SUMMARIES OF SESSION II

Bionomics of Lice

Dr. Busvine: In reviewing our knowledge of louse biology, I was struck that an enormous amount of work had been done during the two world wars. During World War I a great deal was done by Nuttall, Keilin, and Bacot in England and by Hase and Hilda Sikora in Germany. Buxton and his associates, of whom I was privileged to be one, made further advances during and after World War II. The great contribution in the United States was Culpepper's technical advance in adapting louse colonies to feeding on rabbits. One could almost say that the work done at this time was enough to give us a good picture of individual louse biology, with very few outstanding questions. During the 1960's two American papers dealing with the biology of louse colonies reared on rabbits appeared. These were useful in confirming the general similarity of such colonies to those reared on man, but they added little more than technically useful information. More recently, Ludwig in Germany has been studying the ability of different species to feed on the blood of mammals other than their normal hosts. The inconsistent nature of the suitable animals is rather surprising and cannot be explained by their systematic relations.

Dr. Kryński has shown in Poland that louse populations exhibit a very wide range in susceptibility to harmful microorganisms, including *Rickettsia prowazeki, Staphylococcus aureus,* and *Yersinia* species. Lice are also affected by the various antibiotics. Both the regenerating powers of lice and the harm they cause vary in relation to environmental conditions, particularly temperature. The severity of inoculation affects these reactions at different temperatures. Such studies may be useful if we ever find it helpful to reexamine the possibility of louse control through microorganisms pathogenic to lice.

We are still ignorant of any population checks on the proliferation of lice, whether from microorganisms or other causes. It has generally been believed that delousing has been responsible; by that I do not mean insecticiding or even washing, but such a simple thing as picking off lice and killing them with the fingernails or matches.

In the discussions that followed the opening papers, several speakers questioned the observations I quoted from early researchers of the distribution of infestations, in which heavier and heavier infestations were quite rare. It is difficult to decide this point because the people who raised these objections were not able to supply quantitative data. The frequency of mentions of high infestation levels in Burundi and elsewhere suggests that in some circumstances this natural check may not operate fully. It is possible that under conditions of sustained poverty and malnutrition a kind of listlessness supervenes, rather in the way sick animals cease their grooming and become heavily infested with ectoparasites. This is another subject that deserves further study, because presumably only very heavy infestations of lice lead to epidemics of disease.

Conventional Louse Control Methods

Dr. Weidhaas: The panel included presentations and discussion on louse powders, impregnants, fumigants, synergists, repellents, ovicides, systemic toxicants, and physical agents for control.

We did not develop much discussion about systemic toxicants. The data that Mr. Cole presented, along with published data, indicate that these materials can be effective in killing lice. One point that was not really brought out is that the side effects of these materials have caused some people to question their usefulness when their use cannot be controlled.

Drs. Traub and Eldridge noted that we have very little information on the use of repellents against body lice. Dr. Smith very vividly showed that, at least in a test with M-1960, complete protection against body lice is not possible. The question of just how effective repellents would be in giving less than complete protection remains unsolved and requires further research.

Much information was presented on available fumigants. The tests Dr. Grothaus discussed showed that DDVP is not very promising for use in field conditions. Dr. Boese's results are open to interpretation, based on the acceptability of 40 to 80 per cent effectiveness. My general impression is that there is some question as to the use of DDVP for fumigation, except in special cases in which penetration of the insecticide through considerable amounts of clothing is not required.

It appears that the available conventional technology (effective compounds and methods of treatment) is fairly good. Potential future problems related to insect resistance to available insecticides and the development of additional chemical control agents were noted in the discussion. Dr. Gaon pointed out that several compounds are available should resistance crop up. Mr. Cole and Dr. Grothaus summarized the current status of available louse powders and their status in the various developmental schemes. Dr. Gratz also summarized current World Health Oganization recommendations about available compounds.

I think we can conclude that our conventional approaches are relatively good. I would group the problems brought out in the discussions into two general categories. The first is our ability to apply the available technology under varying conditions in a worldwide situation, and the second is concern about future research and development in the light of current problems in the development and use of insecticides or chemical control agents.

The latter area of concern was stressed by several of Dr. Traub's questions. The time lag in the development of new compounds was discussed. In years past, for example, a material went through all the necessary tests in as little as a year when the need for it was great, but when the need has not been so pressing it has taken five to 10 years to test a compound. Dr. Steinberg said that from the toxicologic viewpoint at least three years would be needed for testing. Dr. Smith pointed out that many compounds have become available through their development for agricultural use, and that if the agricultural chemical industry slows its developmental research, we in the public health area will face problems in the future.

