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PESTICIDES AS A CAUSE OF OCCUPATIONAL SKIN DISEASES IN FARMERS

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Abstract: Pesticides are chemical substances used in agricultural production to protect crops against pests. They help to achieve better quality and quantity of crops; however, they also are capable of causing occupational diseases in farmers. Skin is the most exposed organ while spraying the pesticide on fields. Farmers are also exposed to pesticides while mixing, loading the pesticide as well as while cleaning the equipment and disposing of empty containers. Other activities associated with exposure are sowing pesticide-preserved seeds, weeding and harvesting previously sprayed crops. During the first decades of using pesticides the main problem was the risk of acute intoxication among people occupationally exposed. With decrease in the toxicity of improved pesticides, attention was turned to chronic intoxication and environmental contamination. Nowadays, the problem of diseases not immediately related to the toxic potential of pesticides gains increasing interest. The majority of these non-toxic diseases are dermatoses. Most pesticide-related dermatoses are contact dermatitis, both allergic or irritant. Rare clinical forms also occur, including urticaria, erythema multiforme, ashy dermatosis, parakeratosis variegata, porphyria cutanea tarda, chloracne, skin hypopigmentation, nail and hair disorders. Farmers exposed to arsenic pesticides are at risk of occupational skin cancer, mostly morbus Bowen (carcinoma *in situ*), multiple basal cell carcinomas and squamous cell carcinomas. Non-arsenic pesticides, e.g. paraquat, are also potentially carcinogenic.

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Key words: pesticides, occupational dermatoses, farmers, contact dermatitis, urticaria, erythema multiforme, ashy dermatosis, parakeratosis variegata, porphyria cutanea tarda, chloracne, skin hypopigmentation, nail and hair disorders, skin cancer.

Pesticides are chemical substances used in agricultural production to protect crops against pests. These substances may be divided into insecticides (insect killers), fungicides (fungus killers), herbicides (weed killers), rodenticides (rodent killers), repellents (substances used to deter vermin from cultivated land), and fumigants (gaseous chemicals used for clearing plantations of microbes or insects). Pesticides help to achieve better quality and quantity of crops; however, they are capable of causing occupational diseases in farmers. Skin is the most exposed organ while spraying the pesticide on fields [65]. Farmers are also exposed to pesticides while mixing, loading the pesticide as well as while cleaning the equipment and disposing of empty containers [67]. Other activities associated with exposure are sowing pesticide-preserved seeds, weeding and harvesting previously sprayed crops. In the case of contaminating skin with pesticides in field, most farmers wash the skin and change their clothing only after having finished their work – the prolonged exposure increases risk of unwanted effects of these substances, both irritating, allergising and carcinogenic [68].

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The most common clinical form of pesticide-related skin diseases is contact dermatitis, both allergic or irritant. The less common diseases include contact urticaria, erythema multiforme, ashy dermatosis, occupational acne, porphyria cutanea tarda, hair and nail disorders, and skin cancer. These diseases will be described below. Many of the discussed pesticides are no longer in use because of rapid progress on the pesticide market. It cannot be excluded, however, that similar skin diseases may also appear due to some newly introduced pesticides because of structural similarities between the older and newer formulas.

CONTACT DERMATITIS

Pesticide-related contact dermatitis was first described by McCord and Kilkee in 1921 [42]. Pesticide-related contact dermatitis may be both allergic [11, 13, 38, 46, 61, 66] or irritant [37, 38]. Some pesticide components are capable of increasing the skin sensitivity to light which results in phototoxic reactions [26], or may undergo photoactivated chemical reaction which produces a derivative allergising to the skin (photoallergy) [54].

Among all 815 pesticide-related diseases (including poisoning) registered in Japan in 1968–1970, allergic contact dermatitis was diagnosed in 274 cases (33.6%) [41]. Among 122 Taiwanese fruit farmers who were spraying pesticides regularly, contact allergy to pesticides was found in 40%, and clinical symptoms of contact dermatitis – in 30% [22]. In Spain, the prevalence of contact allergy to mercury and carbamates which are compounds of many pesticides was three times as high among farmers compared to the control group [21]. Among 104 Polish farmers treated in a dermatology clinic for eczema, contact allergy to pesticides was found in two persons [45]. In an unselected population of 160 patients in another Polish dermatology clinic, contact allergy to pesticides was found in 46 persons (28.7%) [15]. Among 263 hop growers in eastern Poland, contact allergy to pesticides was found in 66 persons (25.1%) [39].

Some pesticides have shown a very high allergising potential. The organophosphorus insecticide parathion was used for producing experimental contact dermatitis [38]. There were “epidemics” of contact dermatitis among farmers, caused by pesticides with strong allergising properties. In the USA, such outbreaks of contact dermatitis were caused by pesticides Dyrene (2,4-dichloro-6-(o-chloroanilino)-s-triazine anilazine) [59] and Omite-Cr (propagite) [53]. In the district of Magdeburg (Germany), a significant increase of pesticide-related contact dermatits was noted after introduction of the pesticide Nematin which caused 18 of all 22 pesticide allergy cases registered from 1966–1980 [25].

