbons is a cause of this otherwise rare disease. The case for prescription of chloracne can be made on the basis of specific diagnostic features and a clear link with occupational exposure.

We recommend that chloracne following occupational exposure to chloracnegens be added to the list of prescribed diseases for which Industrial Injuries Disablement Benefit (IIDB) is payable.

Yours sincerely

Professor Keith Palmer
IIAC Chairman

July 2013
Summary

The Industrial Injuries Advisory Council (IIAC) has undertaken a horizon scanning exercise to compare diseases listed as occupational by the European Union (EU) and the International Labour Organisation (ILO) with those prescribed under the Industrial Injuries Disablement Benefit (IIDB) Scheme. The Council notes that chloracne, while not presently covered by the Scheme, is included on both the ILO and EU lists of occupational diseases.

Chloracne is a systemic disease, characterised by potentially severe and disfiguring facial acne. Dermatological symptoms can persist for several years. The disease is caused by exposure to certain halogenated aromatic hydrocarbons called ‘chloracnegens’, encountered most often in an occupational setting. Dioxins are the most potent form of chloracnegen.

During the course of review the Council has considered the peer-reviewed published research literature and consulted with experts in the field. Chloracne is a rare disease, usually with an occupational basis. The Council has concluded that chloracne can be prescribed based on its specific diagnostic features, its clear links to occupational exposure and the potential of the disease to cause severe facial disfigurement. IIAC recommends that chloracne be added to the list of prescribed diseases for which IIDB is payable for workers exposed to a chemical capable of causing chloracne (a chloracnegen) at work.

This report includes some technical terms, the meanings of which are explained in a concluding glossary.
The Industrial Injuries Disablement Benefit Scheme

Background
1. IIAC is an independent statutory body set up to advise the Secretary of State for Work and Pensions in Great Britain and the Department for Social Development in Northern Ireland on matters relating to the Industrial Injuries Scheme. The Scheme provides non-contributory, ‘no-fault’ payments for disablement because of accidents or prescribed diseases, which arise out of and in the course of employed earners’ employment.

2. Within this remit, the Council has conducted a horizon scanning exercise to compare diseases listed as occupational by the EU and the ILO with those recognised by the Industrial Injuries Scheme.

3. As one of its findings, the review identified that the disease chloracne is included on the lists of the EU and ILO (as “diseases caused by halogen derivatives of aliphatic or aromatic hydrocarbons”, or “diseases caused by phenols or counterparts or halogenated derivatives thereof”), but is currently not scheduled for entitlement under the UK Industrial Injuries Scheme. This report sets out the case for prescription.

Method of investigation
4. IIAC referred the matter to its permanent sub-committee, the Research Working Group (RWG), which conducted a literature search and reviewed key research papers. The RWG also consulted with two dermatologists with expertise in chloracne (Appendix A) about the diagnostic features of the skin manifestations of chloracne and how it can be distinguished from ordinary acne (acne vulgaris).

Chloracne – the disease
5. Chloracne is a systemic disease, in which skin involvement is the most prominent clinical manifestation. Chloracne is caused by systemic exposure to certain halogenated aromatic hydrocarbons called ‘chloracnegens’. It was first described in 1887 by Von Bettman and by Herxheimer in 1889. They suggested that the condition was caused by chloride exposure and named it ‘chloracne’, owing to the similarity between its clinical features and those of the more common condition, acne vulgaris. Cases of chloracne result from occupational and environmental exposures.

6. Chloracne was once common among workers occupationally exposed to naphthalene and chlorinated biphenyls, including workers from the chemical industry exposed to pesticides. Since the 1960s synthetic resins have replaced these compounds and the incidence of chloracne has fallen dramatically. However, some workers are still being exposed occupationally to relevant chemicals and are at risk of developing chloracne.
7. Dioxins are the most potent of the environmental chloracnegens and, rarely, individuals may become exposed through contaminated industrial waste, contaminated food products or following an industrial accident. A widely publicised accident occurred at a chemical plant near Seveso, Italy in 1976 (Caramaschi et al., 1981). Two kilograms of the most toxic dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) were discharged into the atmosphere during an explosion and subsequently 135 cases of chloracne were diagnosed among 2,000 inhabitants. Elsewhere, hundreds of veterans of the Vietnam War were exposed to dioxin via exposure to a herbicide known as Agent Orange, which was found to be contaminated with TCDD.

