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THE PROBLEM OF POSSIBLE SYSTEMIC EFFECTS FROM CERTAIN CHLORINATED HYDROCARBONS*

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THE use of chlorinated naphthalenes and compounds of allied pharmacological possibilities is extremely wide, and with the steady growth of the use of electricity is certain to expand much farther. For years it has been known that many of these compounds cause a troublesome acne, and there is a large literature upon this phase of the subject. Our investigations have not been concerned with chloracne but with the possibility of systemic effects following ingestion or inhalation of such products. In the spring of 1936, the Halowax Corporation, a division of the Bakelite Corporation, called our attention to three fatal cases of jaundice in workmen using chlorinated naphthalenes and chlorinated diphenyl, and requested that the subject be investigated as rapidly and thoroughly as possible.† In brief these cases were as follows:

Patient 1. Male, age 21. The previous medical history of this man was in no way significant except for the fact that he had an attack of jaundice about 6 weeks prior to his fatal illness. Late in December, 1936, he became badly constipated and had much abdominal pain and distention. When admitted to the hospital he was slightly jaundiced and was evidently very ill. He was somewhat anemic and his skin, particularly upon the arms, face, chest and back, showed many pustules. He died after a brief period in the hospital, and at autopsy was found to

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† The Halowax Company makes many products besides chlorinated naphthalenes, and it has come to our knowledge that all of these products are indiscriminately called "halowaxes" by purchasers and users, and are lumped together as possible causers of acne and even of systemic disease. Since "halowax" is merely a trade designation care should be taken to describe compounds by their chemical names and thus avoid condemnations which are both troublesome and misleading.

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have a cirrhosis of the liver with acute yellow atrophy superimposed upon it. This man had been exposed to low concentrations of vapors arising from a mixture of tetra and pentachlornaphthalenes, together with approximately 10 per cent of a refined chlorinated diphenyl. While both he and others engaged in the same work had chloracne, there were no other disturbances of health in fellow workmen, nor was there any precipitating cause for the acute yellow atrophy such as treatment with arsphenamine or exposure to dangerous concentrations of carbon tetrachloride.

Patient 2. This was a young man who died in February, 1936, after an acute illness characterized by jaundice. He had been exposed to fumes arising from a mixture of penta and hexachlornaphthalenes. There is no record of chloracne. The patient worked with a large number of other people of whom but one (Patient 3), a close friend, had significant illness.

Patient 3. Another young man employed with Patient 2. He became jaundiced in March, 1936, and died after an illness of 2 weeks. A careful autopsy resulted in a diagnosis of acute yellow atrophy of the liver. Here again no history could be obtained as to a precipitating cause, and there was no record of preceding attacks of jaundice.

In addition to these three very recent fatalities, we have learned of four other possible cases, none of them fatal. All of these have had jaundice and the entire group consists of isolated individuals who have been picked out of large groups having the same exposure. In but one instance, Patient 1, is there record of antecedent disturbance of health, and the general health of fellow workers has been good.

Such cases have not been reported in the medical literature and only occasionally can one find reference to systemic effects of any sort. For example, Courtois-Suffit (1934) reports on work done by Touraine and his associates (1934) who examined 60 workers who had been exposed to trichlornaphthalene. Of these 13 were found to have mild digestive complaints, anorexia, nausea and vertigo, but Courtois-Suffit remarks finally, "Absorption is certainly possible and we have for proof of it some of the digestive and general complaints which have been due to it. But they appear to be of little consequence considering the mildness of the digestive troubles and the absence of respiratory phenomena."

In Touraine's cases the exposure was to a trichlornaphthalene, whereas the American cases of acute yellow atrophy were exposed to compounds of higher chlorination. Our own experiments indicate that trichlornaphthalenes require enormous dosage, far beyond anything encountered in industry, in order to produce liver damage. Teleky (1927) reported a number of cases of chloracne in persons exposed to chlorinated naphthalenes with a chlorine content ranging from 14 to 53 per cent. He found that the lower the chlorine content the less the acne. Mittelstädt (1935) examined a number of cases of chloracne due to trichlornaphthalene and reported a number of vague general complaints but nothing in the nature of serious disease. Regarding his animal experimentation, Lehmann (1919) reported that animals fed chlorinated naphthalenes refused to eat after a time and that, whether poisoned by inhalation or by feeding, at death showed "peculiar" lesions in the liver. Flinn and Jarvik (1936) gave subcutaneous injections of enormous doses of chlorinated naphthalenes dissolved in paraffin oil to rabbits. The compounds used were as follows:

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Summary of gross feeding experiments.—Of the various materials fed rats in large doses trichlornaphthalene plus traces of tetrachlornaphthalene was quite innocuous. Tetra and pentachlornaphthalene showed definite liver damage. Penta and hexachlornaphthalenes caused a similar grade of injury. The addition of chlorinated diphenyl to penta and hexachlornaphthalenes increased the toxicity. Chlorinated diphenyl alone produced liver lesions but in the dosage used was less effective than when mixed with highly chlorinated naphthalenes. In no case did the compounds used produce acute yellow atrophy but the lesions observed indicate this might be possible if one found a dosage which could act for the proper period of time.

Feeding Precise Doses by Stomach Tube

The compounds employed were suspended in gum acacia. In figuring the dosage the total amount a man of 50 kg. would inhale in an 8-hour day assuming an air concentration of 20 mgm. per cu. m. was first calculated and reduced to milligrams per kilogram. The rats and rabbits received this dose each day. The compounds used were those employed in the gross feeding experiments and the results were essentially similar though the lesions were less severe.

Subcutaneous Injections

The same gum acacia suspensions were injected subcutaneously into rats and rabbits, the dosage being calculated on the basis of 4 mgm. per cu. m. of air. Again similar results were obtained. In all such experiments there must of necessity be differences in the degree of effect but invariably the liver was the sole organ affected and the lesions were those already described many times.