Allergising or irritant properties of the pesticide preparations may be due to active substances themselves or due to additives like emulgators or preservatives. Moreover, skin reactions may be produced by the degradation product of the active substance or additives. This kind of skin reaction to degradation product was described in workers sorting potatoes for planting - the potatoes were previously impregnated with metham sodium (sodium N-methyl dithiocarbamate) which underwent hydrolytic decomposition into allergising methyl isothiocyanate [58].

Screening for, and diagnosis of pesticide-related contact dermatitis is very difficult because of constant changes in the preparations used. Each year, new pesticide preparations are allowed for trade and older products are banned from the market. However, even if a pesticide is no longer on the market, sensitisation to it may last for many years and eventually re-appear due to cross-reaction with a new pesticide structurally related to the primary sensitiser. Moreover, many products in daily use (rubber, medications, housekeeping means) contain pesticides or chemically related substances capable of provoking relapses of the disease.

URTICARIA

Urticaria is characterised by the presence of transient vascular reaction representing localised vascular oedema in the upper dermis, caused by dilatation and increased permeability of the capillaries following exposure to the eliciting agent. The clinical expression of the reaction are wheals. A case of occupational urticaria to the fungicide captan was described in a gardener, who reacted not only to the captan pulver and solution but also to captan-preserved tulip bulbs [18]. An insect repellent diethyltoluamide (used mostly in housekeeping) was also reported to cause contact urticaria [40]. A more recent case report describes a redwood plant nursery worker, who developed contact urticaria and anaphylactoid reaction to common fungicide chlorothalonil [19].

ERYTHEMA MULTIFORME

The clinical manifestation of this entity is a sudden onset of an erythematous eruption with presence of characteristic lesions called iris, bull’s eye or target lesions, which consist of papules with two or more concentric rings of slightly differing colours. Two cases of erythema multiforme were described, in which the skin lesions appeared a few hours after coming in contact with the organophosphorus insecticide methyl parathion [4, 43]. Another case report describes development of target lesions after accidental massive exposure to another organophosphorus insecticide dimethoate in an ex-farmer [55].

ASHY DERMATOSIS

Ashy dermatosis, called also erythema dyschromicum perstans, is a skin disease occurring predominantly in dark-skinned individuals, characterised by the presence of single or multiple ashen macules of variable size and shape. The cause of the disease is by large unknown, however, in 39 banana farm workers the disease was probably caused by exposure to the fungicide chlorothalonil (TCPN) [47].

PARAKERATOSIS VARIEGATA

This is disease of unknown etiology, characterised by ashy dermatosis-like eruption at the onset, which progressively involves the entire skin and turns gradually into poikiloderma (skin atrophy with speckle-like discolorations). Two farmers with parakeratosis variegata were recently described, in whom the disease was attributed to the exposure to pesticides and fertilisers [50].

PORPHYRIA CUTANEA TARDA

This is the most common form of porphyria, characterised by cutaneous photosensitivity that causes scarring bullae, hyperpigmentation, excessive hair growth on the face, and sometimes skin thickening and hair loss. Pesticide-related porphyria cutanea tarda was described in three workers employed at production of herbicides 2,4-dichlorophenol (2,4-T) and 2,4,5-trichlorophenol (2,4,5-T) [7]. An outbreak of the disease from 1955–1959 was caused by eating wheat seeds which had been preserved with the fungicide hexachlorobenzene [56].

CHLORACNE

This is an inflammatory disease of pilosebaceous unit (complex of hair follicles and sebaceous glands) similar to ordinary acne, caused by chlorinated polycyclic aromatic hydrocarbons, among them by pesticides or their contaminants. Some researchers regard chloracne as a form of irritant contact dermatitis [23]. However, there is more evidence against this hypothesis [16]. Acnegenic properties of chlorine compounds are most apparent under regular exposure. Chloracne was found in over 80% of workers involved in production of the insecticide and herbicide pentachlorophenol [14, 31]. A case of chloracne following exposure to pentachlorophenol-impregnated wood has also been reported [17].

Pesticide spraying is also associated with risk of developing chloracne. A case of a young farmer was reported, who developed chloracne due to exposure to neburone in a herbicide [3]. In another case report, a 53-year old man developed chloracne after having worked for many years as a pesticide sprayer [49].