Epidemiology
8. The prevalence of chloracne in the UK is unknown but there are thought to be fewer than 4,000 cases worldwide, indicating that this has now become a rare disease. In the UK, a total of eight new cases were reported to The Health and Occupation Reporting network (THOR http://www.medicine.manchester.ac.uk\coeh\thor) between 1993-2011, although not all cases would be known to dermatologists and not all dermatologists nationally participate in this reporting scheme.

Toxicology
9. All chloracnegenic (chloracne-inducing) compounds are known to share structural features including two benzene rings with halogen atoms occupying at least three of the lateral ring positions. The position of the halogen substitutions appears to be critical to chloracnegenic activity.

Figure 1: Chemical structure of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)

10. Chloracnegens are absorbed into the body by direct contact (through the skin), inhalation, or ingestion. The average concentration of dioxin in a healthy individual with no prior history of occupational or environmental exposure is less than 10 parts per trillion, but it is over several hundreds of parts per trillion in patients with chloracne. There is no known lower limit of exposure to chloracnegens below which the disease is certain not to occur. Likewise there is no known exposure level above which it is certain to occur.

Clinical features
11. Chloracnegens are highly lipophilic (fat soluble) and can remain in body fat for long periods. Hence, chloracne may be long-lived. Clinical symptoms normally occur 2 to 4 weeks after exposure to chloracnegens, but are often still present 2 to 3 years following cessation of exposure and are sometimes still present after 15 to 30 years.
12. Following exposure, inflammatory comedones and straw-coloured cysts develop. Occasionally, pustules and non-infectious abscesses develop. The distribution of these lesions in chloracne is characteristic. Initially skin lesions appear on the face and neck, and later extend to trunk, extremities, genitalia or other areas. Comedones appear on the face and neck, especially below and to the outer side of the eye (malar crescent) and in the postauricular triangles (behind the ears). The ear lobes, suboccipital hairline and groin are often involved. The skin around the nose and above the eyes is usually spared. The cysts typically affect the neck, shoulders, chest, back, penis and scrotum. Other skin effects include decreased sebum secretion with skin xerosis, pigmentation, porphyrinopathy, hirsutism, skin thickening, palmoplantar hidrosis and palmoplantar hyperkeratosis.

13. Rarely, individuals with chloracne may develop non-cutaneous systemic manifestations including fatigue, anorexia, liver dysfunction, hyperlipidaemia, anaemia, transient weight loss and delayed nerve conduction on testing. Such systemic features do not occur in the absence of the skin disorder and tend to resolve well before the skin lesions.

14. If chloracne is suspected in a patient, chloracnegens can be assessed in serum and various tissues by direct chemical analysis or a biological assay. However, diagnosis rests on the specific clinical features of the disorder as assessed by a specialist in skin diseases.

15. Chloracne, in contrast to ordinary acne, appears to be resistant to all tested forms of treatment. The only way to control the disease is to prevent exposure to chloracnegens.

**Differentiating chloracne from acne vulgaris**

16. Chloracne and acne vulgaris are separate clinical entities, each with its own distinctive pathology. Differentiating chloracne from acne vulgaris requires consideration of the clinical features, anatomic localization, age of onset and exposure history. Chloracne differs from acne vulgaris in that it can occur in any age group, including older adults, whereas common acne normally develops in adolescence. While the overall pattern is clearly acneiform, it also differs from typical acne in the peculiarly dark colour of the comedones, as well as the general peppered distribution in areas not prone to acne vulgaris. Chloracne lesions rarely manifest as inflammation, whereas in acne vulgaris inflammation is a common feature. Colonization by the microorganism *Propionibacterium acnes* is a cardinal feature of acne vulgaris lesions, but not at all in chloracne. While the pathogenesis of acne vulgaris involves excessive sebum excretion and the skin surface is oily, chloracne is usually associated with cutaneous xerosis and the disappearance of sebaceous glands, meaning that the skin is dry. In fact, the disappearance of sebaceous glands is a key, almost diagnostic, feature as there is no other disease in which sebaceous glands become depleted. The points of distinction between acne vulgaris and chloracne are summarized in Table 1.
Table 1. Differential diagnosis of acne vulgaris and chloracne

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Acne Vulgaris</th>
<th>Chloracne</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td>Adolescence and early adulthood</td>
<td>Working age, with no previous history of acne</td>
</tr>
<tr>
<td>Predilection site</td>
<td>Localised, including face, back, chest</td>
<td>Generalised, including the area behind the ear, the cheek, armpit, groin and extremities</td>
</tr>
<tr>
<td>Major lesions</td>
<td>Limited comedones, papules, pustules, cysts</td>
<td>Myriad comedones</td>
</tr>
</tbody>
</table>

