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EFFECTS OF 2,4,5-T ON MAN AND THE ENVIRONMENT

HEARINGS

BEFORE THE

SUBCOMMITTEE ON ENERGY, NATURAL RESOURCES, AND THE ENVIRONMENT

OF THE

U.S. Congress. Senate.

COMMITTEE ON COMMERCE

UNITED STATES SENATE

NINETY-FIRST CONGRESS

SECOND SESSION

ON

EFFECTS OF 2,4,5-T ON MAN AND THE ENVIRONMENT

APRIL 7 AND 15, 1970

Serial 91-60

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Dr. Julius E. Johnson
Vice President, Dow Chemical Co.

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Senator HART. The hour being 12:25, I suggest we recess until 2:15.

(Whereupon, at 12:25 p.m., the hearing was recessed, to reconvene at 2:15 p.m. this same day.)

AFTERNOON SESSION

Senator HART. We resume this afternoon to hear first from Dr. Julius Johnson of the Dow Chemical Co. If a corporate entity can have a spirit attached to it, the comparing is a distinguished corporate constituent of mine.

STATEMENT OF DR. JULIUS E. JOHNSON, VICE PRESIDENT AND DIRECTOR OF RESEARCH, THE DOW CHEMICAL CO.; ACCOMPANIED BY ETCYL BLAIR, DIRECTOR OF DOW AGRICULTURAL CHEMICAL RESEARCH; V. K. ROWE, DIRECTOR OF THE DOW TOXICOLOGICAL LABORATORY; AND GEORGE LYNN, DIRECTOR OF GOVERNMENT REGULATORY RELATIONS OF THE DOW CHEMICAL CO.

Dr. JOHNSON. Thank you, Senator Hart.

I have with me Dr. Blair, director of Dow Agricultural Chemical Research, Mr. Rowe, director of our Toxicological Laboratory, and Mr. George Lynn, director of our Government Regulatory Relations.

Senator HART. Thank you. You are all welcome.

Doctor, you have given us a statement. We will order it printed in full in the record and as you go along, if there is any extension or summation you care to make, the record will contain the full statement in any event.

Dr. JOHNSON. Senator Hart, the policy decision has already been made and announced this morning. I will, however, with your permission, read my testimony, all except the last part which deals with some historical matters that already appears in the record.

Then, if you would permit, I would like to make some additional comments which may be appropriate to the process of shortening the time interval between the discovery of a suspected toxic phenomena and taking appropriate action.

I would also like to refer back to some earlier work done under Senator Ribicoff's guidance in his committee and quote at least one passage from that work published in 1966, which I think is appropriate to the issue, if I may do so.

Senator HART. By all means.

Dr. JOHNSON. Thank you.

Mr. Chairman, I am Julius E. Johnson, vice president and director of Research and Development of the Dow Chemical Co., Midland, Mich. I also served as a member of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health, May 8, 1969, to November 7, 1969, chairman, Emil M. Mrak.

I have with me George Lynn, director of Government Regulatory Relations of the Dow Chemical Co. V. K. Rowe, director of the Dow Toxicological Laboratory and Etcyl Blair, director of Dow Agricultural Chemical Research, are also present to assist if necessary.

This statement is concerned with the herbicide 2,4,5-trichlorophenoxyacetic acid, which has often been referred to as 2,4,5-T and

the chemical intermediate 2,4,5-trichlorophenol used in the manufacture of 2,4,5-T.

An announcement was issued October 29, 1969, by Dr. Lee Dubridge of the Office of Science and Technology which referred to birth defects observed in tests by the Bionetics Laboratories using 2,4,5-T in various dosage ranges in mice and rats.

This announcement preceded the final report of the Panel on Teratology of the Mrak Commission appointed by Secretary Finch which, since May 8, 1969, had been reviewing the effects of pesticides upon health and the quality of environment. At the time, October 29, 1969, members of the Mrak Commission had not seen the Bionetics report on teratology.

Following the announcement by the Office of Science and Technology, I became particularly concerned because Dow is a manufacturer of this herbicide. Consequently, I made a diligent effort to trace the source of samples used and learned that the 2,4,5-T sample came from the Diamond Alkali Co. (which no longer makes 2,4,5-T).

Moreover it was learned that 2,4,5-trichlorophenol also tested by the Bionetics Laboratory came from Coleman-Mathison-Bell who had obtained the sample from McKesson-Robbins who in turn had procured it from the Dow Chemical Co.

2,4,5-trichlorophenol is used as an intermediate in the manufacture of 2,4,5-T. Hence, the quality of 2,4,5-T is related to the quality of its intermediate 2,4,5-trichlorophenol. The chemical process used by Dow for manufacture is as follows:

1,2,4,5-tetrachlorobenzene is hydrolyzed in a solution of methanol and sodium hydroxide in water to form sodium 2,4,5-trichlorophenate. This is in turn reacted with sodium monochloroacetate to form sodium 2,4,5-trichlorophenoxyacetate. The solution is acidified to precipitate and recover the 2,4,5-trichlorophenoxyacetic acid.

Since 1950 we have been keenly aware of the possibility of a highly toxic impurity being formed in 2,4,5-trichlorophenol as a side reaction under conditions of elevated processing temperatures. The most sensitive toxic reaction observed in humans to this impurity was manifested by a condition known as chloracne, a skin disorder mostly prevalent on the face, neck, and back.

It is similar in appearance to severe acne often suffered by teenagers. We also knew that if the impurity was present in the 2,4,5-trichlorophenol it could be carried forward to the end product, 2,4,5-T. It is not formed during the manufacture of Dow 2,4,5-T from the 2,4,5-trichlorophenol, nor does it form on storage even at high temperatures. To avoid the impurity in 2,4,5-T it is necessary to keep it out of the 2,4,5-trichlorophenol.

Our early control test was a bioassay. This consists of applying a solution of the material to the inner surface of a rabbit's ear and observing for the typical skin response described in a paper published in 1941 by Dow scientists. I wish to insert in the record at this point the paper entitled "The Response of Rabbit Skin to Compounds Reported to have cause Acneform Dermatitis," by E. M. Adams, D. D. Irish, H. C. Spencer, and V. K. Rowe, published in Industrial Medicine, January 1941.

Senator HART. It will be printed.

(The information follows:)

The Response of Rabbit Skin to Compounds Reported to Have Caused Acneform Dermatitis

E. M. Adams, D. D. Irish, H. C. Spencer, and V. K. Rowe,
Biochemical Research Laboratory, The Dow Chemical Company Midland, Michigan

THOSE of us acquainted with the industrial field have recognized the need of an experimental method for studying skin irritation. We would profit greatly by knowing the potential skin hazards of a substance before it is put into use; we would be able to take proper precautions in the cheapest and most satisfactory manner and many undesirable incidences could be avoided.

In the literature there are many instances of irritation tests upon the skin of animals, but apparently there has not been a comprehensive study. In an attempt to develop an experimental method, we began about six years ago to study the responses of rabbits' skin to various types of substances. We considered the possibility that if enough were known of these responses to different types of compounds, particularly to those with which there has been considerable human experience, then these responses could be organized to form the basis of an experimental method.