The assessment of acnegenic potential of a given preparation is very difficult because the final product may be contaminated with raw materials, intermediate compounds and decomposition products which are not specified on the label. During heating of chlorophenols in the production of pesticides, formation of unwanted chlorodioxins takes place which possess strong acnegenic properties and may contaminate the final product [20]. TCDD (2,3,4,8-tetrachlorodibenzo-p-dioxin) is a strong acnegenic substance of which is present as an impurity in the herbicide 2,4,5-trichlorophenol (TCP) [27]. Acnegenic activity of the chloraniline pesticides propanil, 3,4-dichloroaniline, and methazole is, in fact, attributed to their contaminants: 3,4,3',4'-tetrachloroazobenzene and 3,4,3',4'-tetrachloroazoxybenzene [34].

Chloracne is relatively uncommon among farmers and should be differentiated from elastosis with comedones, which may occur in outdoor workers [27].

HYPOPIGMENTATION OF THE SKIN

This is abnormally diminished coloration of skin resulting from decreased production of melanin, the natural skin dye, by melanocytes. In a pesticide sprayer, hypopigmentation was observed following contact dermatitis reaction to the carbamate herbicide Carbyne [9].

HAIR LOSS

Pesticide-related hair loss was described in a farmer spraying DDT. The hair loss was classified as diffuse alopecia of mixed type [35].

NAIL DYSTROPHY

This condition is characterised by discoloration, deformities, and eventually loss of the nails. Permanent nail dystrophy was described in pesticide sprayers and other persons exposed to herbicides and insecticides diquat, paraquat, and dinitroorthocresol [2, 8, 24].

SKIN CANCER

Of all surveys on cancer among farmers, eight of 12 studies have shown excess in melanoma incidence, and seven of eight studies have shown excess in other skin cancers, which is primarily attributed to sunlight exposure, but also to pesticides [5]. At their workplace, farmers are exposed to various carcinogens, including pesticides [6]. The International Agency for Research on Cancer (IARC) informs about the increased risk of developing skin and lip cancer among professional pesticide sprayers [28]. Workers employed at production of the herbicide paraquat were also found to be at higher risk of developing skin cancer [37].

Strong carcinogenic properties are attributed to arsenic pesticides [1, 63]. Arsenic is carcinogenic metal with a clear predilection for the skin [36]. Until 1960s, arsenic salts were widely used as insecticides and seed-impregnates, and prior to those times acute poisonings were very common which suggests high exposure in many pesticide sprayers [12]. Arsenic compounds were first introduced and widely used in vineyards, therefore the first reported cases of arsenic-related cancer were vintners [10, 52, 62]. A more recent case report of skin cancer related to long-term arsenic exposure was published in 1987 [30]. In a recent study from Costa Rica, skin cancers (lip cancer, melanoma, non-melanocytic skin and penile cancer) occurred in excess in coffee growing areas with extensive use of paraquat and lead arsenate [64].

The effect of arsenic compounds on skin becomes apparent many years after exposure. First cases of palmoplantar keratosis were reported 10–15 years after introduction of arsenic into agriculture [51]. Carcinogenic effect of arsenic may become disclosed many decades after cessation of exposure, as it is in patients who received arsenic as medication. Before World War II, arsenic was used as a drug administered both internally (syphilis treatment, "tonics" for malaise and neuroses) and externally (Fowler's solution for psoriasis) [32, 33, 57, 60]. In such patients, multiple skin cancer appeared 30–50 years after being treated with these arsenic drugs [44, 48]. This may suggest that farmers who were exposed to arsenic pesticides 40–50 years ago, are still at risk of developing skin cancer related to that exposure. Therefore, every farmer presenting to a doctor with skin cancer should be questioned for contact with arsenic compounds and other potentially carcinogenic pesticides. Typical signs of long-term arsenic exposure are palmoplantar keratosis (excessive thickening of hand palms and foot soles) and chronic skin inflammation of distal body parts (acrodermatitis atrophicans). Later on, morbus Bowen (carcinoma *in situ*), multiple basal cell carcinomas and squamous cell carcinomas with ulceration may appear [10, 29]. Occupational skin cancer should be considered in first range in farmers with multiple or recurrent skin cancer, who were involved in spraying of arsenic insecticides in the past. Such patients must be checked also for other epithelial tumours, especially lung cancer.

According to the IARC, spraying and application of nonarsenical insecticides also entail exposures that are probably carcinogenic to humans (Group 2A) [28].

CONCLUSIONS

Most pesticide-related dermatoses are contact dermatitis, both allergic or irritant.

Rare clinical forms are also possible, including urticaria, erythema multiforme, ashy dermatosis, parakeratosis variegata, porphyria cutanea tarda, chloracne, skin hypopigmentation, nail and hair disorders.

Farmers who were exposed to arsenic pesticides are at risk of occupational skin cancer, mostly morbus Bowen (carcinoma *in situ*), multiple basal cell carcinomas and squamous cell carcinomas.

Also non-arsenic pesticides are potentially carcinogenic.

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