In summary, I would recommend that we should recognize the need for continuing research to improve our conventional approaches to louse control and alternate types of materials that could be used within these conventional methods.

Insecticide Resistance

Dr. Busvine: In my opening remarks, I discussed three general resistance topics that seemed relevant to the louse problem. I would like to bring up two of them because they seemed to arouse general interest. In the detection and measurement of resistance,

the simple method that the World Health Organization standardized in 1953 has provided a valuable picture of the world situation. For certain other purposes, such as laboratory studies, different methods have been found more convenient; for example, the beaker test developed in the United States and the impregnated paper method that my colleagues and I use. The latter has recently been adapted for head louse resistance tests, which demand considerable care. When such lice are removed from infested people they are very often damaged and not able to sustain the further exposure of walking about on treated or even untreated paper for 24 hours. They have to be maintained on the human body before they can undergo the test.

Genetic studies of louse resistance, as well as investigations of selection by insecticides in the laboratory, do not indicate that organochlorine insecticide resistance is potentially easy to select in lice. They show that once developed it would persist for a long time in the absence of selection.

Basic principles would suggest that resistant louse strains would tend to arise in areas where extensive use of insecticide would have selected out the resistant genotypes. This might also occur in some areas where excessive agricultural insecticiding has occurred.

Dr. Schoof discussed the state of louse resistance throughout the world. While the emergence of resistant body louse strains has corresponded in many cases to extensive use of insecticides, this has not always been true because there are examples of irregular and unexplained distribution. One anomaly was the persistence of normal susceptibility in head lice, cases of which have recently been confirmed in Britain.

Dr. Sitar of Yugoslavia gave examples of laboratory selection for body louse strains. In the case of malathion there had been very little change in resistance over quite a long period of generations, though we now know that this negative evidence cannot be relied on as we have found all too unfortunately in Burundi. Dr. Sitar's results that show the potential development of resistance to the carbamate carbaryl are an ominous warning that resistance almost certainly will develop if this insecticide is used in the field.

Dr. Perry of the United States gave a very clear picture of his work on the biochemistry of DDT resistance in lice, a subject that no other worker seems to have studied. His results demonstrated the complex nature of this resistance, with several detoxification pathways, and indicated that it would be quite difficult to overcome it through the use of a single synergist.

After some general comments on these opening papers, Dr. Fabrikant described the interesting case of resistance to DDT, and more recently to malathion, in Burundi. This seems to have been a result of the intense and universal lousiness, together with the regular contamination of the people in some of the coffee-growing districts with a variety of insecticides. Although this resistance complicated and delayed the suppression of typhus, it was only one of the factors involved. Furthermore, the Belgians, using draconian methods, stamped out a severe epidemic quite quickly in 1934 without modern insecticides.

You will remember that I emphasized the importance of insecticide formulation in addition to the actual nature of the chemical compounds used. It seemed to me likely that a powder preparation would be best for dealing with widespread lousiness that threatened epidemic disease, because it would be easily and speedly applied and has moderate persistence.

Impregnated garments might be suitable for sanitary personnel or soldiers in a typhus area.

For the disinfestation of small numbers of body louse-infested people in clean, civilized

environments, heat treatment or, perhaps even better, fumigation with a safe fumigant would be best. For head lice, lotions are preferable and should be imperceptible after use. Their cosmetic acceptability is most important if the cooperation of the lousy and their relatives is to be secured. Lotions or ointments would also be suitable for crab lice.

Some doubts were voiced in the subsequent discussion about the absolute preference for powders in reducing general lousiness. It was pointed out that it is something of an indignity to have insecticide puffed up one's sleeves and down one's neck with dusting guns. It was suggested that where facilities are available that could be adapted to impregnation, such as laundries, this method might be used. Dr. Makara of Hungary advocated impregnation by spraying undergarments.

It must be remembered, however, that neither of these methods is as rapid as powdering since they require that the infested people undress. Laundry impregnation would presuppose a considerable amount of organization and the possession of several sets of clothing by the infested people. It might be useful to discriminate between the sort of fire-brigade action necessary during an epidemic in which large numbers of people must be treated, and more lasting attempts to reduce lousiness in endemic areas. Powders would be best for the former; perhaps impregnation methods for the latter.

Experimental Louse Control Methods

Dr. Smith: The panel divided their discussion more or less naturally between the use of insect hormones and the use of genetic and biologic control methods.

