07 2809

Herbert F. Schoof.[1] *The occurrence and distribution of resistance in lice.* Although DDT was first used intensively in the control of body lice (*Pediculus humanus humanus*) as early as 1943, resistance to this compound in body louse populations was not reported until 1950-51 in Korea (*7*). Before then the effective application of DDT against this louse to control and prevent epidemic typhus in war-torn Europe and Asia had marked one of the most astounding achievements in the history of public health work. During the Korean conflict, however, 10 per cent DDT dusts did not control lice on Korean military personnel, and laboratory tests confirmed that the louse populations were no longer susceptible to the compound. Although the lice also proved resistant to methoxychlor, they were susceptible to gamma-HCH, dieldrin, chlordane, and pyrethrins (*6*).

DDT resistance in P. h. humanus

The discovery of DDT-resistant body louse populations in Korea was followed by detection of similar resistant populations in Japan (*2, 9*). Questions were subsequently raised about the efficacy of DDT dust treatments in Syria, Jordan, and Eastern Europe. Tests by Busvine (*4*) of a laboratory strain of lice from Egypt originally obtained in 1950 showed it to be nine times more resistant to DDT than a strain from Great Britain. Further investigation of the situation in Egypt by Hurlbut and coworkers (*8*) demonstrated that only two-thirds of the persons treated with DDT were free of lice. In Brown and Pal's (*3*) excellent summary of arthropod resistance, the data from various workers from 1952 to 1955 show the occurrence of DDT-resistant louse populations in Korea, Japan, and France; susceptible populations in Yugoslavia, Greece, France, and West Germany; and subsusceptible populations in France and Egypt. From the European tests it was readily apparent that the body louse populations varied greatly in their response to DDT, a fact best shown by the work of Nicoli and Sautet (*15*). Of 118 louse samples collected in southeast France, 95 were recorded as susceptible, 18 were subsusceptible, and five were highly resistant. Certain of these samples also showed resistance to HCH. In contrast to the resistance picture in France, Lepes (*10*) found that louse populations susceptible to DDT still prevailed in Yugoslavia despite eight years of that compound's use as a lousicide there.

Between 1953 and 1956 and from 1958 to 1963, the World Health Organization conducted global surveys of the susceptibility of body lice not only to DDT but also to gamma-HCH and pyrethrins. Samples from 27 countries (*18*) and 22 countries (*19*) were tested. The initial survey showed high levels of DDT resistance in Syria, Hong Kong, France, Japan, and South Africa. Moderate resistance levels were found in some countries (Senegal, French Guinea, Sierra Leone, Chile, and Peru), but susceptibility proved the rule in Italy, Norway, Portugal, Yugoslavia, India, Pakistan, and Afghanistan.

In the second survey, samples from Mozambique, Madagascar, Nigeria, and Sierra Leone showed susceptibility to DDT. Lice from Tanzania, Uganda (two locations), and South Africa were slightly resistant, but one sample from Uganda and one from the Sudan showed high resistance. In Asia, resistant populations were detected in many parts of Afghanistan, but in India and Pakistan the lice remained susceptible. In the eastern Mediterranean area, collections from 16 sites in Egypt revealed high levels of DDT resistance. Similar resistance was apparent in one sample each from Libya and the Gaza strip. One sample from Jordan, where gamma-HCH had replaced DDT, showed the lice to be susceptible to the latter. In Europe, samples from eight localities in Yugoslavia were susceptible, but in France three of four

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samples showed some resistance. In the Americas, samples from Chile revealed one of five samples to have a high level of resistance.

HCH resistance in P. h. humanus

Because gamma-HCH proved highly effective against DDT-resistant body lice, it became a common substitute for DDT. In many areas, however, body lice developed resistance to gamma-HCH—even in localities where the compound had been employed for other types of vector control. Widespread resistance to gamma-HCH was detected in all the samples from Japan (*18*), and resistant samples also were found in Norway, Yugoslavia, South Africa, and Hong Kong. In their 22-country survey, Wright and Pal (*19*) reported gamma-HCH resistance in collections from one locality each in Sudan and Chile. An increase in tolerance to gamma-HCH was noted in Egypt, but in the remaining 19 countries the species proved susceptible to the compound.

Gamma-HCH resistance in body lice also was reported by McLintock and coworkers (*13*) in Iran and by Turner (*17*) in Cairo, Egypt. Although certain gamma-HCH-resistant body louse populations arose from the use of the compound as a lousicide, in other instances the resistance apparently developed from its use to control bedbugs and mosquitoes. As with DDT, there were also some areas (Afghanistan and the Gaza strip) where application of HCH as a lousicide did not cause the development of resistant populations. Barnes and coworkers (*1*) reported that 1 per cent lindane dust failed to control Korean lice. In laboratory tests the lice were shown to be resistant to DDT but not to malathion or lindane.