Acneform dermatitis, characterized by such lesions as folliculitis, comedones, nodules, papules, pustules, and inflammatory changes, has been reported arising from exposure to quite varied substances including petroleum oils and greases, shale oil, paraffin, zinc oxide, chlorine, tars, pitches, chlorinated diphenyls, chlorinated naphthalenes, and crude chlorinated phenols.[1, 2, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14, 15, 16, 17, 18, 19, 20, 23, 24, 26, 27, 28, 29, 30, 32, 33, 34] The recent occurrence in this country of such an acneform eruption,[4, 8, 12, 26, 29] sometimes called "chloracne," has attracted particular interest, and we included in our animal studies five types of substances known to cause the reaction. Today we wish to describe the unusual response of the rabbits' skin to these materials and to consider its possible significance.

Experimental Part

IN OUR experiments, materials have been applied to the inner surface of the ear of albino rabbits and to the shaven belly. The undiluted materials have been used as well as solutions of various concentrations in olive oil, paraffin oil U. S. P., propylene glycol, ethanol, and water. Liberal applications were made on the ear without any covering. The applications on the abdomen were made in a small cotton pad which was covered by a large bandage of filter cloth held in place by adhesive tape. Applications were made once a day, five days a week, for four weeks or until a marked reaction resulted.

The responses obtained following the application of some hundreds of test substances are easily arranged according to type.

Certain of the strongest irritants produce a rapid destruction of the tissue (necrosis), without the skin having an opportunity to show an active response. Irritants with milder and slower actions than this have some effect upon the tissues, as a result of which we see certain responses on the part of the tissue. Most irritants have resulted in responses in the rabbits' skin which tend to develop rapidly and to subside in a short time. This relatively rapid response, which we have termed a simple irritation or reaction, may include, depending upon the severity, any of the following: hyperemia, congestion, inflammation, exfoliation, edema, blistering, sloughing, exudation, crustation, necrosis, induration, hair loss. Microscopically one may see hyperemia, congestion, hemorrhage, edema, blistering, leucocytic infiltration, sloughing, and various degenerative changes.

One type of response has been observed, however, which requires a somewhat longer interval in which to become apparent, and which has a much more prolonged course. This latent reaction is a proliferative response which may possibly occur in any of the structures of the skin, but that about which we are particularly concerned now is epithelial hyperplasia, with its resultant thickening of the skin, follicle enlargement and sequellae.

Naturally responses vary to some extent, and we have observed various combinations of these reactions, depending upon the substances applied to the skin and the intensity of action.

For purposes of classification we have arbitrarily divided the proliferative response into the following *five groups according to intensity:*

1. Least detectable.
2. Very slight.
3. Slight.
4. Moderate.
5. Severe.

While there are naturally no sharp breaks between these, and some overlapping occurs, division was rather easy and has been very useful.

Least detectable epithelial hyperplasia: This degree of response is manifest as an increased prominence of the hair follicles on the inside of the ear. The little dots that one sees on the inside of the ear simply become slightly larger. After exposures are ended this enlargement regresses in a short time, leaving the skin apparently normal

This degree of response is commonly seen as part of a mild simple irritation which is maintained by repeated exposures. Thus far we have been unable to attach a particular significance to this intensity of reaction.

Very slight epithelial hyperplasia: This reaction appears on the ear as a slight enlargement of the hair follicles, which protrude and become hard, causing the ear to feel rough. The thickness of the ear may be increased. A very slight scaly exfoliation may accompany this degree of response, but seldom is there any detectable hyperemia or hair loss. On the abdomen one seldom sees any gross evidence of hyperplasia.

Slight epithelial hyperplasia: In this reaction the ear increases in thickness to about twice normal and feels slightly stiffened and "leather-like." There is some hyperemia, scaly exfoliation, and hair loss. The hair follicles become slightly enlarged, raised and hard. On the abdomen there may be a slight thickening of the skin and an exfoliation, but enlargment of the follicles is not apparent.

Moderate epithelial hyperplasia: This reaction consists of a thickening of the ear to 3 to 4 times normal as a result of which it is quite stiff and leathery. The follicles on the ear become moderately enlarged, raised and hard, causing the surface of the ear to feel like the coarsest of sand paper. After a time the protruding hard masses can be easily expressed by the finger-nail or by bending the ear. At times the enlarged follicles are not apparent until after considerable exfoliation has occurred. A moderate hyperplasia is usually accompanied by a slight to moderate hyperemia. Exfoliation of a granular or scaly type is of moderate intensity and hair loss is nearly complete. After a number of weeks the ear is completely denuded of hair, slightly pitted, with a slight or moderate hyperemia and possibly some exfoliation. The abdominal skin may show a greater simple irritation than does the ear; hyperemia, edema, and even sloughing and exudation have occurred. Hyperemia is usually maintained during the course of thickening. The abdominal skin finally becomes hard and stiff, followed by a marked scaly and granular exfoliation, which persists for weeks.

Severe hyperplasia: This reaction is usually preceded by a marked simple irritation, including even necrosis; however, there may be only hyperemia and edema. As a severe hyperplasia progresses, a marked hyperemia is evident until obscured by the thickened epithelium. The thickness of the ear is increased to many times normal, ears at least 1 cm. thick having been formed. As a result they become very stiff, hard, and heavy. Exfoliation at first has a granular consistency, later flaky, and persists for months. The enlarged hair follicles are buried under the thickened epithelium and become apparent only after considerable exfoliation has occurred. From them large masses of keratin may be expressed leaving pits that may reach 2 to 3mm. in width.

On the abdomen the hardened mass of epithelium cracks and lifts off in large pieces like portions of a cast. Often beneath these is a soft, cheesy, foul-smelling material, which soon dries and comes off revealing a markedly exfoliating skin beneath.

The exfoliation often has a granular consistency at first, which later becomes flaky. There is a complete hair loss.

This proliferation of the epithelium seems to progress only to a certain extent, even with repeated applications of the provoking agent. The slowness and persistence of this latent reaction is to be emphasized. The maximum of a severe hyperplasia usually has occurred in the neighborhood of two weeks, the largest amount of exfoliation around four weeks, and a scaly exfoliation and hyperemia have persisted for months.

Although we make exposures upon both ear and belly, the skin of the ear appears to respond in the most satisfactory manner. There the mildest reactions are more apparent and the enlarged follicles are more easily seen. As a rule the abdominal skin shows a more marked simple irritation.

Histology

MICROSCOPIC examinations were made using 10% formalin as fixative, paraffin for imbedding, and hematoxylin-eosin as stain.

The slightest hyperplastic response is shown by a very slight increase in thickness of the epithelium and the development of small projections (like papillae) of but a few cells in size. The early stages of more severe responses show increasing degrees of thickening of the surface and follicular epithelium. Numerous projections reach downward from the surface epithelium, nearly to the cartilage of the ear. The follicular epithelium spreads outward and downward, often completely engulfing hair follicle and sebaceous glands. Apparently there is also a hyperplasia in the corium. Accompanying this hyperplasia, one may see congestion, even occasional hemorrhages, edema, and leucocytic infiltration.

Later the rate of proliferation apparently lessens and those changes resulting in keratinization become more evident. As those changes leading to keratinization progress from the lowermost layer of the epithelium, which constitutes a basal layer markedly displaced from the original, large masses of material are thrown off. Thus in one section of abdominal skin we see a thick layer of partly keratinized and degenerate tissue being thrown off above a flat, normal-appearing stratum corneum. At the hair follicles most of the tissue undergoes complete keratinization, forming the hard plugs that may be expressed. Completely engulfed follicles and glands are destroyed as the hyperplastic epithelium is keratinized and thrown off.