Discussion

These experiments leave no doubt as to the possibility of systemic effects from the chlorinated naphthalenes and chlorinated diphenyl. As in the case of the effects upon the skin, the degree of chlorination seems to determine the systemic toxicity, and it is a striking thing that when trichlornaphthalene is reached systemic effects are never marked and are produced with the greatest difficulty. It is most remarkable, too, that all the compounds tested attack the liver and the liver alone. During the past few months we have determined the organically combined chloride in the livers of animals very severely poisoned by penta and hexachlornaphthalenes but have found no increase over normal figures, though the livers, as determined histologically, were very severely affected. At the present time we are conducting inhalation experiments on a chlorinated diphenyl containing 55 per cent of chlorine instead of 64 per cent as in the case of the experiments reported in this paper and on a compound with a chlorine content between tri and tetrachlornaphthalene. We are also determining the degree to which the diet may increase or decrease toxicity, this being suggested by similar work upon carbon tetrachloride.

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and on many field determinations of different compounds in the air of workrooms, it appears safe and it is certainly easily attained, to ventilate so that the air breathed does not contain more than 0.5 mgm. per cu. m. of any of these compounds above trichlornaphthalene. In the case of the latter compound concentrations of 10.0 mgm. are permissible. We know from many examinations in many different plants that such concentrations have been greatly exceeded during the past 20 years, and we are conscious of the fact that our rat exposures have been inexorably constant whereas human exposure is never so ordered. Time and careful observation may change these opinions as to standards, but today we are convinced they are safe. Impregnating tanks and other arrangements utilizing the chlorinated hydrocarbons are easy to hood and to safeguard. Compared with benzene, lead tetraethyl and many other compounds, these substances are very little toxic and operations employing them can easily be safeguarded. It may be argued that where possible trichlornaphthalene should be used, but this compound will cause acne and if employed very carelessly might do more. Furthermore, higher chlorination is often essential for highly practical reasons. The solution consists in thoroughly adequate ventilation plus good housekeeping around all wax containers.

A final word of caution bears upon the use of carbon tetrachloride as a wax solvent. Obviously this compound adds readily to the toxicity of the highly chlorinated waxes. If carbon tetrachloride is used, ventilation should be excellent, but in our opinion it would be better to dispense with carbon tetrachloride and depend on other solvents, especially upon those containing no chlorine.

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Discussion

Dr. Cecil K. Drinker: We have had quite a long morning, but since Dr. von Oettingen has to leave, I am going to ask him to say a word.

Dr. W. F. von Oettingen (Director, Haskell Laboratory of Industrial Toxicology, Wilmington, Delaware): I wish to congratulate Dr. Drinker and his group on the very interesting and excellent work on the subject. I also wish to congratulate the Halowax Corporation on the fact that they didn't spare any effort to elucidate the problem so that the dangers which apparently are connected with the use of this material can be controlled.

I personally believe that there is no toxic material which cannot be used safely if it is handled properly. In order to handle such materials properly during the different operations it is absolutely essential to be familiar with the toxicity and especially with the mechanism of the action. Since there is no animal which corresponds in all its physiological characteristics to the human being it is important that such compounds be studied with different species of animals so that one can get a cross-section of the potential dangers.

In addition, this fact illustrates the importance of the pre-employment and periodical examination of workers in such work. As was pointed out by Dr. Drinker, there are individuals who are apparently more susceptible to certain toxic agents than others. On the other hand, we have to try to detect the very first signs of incipient poisoning in order to prevent more serious damage. In the present instance it is very difficult to find these very first symptoms because there are no adequate methods, but I trust that in time the scientific profession will supply the medical profession with adequate methods which will allow the physician to determine incipient damage of the organ before serious clinical symptoms become manifest.

Thank you.

Afternoon Session

Dr. Cecil K. Drinker: In this discussion I will call on one or two individuals and I shall expect others to speak as their notes incline them to. First of all I shall ask Dr. Sayers if he will open the discussion for us.

Dr. R. R. Sayers (Chief, Division of Industrial Hygiene, National Institute of Health, U. S. Public Health Service, Washington, D. C.): Dr. Drinker, Ladies and Gentlemen: It gave me a great deal of pleasure to have the opportunity to listen to the excellent and interesting discussion and presentations made this morning. Dr. Drinker, and I might add, the members of the Halowax Corporation, have discussed this matter with us, as well as the manufacturers of the diphenyls.

We have been doing some work but not nearly as extensive as that carried on here. The work that we have been doing seems to confirm the work that Dr. Drinker has carried on. I think there are certain parts of it that we can very well keep in mind.

We are dealing with toxic substances, but we are dealing with toxic substances each and every day in industry—harmful substances, hazardous substances. That these can be controlled is well known, no matter what they are, and that we can use them and use them in a safe manner. Dr. Drinker has called your attention to the fact that this apparently has been done and can be done in any of the plants where halowax is used. I have information from one or two of the other men who are in the audience that in plants where damage has been done—skin damage and apparently liver damage to some of the workers—the manufacturers have since corrected the conditions and apparently have adequate engineering control supplemented with adequate medical control.

After all, the proof of the pudding is in the eating. If the man does not get the disease your engineering control is successful. If he does get the disease, no matter what you have done in the way of engineering, you haven't been successful. We must go hand in hand. Neither profession alone can be successful. We have got to work together whether we like it or not. I happen to like it.

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smart enough to use every one of them successfully. If this material is particularly adapted for a certain purpose we should use it. Another material that was used previous to this for insulation purposes, which was flammable, caused a disaster in which approximately 167 men lost their lives. I say approximately 167 because they were never just sure whether it was 167 or 168. It might have been one or two more but they were quite sure that 167 lost their lives. It happened when they had insulated a cable with this material. They had an armored electric cable. It was covered with lead armor on the outside. It was 1200 feet long and was being lowered into a mine shaft approximately 3000 feet deep. It was lashed to a steel rope. It slipped and fell to the bottom of the shaft. When the foreman was inspecting it he set it on fire with his carbide cap-lamp. The carbon monoxide from the fire killed those men that were in that mine. Many of course escaped.