On the subject of insect hormones and their derivatives or antagonists, Dr. Vinson reported the results of tests with synthetic mixtures that mimic the activity of juvenile hormone and with Stauffer JH-1. The latter was several hundredfold more active against body lice than Williams' original mixture. When applied topically to the female, it blocked embryogenesis in the eggs the female laid for one to three days. Nymphs placed on pads impregnated with JH-1 either died during the next molt or underwent a lethal supernumerary molt. Dr. Vinson recommended that JH-1 or another hormonomimetic compound receive advanced biologic and toxicologic evaluation leading to an eventual field trial.

Dr. Robbins pointed out that juvenile hormone-like compounds have the advantages of being highly active and relatively simple and inexpensive, and that they readily penetrate the cuticle. A number of highly potent ecdysteroids have also been developed that disrupt insect growth, development, and reproduction. These molting hormone analogs are complex molecules that are not easy to manufacture and are generally not active by contact.

An alternative is the development of simple compounds that interfere with the biosynthesis and metabolism of ecdysone. A number of structurally simple azasteroids have been developed that are several thousandfold more active than the original compounds as inhibitors of molting or metamorphosis. Dr. Robbins discussed the structure of several of these compounds.

Mr. Cole reviewed a program for the evaluation of compounds with hormone-like activity against body lice for toxicity and the induction of sterility. The results with 12 compounds from commercial sources or that Dr. Robbins' group had synthesized were presented. They induced sterility ranging from 30 to 100 per cent.

In the following discussion Dr. Fox inquired about the compounds' stability or residual effectiveness. Dr. Vinson had not tested the durability of treatments with JH-1, but Dr. Robbins mentioned that several JH compounds were not stable in the field. Dr.

Smith noted recent reports that although JH-1 has a short residual life as a mosquito larvicide, the length of its effectiveness could be greatly extended by incorporating it in synthetic plastic materials, a method that might not be applicable to its use against lice, however.

Drs. Perry, Robbins, and Schoof discussed the breakdown of some juvenile hormone compounds such as Zoecon 515 and agreed that although an emulsifiable concentrate broke down readily, a microencapsulated material worked very well.

The possible prices of hormonal mimics were also discussed. It was indicated that the prices might be comparable to those of the more expensive insecticides. Dr. Smith asked Dr. Vinson to comment on the type of treatment, or treatment schedule, that might be required in a field test of JH-1, and the amount of time required by the treatment to eliminate a louse infestation on a treated individual. Dr. Vinson pointed out that he had not recommended an immediate field test but rather more of the evaluation needed before a field test. He assumed that application would be by spraying or dusting clothing.

Dr. Busvine suggested further comparative evaluation of juvenile hormone mimics, molting hormone mimics, and hormone inhibitors before field trials are contemplated. Dr. Gratz mentioned some of the problems that occur in using the compounds, including the need for toxicologic information, and inquired about the availability of information about their toxicity. Dr. Robbins said that the acute oral toxicity data about some juvenile hormone-type compounds seem quite good, and that some of the potent molting hormone inhibitors had LD_{50}'s of 4g/kg or more, and that some Zoecon compounds had LD_{50}'s of 10 g/kg. Dr. Vinson mentioned that he could not be sure how much the slower action of JH-1, compared to DDT, might contribute to maintaining a typhus epidemic since even clothing treated with DDT retained infected dead lice and louse feces. Dr. Wisseman noted that some louse infestations persist among populations treated with conventional insecticides.

The panel felt that the entire field of juvenile hormone mimetics, molting hormones and their mimics, and molting hormone inhibitors merited vigorous exploration and exploitation.

Drs. Eldridge and Weidhaas discussed the use of sterility and other genetic techniques to control insects other than lice, and noted that several research groups exploiting these materials had not included lice among the insects likely to be susceptible to genetic control. The obvious difficulty is the requirement that lice be released on the bodies or clothing of infested people.

Discussion brought out a few imaginative and theoretically possible genetic manipulations that might be applied to lice, but it was obvious that genetic techniques were considered of little potential value against lice.

Drs. Weidhaas and Jenkins discussed the possibility of biologic control of lice. Although Dr. Jenkins presented a very comprehensive list of reported lice pathogens, no available biologic agents seem to promise louse control. The agents known to be pathogenic to lice are also pathogenic to humans. Possible lines of research in this area include the evaluation of such widely used pathogens as *Bacillus thuringiensis* against lice or the rearing of strains of pathogens in a way to select strains that would be pathogenic to lice but not to man. Dr. Reeves pointed out that the search for pathogens has generally been connected with studies of human diseases so that the louse pathogens studied have been natural human pathogens, and that useful pathogens not infective to man might be found by searching for dead or dying lice of strains not infected with human diseases.