The sebaceous glands have seemed to be inactive. One sees them, apparently normal, being engulfed by proliferating epithelium. Some glands, of normal size and appearance, are seen opening into the pits or cysts; others are seen with their

ducts extending through large masses of keratinized epithelium.

Sections taken at a late stage show an atrophic or very slightly thickened surface epithelium and numerous large pits surrounded by slightly hyperplastic epithelium. The corium may still be thicker than normal.

Ultimately there is a tendency for the pits to broaden out and become shallower, and one sees a very irregular atrophic epithelium.

Discussion

THERE are certain points which indicate a relationship between this reaction observed in the rabbit and the acneform dermatitis of man. First, the reaction in the rabbit was produced by 5 types of substances known to cause an acneform dermatitis in man. They were chlorinated diphenyls, chlorinated naphthalenes, chlorinated diphenyloxides, crude chlorinated phenols, and petroleum oils. A few other types of substances have produced the epithelial hyperplasia, but there has been no exposure of these on man. Wacker and Schmincke[21] reported the experimental production of epithelial hyperplasia with various oils, fats, and paraffin. Sachs,[25] and others, apparently, have produced the identical epithelial hyperplasia in rabbits with a number of dyes. In his review of the pertinent literature, Sachs states that the most common dermatosis arising from exposure to aniline and coal tar dyes is eczema; however, warty growths and acneform dermatitis have also occurred. Thus it appears probable that the development of an outstanding hyperplastic response of the rabbits' skin is specific for those substances capable of causing an acneform dermatitis in man, and possibly, the related papular and warty eruptions.

Secondly, by gross and microscopic examination, the enlarged follicles produced in the rabbit resemble the comedones, nodules, and cysts of the dermatitis in man. In both cases there is a relatively large pit or cyst whose walls are composed of epithelium and which contains varying amounts of keratinized epithelium, and at times hair, hair follicles, and debris.

In both the rabbit and in man there is hyperplasia of the epithelium. Proliferative changes have not been stressed in descriptions of the human reaction and probably have not been seen to a greater extent because tissues were taken at relatively late stages of the reaction. There are reports of increased numbers of mitoses and of thickening of the rete Malpighii.[3, 24, 30, 34, 35] Prosser White[34] describes acanthosis in the "primary papule" and considers one important factor in the production of oil folliculitis to be the chemical irritant causing auxetic cell growth. The ability of tar to cause active mitosis is well known.[11] Bornemann's[3] first case, examined at a late stage, showed more mitoses than normal and slight thickening; but in his second case, examined at an earlier stage, the thickening of the epithelium was much more marked.

Although mention is often made of sebaceous cysts in descriptions of the acneform dermatitis only two instances were found of the specific retention of sebaceous glands in descriptions of the microscopic picture. Jones and Alden[12] reported slight edematous changes in a few glands they saw; Cargil and Acton[6] said that the sebaceous glands were unaffected. Bornemann[3] felt that the cysts were of sebaceous origin but admitted the difficulty of proof, and his description shows them to be essentially epithelial structures.

These facts, together with our experimental results, indicate that the so-called "sebaceous cysts" of the acneform dermatitis in man are directly the result of an epithelial hyperplasia. Their content of sebaceous-like material is probably due to the occurrence of inflammatory and degenerative changes in the mass of epithelial tissue. Of course, the retention of sebum may also occur and influence the picture to some extent, but this appears to be a secondary reaction. Bacterial infection may be a factor influencing the nature of the reaction.

Conclusions

THERE have been a number of hypotheses concerning the formation of this acneform eruption in man.[24, 35] We feel that evidence shows the acneform dermatitis to be the visible response of the skin to an irritant acting upon it from the exterior, and that this response takes the form of first epithelial hyperplasia, second inflammatory and degenerative changes, and finally regenerative processes.

And in conclusion, it is possible that this apparently unusual response of the rabbits' skin offers us an experimental method which will indicate the ability of substances to produce an acneform dermatitis in man.

Bibliography:

1. Beitmann: "Chlor-akne," eine besondere Form von professioneller Hauterkrankung. *Deut. med. Wochnschr.* 27, 437-440 (1901).

2. Blaschko: *Dermatol. Zeit.* 18, 70-72 (1911).

3. Bornemann, W.: Ueber die Histologie der Chlorakne, *Arch. f. Derm. u. Syph.* 62, 73-89 (1902).

4. Buttles, M. G.: Acneform Dermatosis Produced by Ortho-(2-Chlorophenyl) Phenol Sodium and Tetrachlorophenol Sodium, *Arch. Derm. and Syphil.* 35, 251-254 (1937).

5. Courtois-Suffit, Touraine et Ménétrel: Etude sur l'intoxication professionnelle par le trichloro-naphtalène, *Annales de méd. lég. de crimin.* 14, 422-427 (1934).

6. Cargil, D. F., and H. W. Acton: Jute Dermatitis, *Indian J. Med. Res.* 12, 257-260 (1924-5).

7. Dotton, W. F.: Petroleum Dermatitis, *Medical Record*, 140, 550-552 (1934).

8. Duvoir, M., Apropos des dermatoses professionnelles par le trichloronaphtalène, *Annales de méd. lég. de crimin.* 14, 539-544 (1934).

9. Fulton, W. B., and J. L. Mathews: A Preliminary Report of the Dermatological and Systemic Effects of Exposure to Hexachloro-naphthalene and Chlordiphenyl: Penna. Dept. Labor, Special Bull. No. 43 (1934).

10. Herxheimer, K.: Ueber Chlorakne, *Munchen. Med. Wochnschr.* 46, 276 (1899).

11. Jamison: Treatment of Eczema with Coal Tar, *Ann. de derm. et de syph.*, Jan., 1900, page 22. Quoted by R

Prosser White, The Dermatergoses, H. K. Lewis and Co., Ltd., London, 1934.

12. Jones, J. W., and H. S. Allen: An Acneform Dermatergosis, *Arch. Derm. and Syph.* 33, 1022-1034 (1936).

13. Lewin, L.: Ueber allgemeine und Hautvergiftung durch Petroleum, *Virchow's Arch. f. Pathol., Anatomie u. Phys.* 112, 35-69 (1888).

14. McEwen: Acne due to Tar, *J. Cut. Dis.* 35, 853 (1917).

15. Mackenzie, S.: A Case of Tar Eruption, *Brit. J. Derm.* 10, 417 (1898).

16. Mayers, M. R., and M. G. Silverberg: Skin Conditions Resulting from Exposure to Certain Chlorinated Hydrocarbons, *J. Indust. Hyg. & Tox.* 20, 244-256 (1938).

17. Nicolas and J. Lacassagne: Un cas d'acné chlorique, *Bull. soc. franç. dermat. et syph.* 36, 223 (1929).

18. Nogues-Moné, S., and M. Gray-Barbera: Contribution à l'étude des poikilodermies à propos de trois cas de toxidermie folliculaire et pigmentaire d'origine exogène, *Ann. de derm. et de syph.* 5, 379-401 (1934), 7th series.

19. Ogston, O.: On the Local Effects of Crude Paraffin, *Edin. Med. J.* 17, 544-547 (1871-2).

20. Oppenheim, M.: Affections of the Skin Caused by Occupation and Profession, The Medical Press 169 (N.S.), 46-49 (1924).