Here we have one hazard, a fire hazard. Now we have another one, a health hazard due to the toxic materials. We have to evaluate them. Certain of these materials, I am informed, are also flammable. I am not just sure how flammable they are but flammability probably decreases as your chlorination increases. But your toxicity also increases as your chlorination increases, according to Dr. Drinker, and I think that checks with other findings. We have these hazards to balance but we can control them. I feel quite confident that we can.

Perhaps we can find other substances that are better even than this material. At the present time I am advised that we have no better. I am advised that in ships, such as submarines, it is quite important to have a non-flammable substance for the insulation of their electrical wire.

DR. CECIL K. DRINKER: Dr. Gray, would you care to say a word?

DR. ALBERT S. GRAY (Director, Bureau of Occupational Diseases, State of Connecticut Department of Health, Hartford, Conn.): Dr. Drinker, I don't think there is anything that I can say except that we used this material in Connecticut and we had a number of so-called cases. All I can say is a confession of ignorance on our part at that time and I was very glad to see that your digging into the literature as thoroughly as you have hasn't elicited any further information than we were able to get, basically. About all we could find was about the two cats that our friend, Lehmann, experimented with. We got in touch with him and he confessed that the amount that he had given the cats and his method of determining it were probably subject to very serious scientific criticism, and we agreed with him on that point.

We felt, and I am very glad that it is what you feel as a result of your experiments, that if we put in an efficient ventilation system sufficient to prevent the dermatitis, we probably wouldn't have liver damage. That is what we did entirely empirically.

I think that is about all I have to say. I have been delighted to be here and to have as many members of my staff here as I could jack out of the office. We have been delighted to listen to the discussion.

DR. CECIL K. DRINKER: May we now make the discussion general and those who have questions please volunteer.

MR. MANFRED BOWDITCH (Director, Division of Occupational Hygiene, Massachusetts Department of Labor and Industries, Boston, Mass.): I would like to second very strongly what Dr. Sayers has said with regard to the approach to this problem in proper control rather than by prohibition, which seems to me wholly unnecessary not only in this case but in the case of other toxic substances with which we have to deal. The problem of proper ventilation seems to me relatively simple from what I have heard of the situation thus far. The problem of maintaining that ventilation properly does not seem to me quite so simple. I think it is going to be quite necessary that there should be a very adequate inspection of the plants using the materials and I can assure you that that will be the case here in Massachusetts.

When this trouble first broke in this state a little over a year ago we issued a quite strongly worded warning letter to all plants using these substances and it has all along

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been my plan to follow that up with a further letter bringing the situation as we now know it, as a result of Dr. Drinker's work, to the attention of users in this state. In that letter we shall unquestionably advocate the concentrations that Dr. Drinker has suggested this morning.

One point that I think is worth commenting on in that connection is the question of identification of the substances. It is extremely important from the state administrative point of view that employers using these substances should know what they are using. They are identified at present only by numbers. If we list those numbers in a warning letter which we send out there are likely to be changes in those numbers. The Halowax Corporation is a progressive concern and it is going to be putting out bigger and better halowaxes all the time. The company's coöperation in this present investigation has been such that I feel assured that they will take the proper steps to see that we in the state offices and also the users of the products will know what we are using.

I wonder whether Mr. Brown would care to say anything about that.

MR. SANDFORD BROWN (President, Halowax Corporation, New York, N. Y.): There are some aspects of this situation on which I think I can enlighten the medical and state and civic authorities, with respect to the commercial and practical aspects. If you go into the research laboratories of any large chemical manufacturing company today you will find anything from one to a thousand different new chemical products which have not yet been put on the market. Some of those may or may not be toxic. The problem so far as the chemical manufacturer is concerned is a question of timing. You have heard this excellent presentation given this morning by the Drinker brothers as to the work that they have done here. Should you take a product of which you have developed, say, 5 or 10 gm. and spend $50,000 on research to determine whether or not it is toxic or should you wait until you have determined whether you have a market for it?

If you are producing only one hundred substances a year you can see that that would run into boxcar numbers in the way of dollars and cents before you ever sold any. That is the problem we have had in this case. It has been on the market for 25 years. Until within the past 4 or 5 years there has never been any intimation that it would cause any systemic effects. Thousands and thousands of workmen have dealt with millions and millions of pounds of certain of these materials, particularly the trichlornaphthalenes. Then we come to the higher stages, combined with chlorinated diphenyl and other products, and suddenly this problem is presented to us.

We had asked various authorities interested in public health, going back over a period of 15 to 20 years, to investigate it but there wasn't much enthusiasm for it. Mr. Bowditch suggested that we take it up with the Drinker brothers at this institution, which we did. You know the results of that work.

Now so far as these changes are concerned, they are beyond our control to a certain extent. We will manufacture a product—let's call it 1234. It has certain chemical and physical characteristics. It is supplied to a cable manufacturer. It is composed of certain constituents. There may be some tetrachlornaphthalene, trichlornaphthalene, paraffin, a little pitch or bitumen, and possibly some chlorinated diphenyl. It does a certain job but he wants it to a little more plastic or he wants its viscosity or the specific gravity changed. Possibly by a change in those constituents of only 1 per cent we can get that particular property. We can't sell it to him as the same product so we put a new number on it. Basically, however, if the variation in the chlorinated naphthalene or the chlorinated diphenyl constituent hasn't changed, the toxic property of that will not change.

When it comes to a question of coöperating with the state authorities in that connection, if there were some major change made in a product we would have no hesitancy in advising them and we would also advise our customers. Virtually every consumer of these materials at some time or another has been given their technical or chemical designation along with their various properties, whether they be physical or chemical.