Pathogenic factors

<table>
<thead>
<tr>
<th>Inflammation lesions</th>
<th>Common</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sebum production</td>
<td>Increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Microflora</td>
<td>Propionibacterium acnes and Propionibacterium granulosum</td>
<td>No bacteria</td>
</tr>
<tr>
<td>Androgen</td>
<td>Dependent</td>
<td>The role of androgens in chloracne is unknown</td>
</tr>
</tbody>
</table>

Histopathology

<table>
<thead>
<tr>
<th>Sebaceous gland</th>
<th>Hypertrophic and atrophic scarring</th>
<th>Gradual replacement with keratinocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweat gland</td>
<td>Uninvolved</td>
<td>Palmoplantar hyperkeratotic lesions; acrosyringial plugging</td>
</tr>
<tr>
<td>Hair follicle</td>
<td>Thinning of the infundibular epithelial wall sebaceous gland duct</td>
<td>General hyperplasia of the infundibulum and significant thickening of the upper follicle</td>
</tr>
</tbody>
</table>

Therapy

| Effective under treatment of antibiotics | Resistant to therapy retinoids and other treatment |

Consideration of the evidence

17. When reviewing the evidence, the Council sought reports that described the occurrence of chloracne in workers exposed to halogenated hydrocarbons where the dose, mode, or duration of exposure was identified. The Council also considered comparative data collected in the context of environmental exposure to dioxins.

18. Outbreaks of occupational chloracne have tended to mirror the technological advances of the twentieth century. In the 1920s, halogen waxes, chlorinated naphthalenes and biphenyls were recognized as causes of chloracne, whereas in the 1940s, chloronaphthalenes and polychlorinated biphenyls (as used in the shipbuilding industry) were identified. More recently, chlorinated phenols and benzenes used as herbicides and insecticides have been a source of chloracne. The Council found
evidence that some workers continue to be exposed to relevant chemicals at work and that cases of chloracne are still arising. Contemporary occupations and exposures vary from shoemaking (halogenates in glue) (Passarini et al., 2010), to fire fighters occupationally exposed to polychlorinated biphenyls (Orris et al., 1986).

19. In addition, cases of chloracne have recently been reported in discovery chemists synthesising novel polycyclic halogenated chemicals, which were classified as triazoloquinoxalines. Seven male pharmaceutical chemists experienced the onset of a facial and truncal chloracne eruption during 1997. Six of the men worked in one laboratory; the other worked elsewhere but had visited the laboratory in question. The chemists were employed discovering novel organic compounds in the pharmaceutical industry (Gawkrodger et al., 2009). These chemicals had not previously been known to be chloracnegenic but had a structure in keeping with that detailed in Figure 1.

20. In instances where chloracne develops in an individual with no known exposure to a chloracnegen, environmental or occupational, but exposure to one or more novel substances at work, formal toxicological assessment may be indicated.

21. A study of former chlorophenol workers found high serum dioxin levels, both in those with chloracne and those without it (Collins et al., 2006). Therefore, occupational exposure to chloracnegens does not necessarily result in the development of chloracne in all individuals.

22. In a longitudinal cohort study of workers occupationally exposed to chloracnegens, the mean duration of residual chloracne was 26 years and in some workers it had been present for 30 years (Moses et al., 1984). Skin examination in 288 veterans of the Vietnam War, 17 to 22 years after exposure to the herbicide Agent Orange, indicates that chloracne can persistent in the long term: 11.5% of subjects had the disease (Panteleyev et al., 1991).

**The case for prescription**

23. When considering the case for prescription of a disease and its occupational exposure, the Council must adhere to statutory requirements (see Appendix B). A disease may only be prescribed if there is a) a recognised risk to workers in an occupation and b) the link between disease and occupation can be established or reasonably presumed in the individual case. Where the clinical features of a case are not specific to occupation, the Council looks for evidence of work causation “on the balance of probabilities”. However, in some circumstances attribution is possible on the basis of specific clinical features of the disease, and more rarely the disease only arises from occupation or specific occupational activities. One recent example in which the Council recommended prescription on the basis of clinical features of the disease is bronchiolitis obliterans due to diacetyl, or closely related food flavouring (‘Bronchiolitis obliterans and food flavouring agents’, Cm. 7439, July 2008).