Malathion resistance in P. h. humanus

Barnes and coworkers (*1*) and Shawarby and colleagues (*16*) found that 1 per cent malathion dust would control DDT-resistant body lice. The LC_{90} for this compound ranged between 0.025 and 0.07 per cent. Malathion has since become the insecticide of choice, particularly where louse populations show evidence of resistance to both DDT and gamma-HCH. To determine the potential of body lice for developing resistance to malathion, Cole and coworkers (*5*) selected three strains of lice from three different regions of the world with malathion for 22 to 44 generations. No resistance appeared, but the investigators stated that such negative data did not prove that resistance could not develop in field populations. The wisdom of this statement was confirmed by Miller and coworkers (*14*) in 1969 studies showing that during a typhus outbreak in Burundi, body lice taken from inhabitants had a marked resistance to malathion test papers. The LC_{50}'s for these lice were 6.4 per cent in two areas and > 12.8 per cent in a third area as compared to 0.1 per cent for susceptible laboratory strains. Data from the United Arab Republic also suggest that malathion resistance is developing there.[1]

Resistance in *Pediculus humanus capitis* and *Pthirus pubis*

P. h. capitis and *P. pubis* are the two other species of lice commonly found on man. Although the infestations of these two species are controlled with the same chemicals used in body louse control, resistance has generally not been a critical factor in suppressing infestations. There are no reports of resistance in crab lice and the general absence of resistance in head lice has been puzzling, particularly since specimens of this subspecies taken from individuals infested with resistant body lice have proved susceptible to DDT. In 1971, however, Maunder

[1] Information Circular on Insecticide Resistance, Insect Behaviour, and Vector Genetics, WHO, VBC/IRG 70.12.

(*12*) described resistance to DDT and gamma-HCH in head lice in England. Reports from health workers in East London indicated control failures in attempting to free children of head louse infestations by use of standard commercial DDT or HCH preparations. Tests were then conducted in which 1 per cent DDT or 1 per cent HCH was applied to six individuals with moderately heavy infestations. The results showed no appreciable reduction in the number of lice. Laboratory tests confirmed the resistance to these two compounds but revealed the lice to be readily susceptible to malathion, propoxur, and carbaryl. Treatment of 120 infested children with malathion and carbaryl liquid preparations showed that individuals treated with 1 per cent carbaryl or 0.25 per cent malathion had no live lice 24 hours later. Maunder (*11*) later revealed that more than 20 areas in Britain had witnessed failures in the use of DDT and HCH against head louse infestations. In a large-scale trial in which 3,000 infested persons were treated with 0.5 per cent malathion lotion, all of the individuals were free of lice the next day.

Conclusion

The resistance pattern in lice is generally like that encountered with the use of insecticides against other arthropod vectors: the level of resistance varies with locality and with the amount of exposure the insect population has had to the insecticide. As has been true with mosquitoes, however, continued use of the same chemical in some countries (e.g., DDT in Yugoslavia) fails to induce resistance, presumably because of the genetic makeup of the louse population. In contrast, resistance to one or more compounds in other areas is readily invoked. The sequence of replacing DDT with cyclodiene and then organophosphorus compounds to overcome resistance parallels that in trying to control houseflies and mosquitoes. A similar parallel also exists that resistance to a chemical may develop in an insect population even though that chemical has not been used against the target species but only to control other vectors or possibly agricultural pests. Thus, it is obvious that the development or lack of development of resistance to pesticides in a louse population can never be a foregone conclusion. Our chief defenses against resistant louse populations are: (1) alertness for changes in the susceptibility levels of the population, (2) continued search for substitute lousicides, and (3) improved operational procedures for using the available compounds.

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07 2807

Albert S. Perry.[1] *Biochemistry of DDT resistance in the human body louse pediculus humanus humanus.* The failure of DDT to control the human body louse was first observed in Korea in 1950-51. Laboratory and field studies conducted by several investigators (*3, 6, 10, 11, 12, 13, 26*) demonstrated beyond doubt the presence of physiologic resistance to DDT in louse strains from different geographic areas. Comprehensive reviews on this subject have been published by Wright and Brown (*24*) and more recently by Brown and Pal (*5*).

Resistance to DDT in insects is in large measure due to the insect's ability to detoxify the compound by dehydrochlorination, via hydroxylation, or by some other mechanism.

The isolation and characterization of the enzyme DDT-dehydrochlorinase (*22, 23*) that catalyzes the degradation of DDT to 2,2-bis(*p*-chlorophenyl)-1,1-dichloroethylene (DDE) and purification of this enzyme (*9, 14, 16*) gave credence to the hypothesis that dehydrochlorination is an important mechanism of DDT resistance in the housefly and other insects, although notable exceptions exist (*4, 19, 20*).

Another route of DDT metabolism is via hydroxylation. In this pathway DDT is converted to 4,4-dichloro-α-(trichloromethyl) benzhydrol (dicofol). The enzyme responsible for this biotransformation was first isolated from the microsomal fractions of homogenates of *Blattella germanica, Musca domestica,* and *Triatoma infestans* (*1, 2*). This so-called "mixed-function oxidase" system requires NADPH and molecular O_2 for activation. In recent years numerous investigations have shown the involvement of this enzyme system in catalyzing the oxidation of many organophosphorus and carbamate insecticides, as well as several organochlorine compounds.

Following the successful colonization of the original DDT-resistant Korean strain of body lice at the U.S. Department of Agriculture laboratories in Orlando, Florida, we became interested in determining the mechanism of DDT resistance in this strain. Collaborative investigations were therefore undertaken between the U.S. Public Health Service and USDA laboratories. The highlights of these investigations (*17*) are described below.

DDT was found to be absorbed very slowly from acetone or benzene solutions when applied topically to either susceptible or DDT-resistant lice, though the resistant strain could tolerate larger quantities of applied DDT without suffering any harmful effects.

Feeding lice through freshly dissected chick skins on citrated human blood containing different concentrations of radioactive DDT showed that the resistant strain could tolerate 100 p.p.m. of DDT in the blood with negligible mortality, whereas 10 to 25

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