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with which all manufacturers of chemicals are confronted today, particularly in the synthetic organic field where the development is so rapid that our sales departments can't even keep up with the research departments sometimes, in knowing what they are doing.

MR. F. R. KAIMER (Assistant to Manager, York Wireworks, General Electric Co., York, Pa.): I am certainly pleased to have this opportunity to say a few words with reference to the experience we have had at our York plant. I perhaps should say that again in this case experience alone has been the best teacher. I have lived with the problem at York with the men who went through the experience from its beginning.

It is only 1½ years ago that we had in the neighborhood of 50 to 60 men afflicted with various degrees of this acne about which you all know. Eight or ten of them were very severely afflicted—horrible specimens as far as their skin condition was concerned. One man died and the diagnosis may have attributed his death to exposure to halowax vapors but we are not sure of that. There was an atrophied condition found as a result of the autopsy but we are not definitely sure that it was or was not connected with his work. Knowing the man as I did when he was employed, with the superficial examination that he had, he appeared to me very thin, pallid in his appearance, and I would not say from my poor knowledge of the physical make-up of the human being that he presented a healthy appearance. However, it was only for a 6 months' period from the time of his employment that he complained of this constipated condition and we advised that he see his home physician. It rapidly developed to the point where he was in the hospital and in a very short time he died.

More serious than that perhaps is the fact that we had 50 other men in very bad condition as far as the acne was concerned. The first reaction that several of our executives had was to throw it out—get it out of our plant. They didn't want anything like that for treating wire. But that was easily said but not so easily done. We might just as well have thrown our business to the four winds and said, "We'll close up," because there was no substitute and there is none today in spite of all the efforts we have made through our own research laboratories to find one.

But we did develop—and I was most closely associated with it—and set up a routine for bringing these men back to normal health conditions. A number of them were sent to Dr. John H. Stokes and to Dr. O. H. Perry Pepper of the University of Pennsylvania Hospital, and the others to Dr. Isaac R. Pels at Johns Hopkins. Through their recommendations and studies we employed a trained nurse and two local physicians and you might say established a small hospital and its facilities at the plant. Through the application of quartz light, x-ray, mechanical removal of comedones and the treatment of pustules that developed in later stages, an utterly strict routine where the worst cases were administered to each day for a period of 15 to 20 minutes, another group who were less serious three times a week, and still another group once a week, we have in this year and a half brought each and every man back to a normal skin condition. Those who were very seriously afflicted do show scars, but otherwise their skin is as healthy in appearance as my own. I tell you we are very proud of the fact that they are still all employed and the amount of halowax that we are using today is even greater in quantity and in types than we were using a year and a half ago.

With the adequate ventilation system we have installed, with the routine for change of clothing from street clothing to work clothing when they come to work and the reverse of that process, with the assurance that a shower will be taken before the street clothing is again put on, we have found no recurrence of this skin trouble. Each and every man working with halowax products, either from solution, from solid compounds or handling the wire insulated and treated with it, is examined twice yearly with a complete physical examination, including blood analysis and efforts to determine any liver damage.

However, there is the point which was very definitely brought out this morning. We do not know as yet when this thing starts. I believe it would be of great help

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to us all in industry if some very fundamental work was done on humans, as Dr. Jones mentioned before we came into this meeting, some control in fundamental work to determine some method whereby we may determine the inception of any liver disorder.

We have had our men examined in groups three times since the trouble developed and nothing has shown up in any one man. We have learned and appreciate the fact that we must handle hazardous materials, but we have learned how to handle them. It has been a very great experience for us and for myself, and again the best teacher.

DR. CECIL K. DRINKER: Can you recollect the air concentration that you are maintaining now with your present ventilating equipment?

MR. F. R. KAIMER: We have had two examinations made of the air by Mr. William F. Hemperly and they average from 0.2 to 0.8 mgm. per cu. m. We recently discovered one condition which was found as the cause of a high reading in one of the examinations. The compound is one that is not manufactured by the Halowax Corporation that is used rather infrequently, perhaps not more than 50 gallons of it in a 6 month period. It is in the form of a paste, reduced with solvent to a paste form, and it was not known that it contained a chlorinated solvent in certain percentage. We discovered it only recently through the analysis of a sample and we found that that was the cause of throwing the results off to a high value. It was then about 8 mgm. per cu. m., I believe. That is going to be eliminated now. That is a combination of toluene and carbon tetrachloride solvent. When that compound is exposed to the air the chlorinated solvent odor is completely masked by the toluene. It is lost. I was able to detect it only by removing the head of the drum and immediately smelling the odor of carbon tetrachloride. As soon as that head was removed for a period of 10 seconds the toluene predominated and we had no knowledge of the other being in there.

MR. ARTHUR G. BEYER (Research Engineer, United American Bosch Corporation, Springfield, Mass.): Do I understand you to say that those men who were afflicted are back on the same job?

MR. F. R. KAIMER: They all returned to normal skin health, as I say, and are working on the same job.

DR. CECIL K. DRINKER: Dr. Schwartz, you have seen a good deal of this general subject.

DR. LOUIS SCHWARTZ (Medical Director, Dermatoses Investigations, United States Public Health Service, New York, N. Y.): I am primarily interested in dermatitis and it was only because of my researches in that field that I happened to come across information given to me by Dr. Gray that there were some cases of yellow atrophy of the liver attributed to halowax. I can only talk from personal experience about the skin cases. I know from what I have seen and from what I have heard from doctors who have been treating these cases that if they are treated like an ordinary acne vulgaris and kept away from further large exposure they all get well, with the same results as acne vulgaris. Those who have large pustules may have scars resulting and those who have superficial pustules or only comedones won't have any scars.

As far as prevention goes, I felt even before this investigation was undertaken that this substance, like any other poisonous substance, can be handled and used in industry provided proper safety precautions are taken, and I so advocated at the meeting in Pennsylvania when this was discussed.