21. Page, C. G., and L. D. Bushnell: Oil Folliculitis, *J. Indust. Hyg.* 3, 62-75 (1921).

22. Pomeroy, H. S.: On a Hitherto Undescribed Form of Skin Disease, *Lancet*, 1874, ii, 724-5.

23. Pusey, W. A.: Case of Acne, *J. Cut. Dis.* 26, 426 (1908).

24. Ross, H. C., and J. W. Cropper: The Problem of the Gasworks Pitch Industries and Cancer. The J. H. McFadden Researches, 1913. Quoted by R. Prosser White, The Dermatergoses, H. K. Lewis and Co., Ltd., London, 1934.

25. Sachs, O.: Klinische und experimentelle Untersuchungen ueber die Einwirkung von Anilinfarbstoffen auf die menschliche und Tierische Haut, *Arch. f. Derm. u. Syph.* 110, 585-644 (1913).

26. Scott, A.: The Occupational Dermatoses of the Paraffin Workers of the Scottish Shale Oil Industry, *Brit. Med. J.* 2, 381-385 (1922).

27. Sézary, P. Vallery-Radot, and Benoist: Mélanose de Riehl, bouton d'huile, hyperkératose folliculaire chez un ouvrier tourneur sur métaux, *Bull. soc. franç. de. dermat. et de syph.* 34, 139-143 (1927).

28. Sulzberger, M. B., A. Rostenberg, Jr., and J. J. Suss: Acneform Eruptions, *N. Y. State J. Med.* 34, 899-908 (1934).

29. Telecky: Die Pernakrankheit, *Klin. Wchnschr.* 6, 845-848 (1927); 6, 897-901 (1927); 7, 214 (1928).

30. Torsuka, R.: Study of the So-called "Oelkratze," Produced by the Industrial Use of Mineral Oil and Turpentine, *Jap. Zeit. f. Derm. u. Urol.* 17, 395 (1917). Abstracted in *Brit. J. Dermatol.* 29, 227-228 (1917).

31. Toujaine, Solente, Ménétrel, and Auburn: Cinquante-quatre cas de dermatitis par trichloronaphthaléne, *Bull. soc. franç. de derm. et de syph.* 41, 265-269 (1934).

32. Turner, J. A.: An Occupational Dermatoconiosis among Zinc Oxide Workers, U. S. Public Health Reports 36, 2727-2732 (1921).

33. Warde, W.: A Case of Oil Folliculitis, *Brit. J. Dermatol.* 12, 212-213 (1900).

34. White, R. Prosser: The Dermatergoses, H. K. Lewis and Co., Ltd., London, 1934, pp. 195-241.

35. Occupation and Health, International Labour Office, Geneva, 1930. See Chlorine, Coal Tars, Paraffin, Petroleum Oils, Pitch, Shale Oil Industry.

Dr. JOHNSON. Thank you.

As early as 1944 we were monitoring the oils removed as impurities from the 2,4,5-trichlorophenol process by the rabbit ear test. It is in these waste oils that the impurities are concentrated.

In late 1964 some workmen developed chloracne and our bioassay program showed that the chloracne potential of the waste oil from 2,4,5-trichlorophenol process was building up to a danger point.

This came about from operating changes made to improve production capacity. Exposure to this waste oil was the cause of the acne in the workmen. (This waste is routinely destroyed by incineration at high temperature.)

The plant was summarily shut down. Bioassays of Dow 2,4,5-trichlorophenol and 2,4,5-T being produced at this time were negative. We confirmed that the principal offending impurity was 2,3,7,8-tetrachlorodibenzo-p-dioxin. Technology had advanced by early 1965 to the point where we were able to develop a gas chromatographic method for the tetrachlorodibenzo-p-dioxin with a sensitivity of 1 p.p.m. in 2,4,5-trichlorophenol and 2,4,5-T.

I wish to insert in the record at this point a paper entitled "The Determination of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in 2,4,5-trichlorophenoxyacetic acid by Gas Liquid Chromatography," by the Dow Chemical Co.

Senator HART. It will be printed.

(The information follows:)

THE DOW CHEMICAL COMPANY
MIDLAND, MICHIGAN 48640

ANALYTICAL METHOD

June 22, 1965 MLW.65.11

THE DETERMINATION OF 2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN IN 2,4,5-TRICHLOROPHENOXYACETIC ACID BY GAS-LIQUID CHROMATOGRAPHY

1. Scope

This method is applicable to the determination of 2,3,7,8-tetrachlorodibenzo-p-dioxin in 2,4,5-trichlorophenoxyacetic acid. The dioxin can be detected at the one ppm level with a lower limit of 0.5 ppm possible at optimum operation conditions.

2. Principle

The 2,3,7,8-tetrachlorodibenzo-p-dioxin is separated from the 2,4,5-trichlorophenoxyacetic acid by means of an extraction with chloroform. The chloroform extract is concentrated and then chromatographed. The 2,3,7,8-tetrachlorodibenzo-p-dioxin in the sample is measured and compared to a known standard.

3. Safety Precautions

2,3,7,8-Tetrachlorodibenzo-p-dioxin is capable of causing a severe delayed skin response (chloracne) upon minimal contact. Samples suspected of containing any of this compound should be handled so as to prevent all skin contact and inhalation. Wear impervious gloves (rubber, polyvinyl chloride, etc.) at all times when contact is a possibility. Clean all equipment with acetone followed by a chloroform wash. Dispose in such a manner as to prevent all skin contact, any potentially contaminated equipment or materials which are not readily cleaned with chloroform, i.e., towels, gloves, etc.

4. Apparatus

(a) Gas chromatograph, Aerograph A-600-D with flame ionization detector, Wilkins Instrument and Research, Inc., Walnut Creek, California, or equivalent.
(b) Recorder, -0.05 to +1.05 millivolt, full span, one-second full response time.
(c) Syringe, Hamilton microliter, No. 701N, or equivalent.
(d) Syringe, Multifit 5 cc, Becton, Dickinson and Company, or equivalent.
(e) Syringe, Yale 1/4 cc, Becton, Dickinson and Company, or equivalent.

(f) Centrifuge
(g) Injector insert, Pyrex glass for A-600-D. Available from Wilkins Instrument and Research, Inc., Walnut Creek, California (Note 11a).
(h) Column, 1/8-inch O.D., 0.081-inch I.D., stainless steel tubing, five feet in length packed with reagent 5(c).

5. Reagents

(a) Solid support, Chromosorb W, 60/80 mesh, Johns-Manville.
(b) Partitioning agent, SE-30, Silicone gum rubber-methyl (Note 11b).
(c) Column packing, five percent by weight of SE-30 on 60/80 mesh Chromosorb W. Available from Wilkins Instrument and Research, Inc., Walnut Creek, California.
(d) Carrier gas, nitrogen, commercial grade.
(e) Chloroform, ACS grade.
(f) 2,3,7,8-Tetrachlorodibenzo-p-dioxin, available from The Dow Chemical Company, Midland, Michigan.
(g) Sodium hydroxide, 1 N solution. Dissolve 40 grams of reagent grade sodium hydroxide in one liter of water.