24. Similarly, the case for prescription in chloracne can be made on the basis of specific clinical features and a particular association with work. Chloracne is a rare disease and the majority of cases can be linked to exposure to chloracnegenic substances. There is strong evidence of an association between work with chloracnegens and the development of chloracne.
25. Chloracne warrants prescription in that the disease can be severely disabling and can have enduring effects, sometimes over several years or decades after exposure has ceased. The condition leads to disfigurement of the face. Other systemic effects are rare and evidence suggests that the non-dermatological systemic effects and their sequelae appear not to persist for more than 90 days following exposure (Suskind, 1985, Bertazzi et al., 1998).

26. Normally, when a diagnosis of chloracne is suspected, a dermatologist will look for supporting evidence of exposure to chloracnegens. For example, employment of the affected person in an occupation that involves the production of chemicals that are either known chloracnegens, or are chemically similar to chloracnegens, and potential exposure to these chemicals. Occasionally, the suspected causative substance may be a novel compound that has not previously been reported to cause chloracne. In this case the consulting dermatologist may have sought toxicology advice about the propensity of the novel compound to cause chloracne. In vitro tests for chloracnegens are available. However, for the purposes of the Scheme, diagnosis by a consultant dermatologist should be sufficient to establish that the disease is present.

**Recommendations**

27. The Council recommends prescription for chloracne for workers occupationally exposed to chloracnegens as shown in the table below.

<table>
<thead>
<tr>
<th>Prescribed disease</th>
<th>Occupation</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 33 Chloracne</td>
<td>Exposure to a substance causing chloracne</td>
</tr>
</tbody>
</table>

28. Diagnosis of chloracne will normally be based on clinical diagnosis by a specialist and occupational exposure to a substance that causes chloracne.

29. The Council suggests that chloracne should not enjoy the automatic benefit of presumption under Regulation 4(1) of the Social Security (Industrial Injuries) (Prescribed Diseases) Regulation 1985), as, in common with most of the ‘C’ diseases, attribution to occupation (as compared with environmental exposure) may require interpretation of complex toxicological evidence in each individual case.

30. The Council intends prescription to relate to the skin manifestations of chloracne. The Council recognises also that psychological sequelae may accompany skin disfigurement and may comprise an important component of the resulting disablement.

31. Decision makers may wish to consider the extent to which any claimed systemic effects can be attributed to work with chloracnegens on the balance of probabilities. In this regard, it should be noted that symptoms such as fatigue, anorexia, and transient weight loss are common in the general population, have many non-occupational causes, and are more likely than not to have alternative explanations in individual claimants with chloracne.
Prevention

32. Chloracne arising from workplace exposure is a preventable illness. The Control of Substances Hazardous to Health Regulations 2002 (as amended) (COSHH) applies to people who work with hazardous substances such as chloracnegens. These regulations require employers to undertake a suitable and sufficient assessment of the risks created by work involving hazardous substances. Where it is not reasonably practicable to prevent exposure to a hazardous substance by substituting it with a safer option or by totally enclosing the work process, employers are required to take measures to prevent exposure as far as is reasonably practicable.

33. Exposure should be adequately controlled by using appropriate work processes/systems, engineering controls and other measures, including local ventilation systems. Suitable personal protective equipment (PPE), including respiratory protective equipment (RPE) may be used, where adequate control cannot otherwise be achieved. Workers handling chloracnegens need to be informed of the hazards/risks and be provided with appropriate instruction and training.

34. Where it is appropriate for the protection of the health of employees who are or who are liable to be exposed to a hazardous material, COSHH requires the employer to ensure that such employees are under a suitable health surveillance programme, http://www.hse.gov.uk/coshh/basics/surveillance.htm.

Diversity and equality

35. IIAC is aware of issues of equality and diversity and seeks to promote them as part of its values. The Council has resolved to seek to avoid unjustified discrimination on equality grounds, including age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, gender and sexual orientation. During the course of the review of occupational chloracne no diversity and equality issues were apparent.
References


Industrial Injuries Advisory Council, Bronchiolitis obliterans and food flavouring agents, Cmd. 7439, July 2008.