About ventilation and safety precautions, I think that while we cannot, with our present knowledge, detect by any chemical tests the early symptoms of intoxication from this substance, the skin offers an easy way of proving whether your method of ventilation is efficient or not. If there are any cases of acne or of this dermatitis occurring in a plant where halowax or the chlorinated naphthalene or chlorinated diphenyls are used, then that shows that there is sufficient concentration of these substances in the air to cause plugging of the follicles and to cause a skin condition. If there is sufficient concentration to do that there may be

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sufficient concentration to cause systemic poisoning in the few people who are hypersensitive to the action of these hydrocarbons. Everybody is not hypersensitive to them. If they were, of the thousands of people who have been handling these substances, more would have contracted this disease and it would have been reported very much earlier. This material was used in Germany as early as 1914 or 1915.

While I cannot add anything to the methods outlined here for safety in the way of ventilation and so forth, I can say that if you go into a plant and find that there is any acne present among the workers with this material you will know that there is sufficient of the substance in the air to cause acne and consequently sufficient perhaps to be dangerous to the few people who are hypersensitive to its action.

DR. CECIL K. DRINKER: There is a practical point in regard to the question of determining these substances in air. My brother pointed out this morning that there are several pieces of apparatus for doing this. It has seemed desirable to a number of the men who are here that during the next couple of years, while we are in a position of learning, that we endeavor, if we can, to confine our analyses to one piece of apparatus, so that at least our results will be as comparable as we can make them from place to place.

I don't know much about this phase of the subject: perhaps, Mr. Cook, you have an idea or two about that.

MR. WARREN A. COOK (Chief Industrial Hygienist, Bureau of Occupational Diseases, State of Connecticut Department of Health, Hartford, Conn.). On the determination of the halowax I wonder if it wouldn't be preferable to have Mr. Hemperly discuss the method he has been using throughout the country for the determination of chlorinated naphthalenes.

DR. CECIL K. DRINKER: I think so far as that is concerned it is best to leave that to discussions with Mr. Hemperly and Dr. Brandt afterward. But the question of determining some uniformity of technic for a while at least is, I think, a matter of general interest to us.

MR. WARREN A. COOK: I am not quite sure that I have in mind exactly what you want in that regard. In connection with sampling?

DR. CECIL K. DRINKER: Yes. In connection with the whole technic of determining the material in air, length of sampling, type of apparatus, and so forth. It has been suggested that we endeavor to agree upon some uniform procedure for that and as figures begin to come in, as they will in the course of the next couple of years, we will at least have them on a comparable basis.

MR. WARREN A. COOK: In that regard there is no question but what the determinations and results of analyses of the concentration of injurious materials in air, correlated with pathological findings or freedom from pathological findings, are real factors in further substantiating toxic limits which are originally given us from animal experimentation. In order to obtain data which are of value along that line it is desirable to know to what extent, in terms of milligrams per cubic meter, workers are exposed to in breathing any potentially injurious material.

It seems to me that one of the things that should be done, which many of the plants and many of the organizations equipped to make determinations of injurious materials in air should do, is to make an effort to develop one group and series of results which will represent average exposures of workers to chlorinated naphthalenes. In getting that figure I think that it is of great importance that we should consider average daily exposure. There is a tendency very often in taking samples of air to determine maximum exposures, to get the exposure over a 15 or 20 minute period when the worker may be actually tending a pot where the material is being used, whereas during the subsequent half hour he may be 40 or 50 feet away from that particular location. Therefore, for one thing, it seems to me it would be extremely desirable to obtain information in as many plants and as many locations as possible of the average exposure, taking into consideration not only the worker's maximum exposure while actually

at work with these materials but also his much smaller exposure and possibly even lack of exposure as he may go to other parts of the room or even to other departments during the course of the day.

Another type of determination which seems to be extremely desirable to have is concentrations of the chlorinated naphthalenes at certain reference points. I believe that Mr. Hemperly very carefully duplicated these reference points in each of the plants where he took his determinations. He took the samples, I believe, at breathing level and a certain measured distance from the pots where the chlorinated naphthalenes were being handled, so that next year he could go back to those same locations or others could take determinations at those same locations, which are definitely fixed and recorded, and learn whether, due perhaps to clogged pipe lines or to fans which might become loaded with the condensed chlorinated naphthalene, there might be poorer ventilation than originally designed and higher concentrations of the chlorinated naphthalene than originally determined.

It seems to me that it would be an extremely desirable thing to have made available for all of us who are making these determinations these reference points so that in Massachusetts and in Connecticut, at one plant or at another, a considerable group of workers could be taking samples at this one particular point with reference to the source of generation of the vapor. Such results would permit a comparison of knowledge between plants.

In that regard it happens that there is a committee of the American Public Health Association which is charged with the development of chemical methods for determination of atmospheric contamination such as that now under consideration. It seems to me that it might be a very desirable project for that committee to consult with the investigator of the Halowax Corporation and suggest to all of those who are doing work of this type, after some discussion, what reference points could be adopted and also what should be done in connection with getting these average exposures. As a matter of fact our committee will discuss that very feature and possibly include it in our report before the A. P. H. A. in October as one of the projects which we shall carry out at that time.

As I have not given this consideration, I am afraid my discussion is not as connected as I might wish it to be. We have a real problem here and one that deserves some study.

DR. CECIL K. DRINKER: Would it be of service to the American Public Health Association Committee if a sub-committee from this meeting, collected perhaps by my brother and those of you involved with these problems, were to make a recommendation to the A. P. H. A. as to the things you have brought up and as to suitable apparatus, and let the final statement come from the Association after they have considered that material?

MR. WARREN A. COOK: I think that would be a splendid idea because we have a bulk of information on this particular material. A number of individuals have given much thought to the development of apparatus, both the combustion method which we have here and also the continuous record type of apparatus which Professor Drinker mentioned this morning. I think that it is a sufficiently important project that a sub-committee made up from this group could give that committee a very definite steer.