6. Chromatographic Conditions

(a) Oven temperature, 225°C.
(b) Inlet temperature, 260°C.
(c) Carrier gas flow rate, 75 ml. per minute as determined by the moving soap bubble technique.
(d) Attenuation, such that a response of at least 50% of scale is obtained from a 1.0 microliter sample of a standard containing 100 micrograms of 2,3,7,8-tetrachlorodibenzo-p-dioxin in one milliliter of chloroform.

7. Preparation of Standard

(a) Again read Section 3.
(b) Weigh, using a micro-balance, one milligram of 2,3,7,8-tetrachlorodibenzo-p-dioxin into a ten ml. volumetric flask.
(c) Dilute to the mark with chloroform.
(d) Inject a 1.0 microliter sample into the chromatograph. See Figure I for a typical chromatogram.

8. Procedure

(a) Weigh 10.0 grams of the sample into a four-ounce bottle.
(b) Add 20.0 milliliters of chloroform and shake for one hour.
(c) Place the solution in a centrifuge tube and, with proper balancing, centrifuge for five minutes.
(d) Using an eye-dropper, draw off as much of the clear chloroform layer as possible into a two-ounce bottle.

(e) Add 25 ml. of 1 N sodium hydroxide to the chloroform extract and shake for 15 minutes (Note 11c).
(f) Centrifuge for five minutes.
(g) Using a five-milliliter syringe, draw off as much of the bottom chloroform layer as is possible into a small vial. Note this volume.
(h) Evaporate to dryness in a hood.
(i) Take up with chloroform to 5.0% of the volume noted in step (g). This final solution represents ten grams of sample per ml. of chloroform.
(j) Inject 1.0 microliter into the chromatograph and measure the response of the 2,3,7,8-tetrachlorodibenzo-p-dioxin. Figure 11 shows a representative chromatogram.

. Calculations

Let:

A = The area of the 2,3,7,8-tetrachlorodibenzo-p-dioxin in the sample.

B = The attenuation of the chromatograph for the sample.

C = The micrograms per milliliter of the 2,3,7,8-tetrachloroditenzo-p-dioxin in the standard.

D = The area of the response from the 2,3,7,8-tetrachlorodibenzo-p-dioxin in the standard.

E = The attenuation of the chromatograph for the standard.

Then.

$$\text{ppm of 2,3,7,8-tetrachlorodibenzo-p-dioxin} = \frac{A \times B \times C}{D \times E \times 10}$$

. Accuracy

The accuracy of this method is $\pm$ 5%, or less, relative.

. Notes

(a) Glass inlet liners have been found to be necessary to provide reproducible results.

(b) Silicone FS-1265 (fluro) has been found to work well as a stationary phase. It also is available from Wilkins Instrument and Research, Inc., Walnut Creek, California.

(c) Any 2,4,5-trichlorophenoxyacetic acid which has dissolved in the chloroform extract must be removed as it will interfere with the chromatographic analysis of the 2,3,7,8-tetrachlorodibenzo-p-dioxin.

* * * * * * * * * * * *

FIGURE I

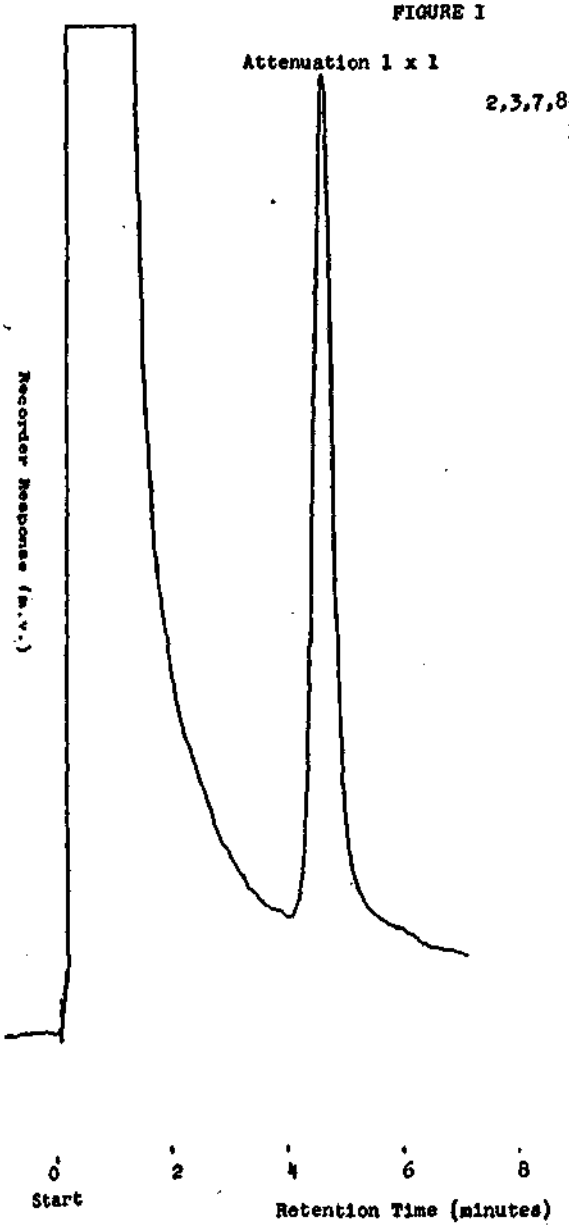
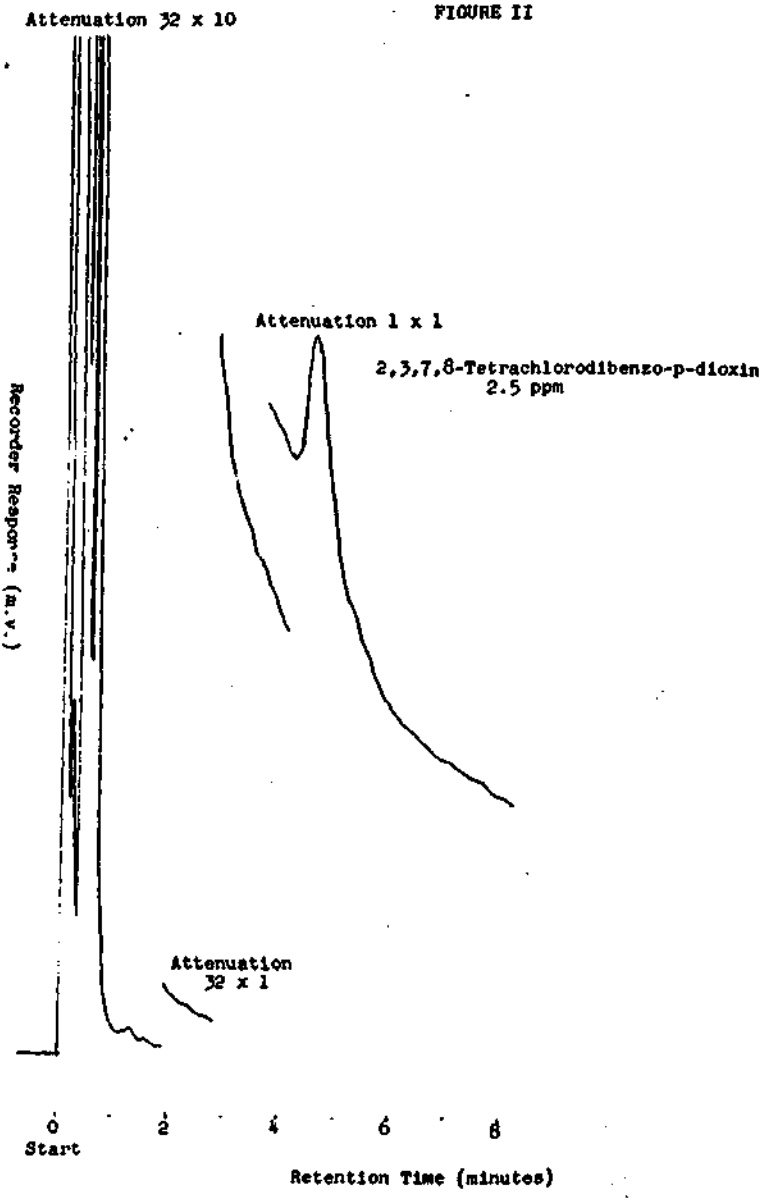