Appendix A: List of experts consulted

Professor David J Gawkrodger
Professor Emeritus in Dermatology, University of Sheffield

Dr John English
Consultant occupational dermatologist, Nottingham University Hospitals NHS Trust, Nottingham
Appendix B: The legal requirements for prescription

The Social Security Contributions and Benefits Act 1992 states that the Secretary of State may prescribe a disease where he is satisfied that the disease:

a) ought to be treated, having regard to its causes and incidence and any other relevant considerations, as a risk of the occupation and not as a risk common to all persons; and

b) is such that, in the absence of special circumstances, the attribution of particular cases to the nature of the employment can be established or presumed with reasonable certainty.

In other words, a disease may only be prescribed if there is a recognised risk to workers in an occupation, and the link between disease and occupation can be established or reasonably presumed in individual cases.

In seeking to address the question of prescription for any particular condition, the Council first looks for a workable definition of the disease. The Council then searches for a practical way to demonstrate in the individual case that the disease can be attributed to occupational exposure with reasonable confidence. For this purpose, reasonable confidence is interpreted as being based on the balance of probabilities according to the available evidence in the scientific literature. An accident at work is specifically catered for within the IIDB scheme. However, if the condition might result from occupational exposure in the absence of an identifiable accident, the Council must consider whether it should be included in the list of diseases that are prescribed for benefit purposes. In these circumstances, it may be possible to ascribe a disease to a particular occupational exposure in two ways – from specific clinical features of the disease or from epidemiological evidence that the risk of disease is at least doubled by the relevant occupational exposure.

Clinical features

For some diseases attribution to occupation may be possible from specific clinical features of the individual case. For example, the proof that an individual's asthma is caused by his occupation may lie in its improvement when s/he is on holiday and regression when s/he returns to work, and in the demonstration that s/he is allergic to a specific substance with which s/he comes into contact only at work. It can be that the disease only occurs as a result of an occupational hazard (e.g. coal workers’ pneumoconiosis).

Doubling of risk

Other diseases are not uniquely occupational, and, when caused by occupation, are indistinguishable from the same disease occurring in someone who has not been exposed to a hazard at work. In these circumstances attribution to occupation on the balance of probabilities depends on epidemiological evidence that work in the prescribed job, or with the prescribed occupational exposure, increases the risk of developing the disease by a factor of two or more. (The logic of this is explained in other Council reports.)

The evidence on chloracne and occupational exposure to chloracnegens is such that attribution can be made in the individual case on the basis of the clinical features.
Glossary

Acne vulgaris  
Simple acne, commonly occurs during adolescence, characterised by comedones, pustules, red skin and sometimes scarring.

Acrosyringium  
A duct within the epidermis that forms part of a sweat gland nearest to the surface of the skin.

Androgen  
A steroid hormone that controls the development and maintenance of masculine characteristics. Examples include testosterone and androsterone.

Chloracnegenic  
Chloracne-inducing.

Comedone  
A dilated (widened) hair follicle filled with skin debris, bacteria, and sebum (oil). Comedones may be closed (whitehead) or open (blackhead).

Hirsutism  
Excessive hairiness in those parts of the body where hair does not normally occur or is minimal (usually, male pattern hair growth in a woman).

Hyperlipidaemia  
An abnormally high concentration of fats in the blood.

Hyperplasia  
An abnormal increase in the number of cells in an organ or a tissue with consequent enlargement.

Hypertrophic and atrophic scarring  
Hypertrophic scarring occurs when there is excessive overgrowth of collagen tissue leading to the formation of a pronounced, raised or enlarged scar. Atrophic scarring occurs due to damage to the fat and muscle supporting the skin's structure, leading to a scar with a pitted, sunken appearance.

Hair follicle infundibulum  
The upper segment of the hair follicle.

Keratinocyte  
A cell of the epidermis (skin) that produces keratin. It is the predominant cell type within the epidermal layer.

Longitudinal cohort study  
A study, which follows individuals with an exposure to a risk of interest (usually over a period of years), and compares their incidence of disease or mortality with a second group, who are unexposed or have a lower level of exposure to the risk of interest.

Palmoplantar hidrosis  
Excessive sweating of the palms of the hands and soles of the feet.

Palmoplantar hyperkeratotisis  
Abnormal thickening of the skin of the palms of the hands and soles of the feet.

Papule  
A small, raised solid pimple or swelling.

Porphyrinopathy  
A syndrome that results from abnormal porphyrin metabolism such as acute porphyria.

Pustule  
A small blister or pimple on the skin containing pus.

Retinoids  
A class of compounds that are chemically related to vitamin A.

Xerosis  
Abnormal dryness of the skin.