[Personnel of the Sub-committee: W. A. Cook, chairman, A. L. Coleman, H. B. Elkins, W. B. Fulton, S. W. Gurney, E. R. Hayhurst, W. F. Hemperly, F. W. Sehl, and A. N. Setterlind.]

MR. HERVEY B. ELKINS (Chemist, Division of Occupational Hygiene, Massachusetts State Department of Labor and Industries, Boston, Mass.): In connection with what Dr. Schwartz has said, I am not sure that I am in complete agreement as regards the use of skin lesions as warning agents. It is my understanding that in insulated wire plants the chlorinated diphenyls are very commonly compounded with the chlorinated naphthalenes. It is also my understanding that these are more likely to cause a severe skin irritation than the straight chlorinated naphthalenes. On the other

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hand, from Dr. Drinker's work one would judge that the straight chlorinated naphthalene was nearly as toxic at least as the mixture of it with a small amount of chlorinated diphenyl.

In the condenser factory where we had our cases there is no chlorinated diphenyl used and no acne of the type described in the reports on the insulated wire factories.

DR. R. EMMETT KELLY (Monsanto Chemical Co., St. Louis, Mo.): I can't contribute anything to the laboratory studies but there has been quite a little human experimentation in the last several years, especially at our plants where we have been manufacturing this chlorinated diphenyl. It has been our observation that although on one occasion we did have a more or less extensive series of skin eruptions which we were never able to attribute as to cause, whether it was impurity in the benzene we were using or to the chlorinated diphenyl, we have never had any systemic reactions at all in our men. We have examined them very closely both from what laboratory tests we thought might help us and from the clinical viewpoint. Also from chlorinated diphenyl alone there have been no cases of systemic poisoning reported.

I don't believe that we can transpose the laboratory results into the actual humans without paying considerable attention to the volatility of different substances and the way they are being used.

DR. JOHN A. HOOKEY (Consulting Dermatologist, Halowax Corporation, Detroit, Mich.): I have had considerable experience with the dermatological angle of this problem. The experience at the Halowax plant at Wyandotte definitely was that the dermatosis did increase when compounds were used rather than the straight chlorinated naphthalenes.

From the discussion we have heard today I think the observation Dr. Drinker made that the chances are that dermatological problems will disappear along with the other is probably true. However, I think that certain precautions, certain insurance measures, you might say, should be taken in hiring men who are going to work with these products, even though we are going to attempt to get the concentrations low. We saw this morning that the effect of these products was on the liver and that if some one working in these products developed liver damage from some other source the chances of his having serious trouble was increased. Therefore, inasmuch as there is no test to tell whether a person has had liver disease, certainly in the preliminary medical examination of applicants for work the history at least should be gone into very carefully for a history of previous liver diseases.

There are other things that should be taken into consideration also. One is the history of syphilis, because syphilis does have an effect on the liver. If there is any history of syphilis I don't think that that man should be hired. A Kahn test should be taken and I think that it would be a good plan to take Kahn tests on men at stated intervals, because they might develop syphilis after they are hired.

I think those things should be done even though we feel that if the concentration of these vapors in the air is kept as low as was recommended this morning, the chances of having toxic effects are very small.

MR. F. R. KAISER: I would like to clarify a point of Dr. Hookey's.

You mentioned at the beginning of your talk that your experience in acne condition was more pronounced from the compounds of various materials with chloronaphthalene than with the straight chloronaphthalenes. Did you mean by that, that the acne condition actually was more pronounced with the compounds than with the straight chloronaphthalene or was that due to the fact that you were in a plant operated in a different fashion? In other words, you handled your numerous wire compounds in more of a batch operation. That is my understanding from Mr. Brown.

Is it a fact that the straight chloronaphthalenes are less harmful in so far as acne is concerned or is it because of the handling of batch compounds?

DR. JOHN A. HOOKEY: That is a question that would be difficult to answer. I based my statement on the fact that in taking a general survey of these cases after I started working with them the men in the plant said

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that they developed acne more often and more severely after they started making compounds. It may be that it was in the method of the handling.

MR. F. R. KAIMER: You say that the condition increases with the increased chlorine content and we are attributing the acne primarily to the chlorine radical. If that is true, what are we to associate insofar as these various other constituents are concerned, such as various plasticizing agents? How much do we know about those insofar as development of acne is concerned? Some of these compounds have a half dozen constituents in them other than chlorodiphenyl and chloronaphthalene. We are at the present time considering the chloronaphthalene as the basic element responsible for the acne condition which we have. We know very little about what the other materials may or may not do.

DR. JOHN A. HOOKEY: I don't know about these other materials. Perhaps Dr. Schwartz would know something more about them.

DR. LOUIS SCHWARTZ: It is well known in industry that there are many compounds that cause acne. For instance, paraffin acnes and oil acnes have been known for a long time. Paraffin acnes, wax acnes, are simply a mechanical plugging of the follicles of the skin by the minute particles of wax that fall on the skin. I think that the acne caused by these chlorinated naphthalenes and diphenyls, because it is caused by both—I was down at the Swan Chemical Company where they make chlorinated diphenyls and they have acne there just the same as over at Wyandotte where they make the chlorinated naphthalenes—I believe that that is caused by the same thing, a blocking up of the follicles of the skin, the formation of the comedone and then the comedone becomes infected and forms a pustule. They don't all pustulate because they don't all become infected. Many of these men never have any pustules. They just have little white elevations on their skin.

In those people who are in the acne age, the youngsters of 18, 20, 22 and 23, acne vulgaris is most apt to occur. The sebaceous glands are most active and they seem to have it much more than the older people in whom the sebaceous glands are not so active.

We keep a clipping of all articles relating to industrial dermatitis in my office and I recently read an article in a German magazine in which they report in Germany a similar acne condition from chlorinated phenols and chlorinated benzenes and solid waxes. It seems that this acne-like condition is not peculiar to halowax or chlorinated naphthalenes or diphenyls but can occur with any condition that blocks up the sebaceous follicles of the skin.