Attenuation 1 x 1
2,3,7,8-Tetrachlorodibenzo-p-dioxin
114.4 micrograms/ml.
Recorder Response (m.v.)
0
Start
2
4
6
8
Retention Time (minutes)

FIGURE II


Attenuation 32 x 10
Attenuation 1 x 1
2,3,7,8-Tetrachlorodibenzo-p-dioxin
2.5 ppm
Recorder Response (m.v.)
Attenuation
32 x 1
0
Start
2
4
6
8
Retention Time (minutes)

Dr. JOHNSON. Thank you.

Senator Hart, the 2,4,5-trichlorophenol plant was redesigned to insure, insofar as possible, the production of a product containing a minimum of the tetrachlorodibenzo-p-dioxin. By so doing we were able to control the quality of Dow 2,4,5-T.

By May 1965 we had the technology to establish a manufacturing specification of no detectable 2,3,7,8-tetrachlorodibenzo-p-dioxin in 2,4,5-trichlorophenol and 2,4,5-T, using an analytical method sensitive to 1 p.m.m. While the plant was being rebuilt, we purchased 2,4,5-trichlorophenol and 2,4,5-T on the basis of this specification.

The new plant came on stream in 1966 and since that time Dow 2,4,5-trichlorophenol and 2,4,5-T have met this specification, and most has contained less than 0.5 p.p.m. of the 2,3,7,8-tetrachlorodibenzo-p-dioxin.

I apologize for repeating these long chemical names but the position and number of chlorines is important.

Senator HART. The day will come when I can pronounce them, even if I can't understand them. I can't do either yet.

Dr. JOHNSON. When the difficulty was encountered in 1964 we notified the Michigan Department of Health, the Institute of Industrial Health, University of Michigan, and various other health oriented individuals in private medicine and industry.

In addition we called a meeting which was held in March 1965 to notify other manufacturers of 2,4,5-T of the difficulties encountered. We described to them the nature of the health hazard and shared our test procedures and analytical standards.

With this background—and firsthand experience—it was only natural that my associates and I would inquire about the identity of the sample used for the Bionetics tests. The 2,4,5-trichlorophenol tested was Dow material and the 2,4,5-T was a Diamond Alkali sample.

It is important to emphasize that 2,4,5-trichlorophenol was reported to show no significant increase of anomalies by the Bionetics Laboratory, but the sample of 2,4,5-T did display a significant increase of anomalies.

This prompted examining our past records of tests run in 1964. The records of analytical determinations of different supplies showed that samples of Diamond Alkali 2,4,5-T in fact did contain tetrachlorodibenzo-p-dioxin up to levels of 16 ppm. It should be emphasized at this point that Diamond Alkali has since stopped manufacturing 2,4,5-T.

I presented the essence of the above information to the Mrak Commission November 7, 1969, and showed pictures of the chloracne observed in humans and pictures illustrating the rabbit ear test. Moreover, I stated that the Bionetics test with 2,4,5-T may have been complicated by an impurity in the 2,4,5-T.

I further emphasized the importance of tests using procedures recognized among experts as being valid and meaningful; the importance of representative materials which could be better obtained by consultation with industry; and the importance of knowledge of composition and purity of the materials tested. These points were made in the course of writing the final draft or recommendations of the Mrak Commission.

In view of our knowledge of the low mammalian toxicity of 2,4,5-T and the absence of reports of increased incidence of birth defects in cattle or sheep grazing rangelands sprayed with 2,4,5-T, we found it difficult to believe that any practical hazard existed from the registered uses of 2,4,5-T.

It became important to gain additional evidence as soon as possible as to whether (1) the sample of 2,4,5-T tested by Bionetics was contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin; (2) if so, could the tetrachlorodibenzo-p-dioxin itself be responsible; and (3) would 2,4,5-T of a specification made by Dow cause similar birth abnormalities.

I asked Dr. Dale Lindsay of FDA if a conference could be arranged with appropriate individuals in DHEW to discuss protocols for tests which would be acceptable to their scientists. Dr. Lindsay asked Dr. McLaughlin of FDA to arrange a meeting which was held November 25, 1969. Present at this meeting were:

Dr. I. Mitchell and Dr. R. Bates of the National Cancer Institute; Dr. J. McLaughlin, FDA; Dr. J. E. Johnson; Mr. D. D. McCollister; Dr. V. B. Robinson; and Mr. V. K. Rowe of Dow.

I requested that Dr. Mitchell identify the test procedure by which we could reexamine 2,4,5-T and the suspected contaminant. Dr. Mitchell replied that tests with Sprague-Dawley rats would be the best procedure for reconfirmation and further stated that, for the purpose, it would be superior to a test with mice.

I offered to underwrite the cost of confirmatory experiments in the laboratories of the National Institute of Health, in the laboratories of a third party (independent of Government or Dow) or in the Dow laboratories open to observation at any time by personnel of the Department of HEW.

Dr. Mitchell stated that he would have confidence in the work if it were done in Dow laboratories. We agreed to repeat the Bionetics work with Sprague-Dawley rats using Dow 2,4,5-T of regular production grade. If this study yielded positive results the Bionetics results would be confirmed. If the results were negative it would be necessary to run further tests on graded levels of the contaminant and on refined 2,4,5-T. It was agreed that Dow would provide samples of 2,4,5-T and 2,3,7,8-tetrachlorodibenzo-p-dioxin to the National Institute of Environmental Health Science laboratories at Research Triangle, N.C.

Moreover—Robinson and Rowe of Dow would visit the NIEHS laboratories in order to confer with them concerning the details of the test methods to be used.

On December 1, 1969, I met with Dr. DuBridge and Dr. Buckley of the OST to apprise them of the possibility of a contaminant in the sample tested by Bionetics and also the information known to Dow. At this meeting the same points were discussed as presented to the Mrak Commission. The plan for additional testing as discussed with Drs. McLaughlin, Bates, and Mitchell of DHEW was also presented.

Dr. DuBridge stated that he would be interested in further information as it developed and was willing to consider new evidence when it was available. I promised to report the results of our work.

Information has been supplied primarily through Dr. Burger of the OST.

On December 11, 1969, Dr. V. B. Robinson and V. K. Rowe met with Drs. Falk, Courtney, and Gaylor at the Research Triangle and discussed with them the design of teratological study to be conducted on Dow regular production 2,4,5-T. Agreement on the design of the experiment was easily achieved and was followed in our studies.

At this meeting Dr. Courtney of the NIEHS Laboratory provided a two gram sample of the 2,4,5-T used by the Bionetics Laboratory. This sample was examined at Dow with the following results:

1. Rabbit ear tests showed a positive reaction characteristic of the contaminant.

2. Analysis by gas liquid chromatography indicated the presence of 27 plus or minus 8 p.p.m. of 2,3,7,8-tetrachlorodibenzo-p-dioxin.

In late December Dr. Burger of the OST requested a review of the chemistry of 2,4,5-T production to be presented to Dr. Baldeschweiler, a consultant of the agency. The information for this report was organized by Dr. Blair of Dow and presented at a meeting with the OST on December 29, 1969 in Washington.

Dr. Blair is on my right.

By January 12, 1970, we had made enough progress in the teratological study in rats with Dow production grade 2,4,5-T to make a report to Dr. Egeberg, Assistant Secretary for Health and Scientific Affairs, HEW. Copies were sent to other involved persons in DHEW and USDA. This report showed that the Dow 2,4,5-T of regular production grade did not cause birth defects as determined by gross examination of fetuses. The dosage levels used were selected in consultation with Drs. Falk, Courtney, and Gaylor of NIEHS.

Furthermore, we were able to report to Dr. Egeberg that a pilot study with pregnant rabbits fed the same 2,4,5-T had not caused birth defects. Dr. H. L. Richardson, pathologist, FDA, observed the results of both of these tests.

These preliminary observations were followed by the more time consuming microscopic examinations of the tissues and detailed skeletal examinations. This work confirmed the preliminary findings.

The final report of the study was presented before the Society of Toxicology in Atlanta, Ga., on March 17, 1970. I wish to insert into the record at this point an abstract of this report entitled "Teratogenic Study of 2,4,5-trichlorophenoxyacetic Acid in the Rat" by J. L. Emerson, D. J. Thompson, C. G. Gerbig, and V. B. Robinson, The Dow Chemical Co.

Senator HART. That will be received.

(The information follows.)

A study to determine the embryotoxicity or teratogenicity of 2,4,5-tricholorophenoxyacetic acid containing less than one part per million of 2,3,7,8-tetrachlorodibenzo-p-dioxin has been completed in Sprague-Dawley derived rats. Five treatment groups, each consisting of 25 females were administered 1, 3, 6, 12 or 24 mg/kg/day of the compound via gavage in 0.25% METHOCEL® on days 6 through 15 of gestation. A single group of 50 females received the suspending vehicle and served as controls. The following parameters were examined: clinical observations, maternal body weights (prebreeding and day 20), number and position of fetuses and resorptions, number of corpora lutea, pup weight and sex, gross external examination of pups, and macroscopic examination for intestinal hemorrhage in pups. Two-thirds of each litter were fixed in Bouin's solution and one-third was prepared for alizarin red-S staining

and skeletal examination. Examination of Wilson sections under the dissection microscope or of alizarin stained skeletons of all fetuses from the 24 mg/kg/day group and an equal number of control fetuses was performed. Representative stained histologic sections through the head, thorax, and abdomen of 10 control and 10 high level fetuses were studied for histopathologic changes.

No clinical or gross pathologic signs of adverse chemical effect were observed in treated dams during the period of treatment or gestation. Similarly, litter size, number of fetal resorptions, birth weights and sex ratio of pups appeared to be unaffected by chemical treatment. Skeletal and visceral examination of high level and control fetuses as well as histopathologic examination of certain fetuses failed to reveal any teratogenic or embryotoxic effects.

The results of this study fail to substantiate the findings reported recently (unpublished data: Bionetics Research Laboratories, Bethesda, Maryland) of serious effects in fetuses obtained from dams given comparable daily doses of 2,4,5-T containing approximately 27 parts per million of the contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

Dr. JOHNSON. Thank you.

In accordance with the plan discussed with the DHEW in December, as soon as the preliminary results of the 2,4,5-T study on rats indicated no fetal anomalies, we proceeded to conduct a teratology study in rats with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Dosages were used which bracketed the levels of the contaminant which were given inadvertently to the rats in the Bionetics study. The results of this experiment indicated that a high of maternal and fetal toxicity was associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Dr. H. L. Richardson of FDA and Dr. C. T. G. King, National Institute of Dental Research, NIH, participated in the observations made on these animals at necropsy at the Dow Laboratories in Midland.

We concluded that the presence of the tetrachlorodibenzo-p-dioxin in the sample tested in the Bionetics Laboratories could have accounted for the observations reported and attributed 2,4,5-T. At this point I wish to insert into the record an abstract of the report as presented to the Society of Toxicology, March 17, 1970, Atlanta, Ga., entitled "Teratogenic Study of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in the Rat" [1] by G. L. Sparschu, F. L. Dunn, and V. K. Rowe, The Dow Chemical Co.

Senator HART. That will be inserted.

Dr. JOHNSON. Thank you.

The detailed results of these tests were also presented by Dow personnel to the scientists of FDA, NIH, NIEHS, in Washington on February 24, 1970.

In addition to our investigations with laboratory animals, we have also utilized the medical records of Dow employees accumulated throughout their Dow careers.

Our physicians have made an in-depth evaluation of the health of male employees who have been exposed to 2,4,5-T in manufacturing operations for from 6 months to approximately 20 years. From the medical data available, over 50 clinical parameters were selected for statistical evaluation. The control population for this evaluation consisted of 4,600 other individuals for whom similar data were available.

After careful study of this information, it was the conclusion of our medical staff that there was no evidence that exposure to 2,4,5-T had resulted in adverse effects.

[1] See p. 470.

It is our belief that the adverse effects reported by the Bionetics Laboratories were the result of a contaminant—2,3,7,8-tetrachlorodibenzo-p-dioxin—and were not caused by 2,4,5-T.

Moreover it is our belief that 2,4,5,-T produced under specifications requiring less than 1 part per million of 2,3,7,8-tetrachlorodibenzo-p-dioxin present no practical hazard when used in accordance with good agricultural practices.

Now, from here on it is historical.

If I may I would like to add some recent information and this like the information presented this morning, was only obtained this past weekend, as a matter of fact.

The Midland Labs extended the work by Dr. Robinson using the Dow 2,4,5-T on rats. This is the production grade of Dow 2,4,5-T. The dosage of 50 milligrams per kilogram, higher than that recommended in the consultation at NIEHS, was administered. At this dose we found one fetus in 203 viable fetuses with intestinal hemorrhage. At the 100 milligram per kilogram dose level; there was 75 percent mortality of the dams and high fetal mortality.

At this point I should point up that these levels of 2,4,5-T put extreme stress on the physiology of the test animal.

The next experiment involved drinking water supplied to rats. This drinking water was saturated with 2,3,7,8-tetrachlorodibenzo-p-dioxin and in this case no effect was detected in 21 litters of 259 pups.

In a third experiment we studied combinations of pure 2,4,5-T with 2,3,7,8-tetrachlorodibenzo-p-dioxin. In this experiment 2,4,5-T was fed at 50 milligrams per kilogram and maintained at a base level throughout all tests to which graded or incremental dosage of additional 2,3,7,8-tetrachlorodibenzo-p-dioxin were added. Bear in that this base amount of 2,4,5-T was administered orally in a single dose each day.