DR. ROYAL MEEKER (Special Agent, State of Connecticut Department of Labor, Hartford, Conn.): I am full of questions. As a statistician I am a little bit suspicious of averages, so I should think that we should take maxima as well as averages in getting at the threshold dose or the dangerous impregnation of the atmosphere with these poisonous compounds. I just wanted to drop that as a hint for this committee to consider in its work.

In spite of what you said at luncheon, Dr. Drinker, I still think it is rather important to determine how the plugging of the pores actually does occur, whether they are plugged as Dr. Schwartz has suggested, from the particles falling on the outside of the skin or whether they are plugged, as so many doctors have informed me, from inside as it were. The fumes are breathed, the substance gets into the blood stream. It is thrown off through the pores of the skin and the pores are plugged. I think it is rather important to determine that because it seems to me, from the slight knowledge that I have of the industrial application of halowax compounds in insulating wires, that the plugging of the skin, if it is just an outside plugging, may take place either from handling a solid substance or from the coating on the wire after it becomes cold.

I haven't heard anybody say anything about those Massachusetts cases of very severe dermatitis and I am not so sure but what there was some question of liver damage there. Nobody has said anything about them at all. There is no question there

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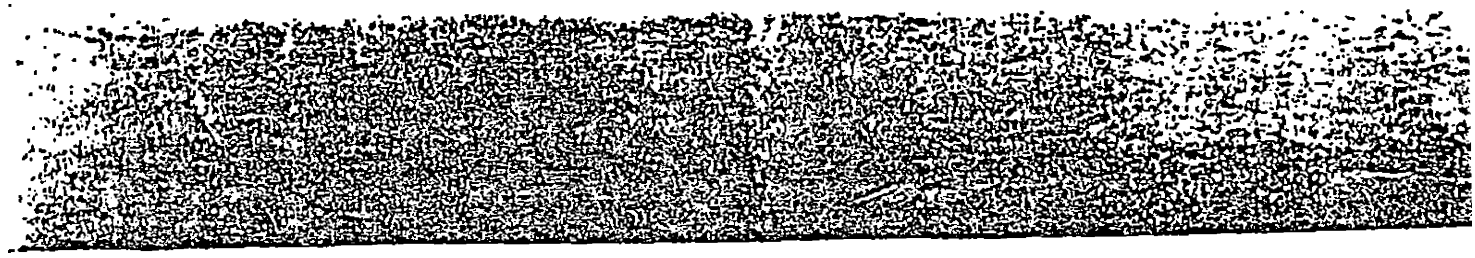

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that the condition, whatever the complications might have been, came from handling cold wire, in a confined area of course.

I think this needs a great deal more study, Dr. Drinker, than you and your associates have been able to give it as yet. All I am curious about is the way we can administer the protective labor laws in order to protect both the employer and the employes.

I listened with very great interest to the expositions of suggested pots for the application of halowax, chlorinated naphthalene and diphenyl. It seemed to me that they left very much to be desired. I don't see why the application of the halowax compound, if it is necessary, as I assume it is, to use this rather dangerous substance, can't be done in a practically closed pot. If you please, Dr. Drinker, I wish you would ask Mr. Reeves of the Rockbestos Products Corporation to tell how they have handled it. If I am any judge of equipment and safety devices they have come as near to eliminating entirely from the atmosphere all contamination from fumigated or evaporated halowax as anyone. All of the application of halowax, either in the melting pots or where it is applied to the wire, is done under hooding and with ventilating apparatus, and it seems to be entirely adequate.

Mr. B. H. Reeves (Vice-president and General Manager, Rockbestos Products Corporation, New Haven, Conn.): I will be very glad to tell of our experience if it will help the picture along. Our experience has been more or less parallel with Mr. Kaimer's in as much as we manufacture the same type of wire. We have avoided the serious picture that he ran into, probably due to the fact that shortly after 1923 we were using benzene as a solvent for asphaltic materials.

We got into anemia difficulties with benzene fumes and had to install a complete ventilating system to remove all those fumes from the machines that applied the compounds to the wire. Following the installation of that equipment we were able to get a substitute for benzene, so we got it out of the picture.

We are still in the same fix as every one else is as far as finding a substitute for halowax. There is none that we know of. Consequently when we went to the use of halowax we had a head start as far as the ventilating system was concerned, since ours was already installed and adaptable to a compound with a benzene solvent rather than a melted halowax compound. In order to keep the fumes of a highly volatile solvent under control we did develop a practically complete enclosure for the container in which the compound was placed and exhausted that container in order to prevent any escape of the fumes from it. When we changed to the halowax compounds we followed the same scheme of applying the compounds and used a completely enclosed pot. There is a hole in one side for the wire to go in and one on the other side for the wire to come out. There is enough exhaust suction on the enclosure to prevent any fumes from getting out of the openings where the wire enters and leaves. Of course periodically it is necessary to open the pot to replenish the compound or make adjustments. In that case we have the ventilating system interlocked with the door that the operator opens so that when he opens it he increases the amount of air travel about ten-fold.

Dr. Royal Meeker: What is the velocity when the door is open?

Mr. B. H. Reeves: With the door wide open, at breathing level the velocity is 200 feet. That is the linear velocity. We check that every week on every opening at every machine with a velometer, a small instrument which is easy enough to operate and reads directly. Whenever the velocity falls below that figure the pipe connecting that machine is taken down and cleaned, because there will be condensation inside the pipe to cut down the air flow and reduce the ventilation efficiency.

Dr. Royal Meeker: What do you think of that trap device shown?

Mr. B. H. Reeves: I don't know what to think of that. I don't know whether it would be practical or not. I was going to ask Dr. Drinker whether in passing the air laden with halowax fumes through the boxes of rats there was any deposit of halowax in the enclosure.

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DR. CECIL K. DRINKER: Yes. It is detectable readily through the outflow pipe.

MR. B. H. REEVES: Those in the far end probably didn't get the concentration.

DR. CECIL K. DRINKER: We change the position of the boxes each day. The ones furthest away move into the nearest position, so that over a period of weeks all are exposed equally.

DR. EMERY R. HAYHURST (Consultant in Industrial Hygiene, State Department of Health, Columbus, Ohio): I would like to ask if it wouldn't be possible to put a cold water line around that trap and deposit it all before the air escapes from the trap.

MR. B. H. REEVES: We have tried cooling the surface of the exhaust pipes in order to concentrate the deposit in one place and make it unnecessary to remove long lengths of the ventilating system. While we have found a slight advantage in doing so it hasn't at all paid for the expense. It is much easier to take the piping down. Consequently I doubt the possibility of removing it all by cooling the surfaces of the trap. It might be possible, by building a labyrinth of refrigerating coils, to collect it. But then you would have the problem of removing it from the coils after you had collected it and it would involve rather complicated procedure.

DR. B. L. VOSBURGH (Medical Director, General Electric Company, Schenectady, New York): We have heard about the possibility of preventing liver damage and skin trouble among manufacturers of wires and cables and so forth, but like the old rhyme, every dog has fleas and the fleas have fleas, we also have customers who use wires and cables in tunnels, in enclosed spaces, splicing them together and doing all sorts of things. I am not at all certain that we know what the concentration of these chlorinated hydrocarbons is under those conditions.

About the time we were having so much trouble at our York factory some of our customers began complaining. We thought we were having a hysteria of halowax mania throughout the country. Some of their complaints were bona fide. We had no difficulty in handling cold wire and the men had no skin trouble. Yet when they did the same thing with possibly the application of heat in tunnels, ships and so forth, they actually did develop trouble.

We have used, of course, the icterus index in following some carbon tetrachloride cases and I wondered what you have to say about that. Is that of no value at all in the case of liver damage in this material?

DR. CECIL K. DRINKER: I don't think so until it gets so extreme that we know it any way.

DR. B. L. VOSBURGH: I did write down a few questions that came to mind. Some of them have been answered and some are foolish but I shall ask them anyhow.

It occurred to me that if trichlornaphthalene has been proved to be practically innocuous, isn't it a problem of research largely for the Halowax Corporation to use only that one material adopted with other known chlorinated compounds to meet the requirements of customers? That is one of the foolish ones probably, but I shall just ask it.

Furthermore, how long is it reasonable to expect the liver to recover after it has been pretty well damaged. I talked to you and you said you hadn't worked that out with the animals as yet.

DR. CECIL K. DRINKER: In that case we set aside a certain number of animals to recover, after knowing that a certain amount of damage had been done. Then we started to kill them but we invariably ran out of rats before they ran out of lesions. We don't know how long it lasts.

DR. B. L. VOSBURGH: Have you given them calcium and glucose as you would with carbon tetrachloride?

DR. CECIL K. DRINKER: Not yet, but we are doing an experiment now with one group on a very high calcium diet and another group on a calcium free diet. The whole question of calcium in the diet, of giving milk daily to these people may be worth while.

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DR. B. L. VOSBURGH: I just had those questions in mind. I would like to hear what Mr. Brown would say as to the possibility of using only this one innocuous chlorinated naphthalene.

MR. SANDFORD BROWN: That would simplify our problem exceedingly, not only from the commercial standpoint but from the toxicity standpoint. But if we did so I think that Mr. Kalmer would be the first to object because he wouldn't be able to get the technical effects he desires in the cable. The same thing applies throughout all the industry where we are using these higher chlorinated products.

The problem as we see it, and it is one which we intend to study further (we have our program for this continuous work that will be done under the direction of the Drinker brothers), is to try to find a line of demarcation and whether or not within this complicated chemical structure there is some one thing that causes the trouble. If we could take hexachlornaphthalene and remove 1 per cent of some unknown constituent with which we are not now familiar and eliminate the toxicity, that would be a lovely solution. Whether we will ever be able to attain that I don't know. That is one of the things we have in mind.

As I said before, that is one of the things with which all manufacturers of these synthetic organic products are confronted at some stage, either in their laboratories or in commercial developments. It is largely a question of timing as to when you should do the work, how much you should do, and whether you know how to do it. You have to learn that first.

DR. CECIL K. DRINKER: Unless there is some other important matter I will declare the meeting adjourned.

DR. R. R. SAYERS: May I say a word more with regard to what Dr. Hookey stated on syphilis? If you are going to eliminate all your workers who happen to develop syphilis during the time they are working for you, you are probably going to lose some very important employees. It would seem that it would be worth while to give serious consideration to seeing that conditions are proper and suitable for them to continue working for you and that they have proper treatment. In other words, I don't believe that is a good or sufficient reason for discharging those employees who do develop syphilis. We have not found that to be true in other places and I question whether this is one of the places. I may be in error.

MR. SANDFORD BROWN: I want to take this occasion to express on behalf of the Halowax Corporation my thanks for the excellent cooperation we have received from various state authorities and our customers as well in this investigation. I believe you have all formed the opinion, based on what you have heard this morning, that our whole motive here is to conduct this on an ethical, scientific and constructive basis.

In collaboration with the Monsanto Chemical Company we have a much more comprehensive program in view to carry on. Therefore we want to continue that same type of cooperation.

There is one thing that I want to bring up in that connection, which will have to be observed by the state authorities, when they go out to make these inspections. That is the necessity of not creating mob hysteria on the part of the workmen in the plants where these inspections are made. Mr Hemperly has run into some very interesting situations in the various examinations he has made. I know that he would be glad to relate them and give the benefit of his experience to the heads of any of these state departments who will have the direction of this work. Otherwise I can see where we will be unable to get the full coöperation of not only the individual workmen but the plant foremen and the management, and we must have that if we are to get the results that we are shooting for over the next several months or years. This thing may continue, probably will continue for years.