I will read the list of results. When 50 milligrams per kilogram of pure 2,4,5-T were administered with zero added 2,3,7,8-tetrachlorodibenzo-p-dioxin, no adverse effects were observed in rats.

When one-hundredth of a microgram per kilogram of the tetrachlorodibenzo-p-dioxin was combined with the 50 milligrams of 2,4,5-T, again no effect was observed. When three-hundredths of a microgram per kilogram per day of the tetrachlorodibenzo-p-dioxin was combined, again no effect was observed. When six-hundredths of a microgram per kilogram of the tetrachlorodibenzo-p-dioxin was combined with the 2,4,5-T, we observed 8 percent of gastrointestinal hemorrhages and one cleft palate in 155 fetuses. When 0.125 micrograms of the tetrachlorodibenzo-p-dioxin was combined we had an increase in the resorptions and some gastrointestinal hemorrhage. We also saw subcutaneous edema in three of the 134 fetuses.

When five-tenths and 1.0 micrograms of the tetrachlorodibenzo-p-dioxin were combined with the base level of 2,4,5-T, we observed an increased incidence in the fetal mortality, in resorptions, in gastrointestinal hemorrhages, and in subcutaneous edema, cleft palates were observed in four out of 14 and five out of 15 litters respectively.

Again I should stress the base level of 2,4,5-T was extremely high, approaching the toxic dose; moreover the base level of dioxin was extremely high.

Is there any further comment to be added on that, Mr. Rowe?

Mr. ROWE. I think you covered it very well.

Dr. JOHNSON. These data were only available yesterday. The microscopic study of soft tissues and skeletal study have not been done. These animals were stressed to the limit of their tolerance of 2,4,5-T and, in addition, to a toxic stress of the tetrachlorodibenzo-p-dioxin.

I personally feel it is important to consider the dosage related to the response with these materials and later I will get into a more definitive discussion of that, if you desire.

Based on the proposed finite tolerance of 2,4,5-T in food but less than the 1 part per million of tetrachlorodibenzo-p-dioxin in the 2,4,5-T the safety factor for humans as derived from animal studies in several thousandfold. This is well in excess of the safety factors judged adequate by toxicologists in some branches of government and many others in the scientific community.

I would like to make a few comments, because the word dioxin has become almost a cause celebre, in order that we get some conception of the amounts involved. If this rather simple illustration is okay, I guess it really isn't very simple but I will try it, if it is all right.

Now, this is assuming what is *not* going to happen. It is assumed that all food ingested by man contained 0.2 part per million of 2,4,5-T. This is not going to happen but I am just making that assumption for purposes of illustration.

The total, 2,4,5-T ingested per day in the food of a person would be three-tenths of a milligram, that is equal to 300 micrograms, a very small amount. If the 2,4,5-T contained 1 part per million of the tetrachlorodibenzo-p-dioxin, the daily food would contain one one-millionth of this 300 micrograms or——

Senator HART. Doctor, back up.

If the two parts per million——

Dr. JOHNSON. Two-tenths.

Senator HART. Had how much dioxin?

Dr. JOHNSON. One part per million.

May I proceed?

Senator HART. Yes.

Dr. JOHNSON. If the two-tenths parts per million of 2,4,5-T in the food of a person contained one part per million of tetrachlorodibenzo-p-dioxin, the food would contain one-millionth of the 300 micrograms or 300 picograms.

A picogram is one-trillionth of a gram and a gram is one-twenty-eighths of an ounce.

If a person ingested this amount of dioxin each day for 100 years, which is an optimistic period, the total amount ingested would be only 11 micrograms. A grain of sugar weighs about 120 micrograms. So this 11 micrograms of tetrachlorodibenzo-p-dioxin would be no more than one-tenth of a granule of sugar and that level affords a 6,000-fold safety factor over the amounts, as we observed, to cause no embryotoxic effects in rats.

I realize that this has nothing but illustrative value, but it is not very much the tetrachlorodibenzo-p-dioxin we are talking about. That is my main point, Senator.

Senator HART. All right, some who are better equipped than I to handle the technical aspects may pursue it with you. I just confess that I will have to inhale it if not ingest it.

Dr. JOHNSON. The simplest way to think of it is one-tenth of the weight of a grain of sugar over a lifetime. Senator Hart, I am not sure how you would like to proceed. I have some other remarks to make which get to this question, perhaps in shortening the time interval. Would you prefer for me to answer questions now or at a later time?

Senator HART. I have a few questions. Suppose we ask a few questions here and if they do not raise items that you intended to discuss, we would welcome the additional reaction.

One very quick one has to do with the test that you report having made on 110 male employees. I am sorry, 130 with no evidence of adverse effect.

Has there been any evaluation made of the effect on female employees or were any exposed?

Dr. JOHNSON. None were exposed, Mr. Chairman.

Senator HART. Was that on purpose consciously?

Dr. JOHNSON. No, the manufacturing plant is not a desirable place for most women to put in their time.

Senator HART. I am not sure you speak for all women. That is another subject entirely.

Dr. JOHNSON. This has unraveled far enough.

Senator HART. I am sorry, I didn't realize there was a vote signal and we must recess to permit me to get to it. So I will be back shortly.

(Recess.)

Senator HART. Doctor, let us ask these few questions and then if they do not raise all of the items that you would like to make additional comment on, we would welcome your making a comment.

When did you first have reason to believe that a dioxin contaminant in 2,4,5-T could cause chloracne?

Dr. JOHNSON. Just a moment, sir, and I will get the exact date.

Senator HART. Yes.

Dr. JOHNSON. Senator Hart, in regard to the 2,4,5-T, it was 1964 when we first developed an awareness of this possible buildup of the dioxin potential in the product—in October.

Senator HART. There was no, as far as you were aware, earlier study here or in Europe that identified tetradioxin as causing chloracne?

Dr. JOHNSON. Not in 2,4,5-T.

Senator HART. Tetradioxin in some formula had been found to cause chloracne?

Dr. JOHNSON. Yes. In 1950 the Germans ran into difficulty with chloracne and they isolated the dioxin. This was in the process of manufacture of 2,4,5-trichlorophenol. We were aware of it.

Senator HART. When did you begin the manufacture of 2,4,5-T?

Dr. JOHNSON. We began the manufacture of 2,4,5-T in 1948. I should point out in addition, however, that we were monitoring our workers for chloracne since 1941. This was also when the rabbit ear test was developed by Dow.

Senator HART. If the German study indicated the tetradioxin as a chloracne cause in 1950, would that have suggested to you any test run on the potential presence or dangers of this contaminant in the 2,4,5-T that you were introducing?

Dr. JOHNSON. Yes, and we monitored products made with 2,4,5-trichlorophenol knowing that the dioxin resided in the intermediate.

Senator HART. Did those tests include any tests to determine the carcinogenicity of dioxin in the formula that you were producing?

Dr. JOHNSON. No, sir, they did not.

Senator HART. Then in June of 1964 you were concerned about the chloracne, and in your testimony you say I think that you notified a number of people. You notified the Department of Health of Michigan and the Industrial Health Institute in Ann Arbor and various other health oriented individuals in private medicine and industry, and you had the meeting in March of 1965 notifying other manufacturers. Why not the FDA and the U.S. Department of Agriculture?

Dr. JOHNSON. At that time, Senator Hart, we considered our obligation discharged by removing the dioxin from our product, by notifying health authorities in the State and we thought we had the problem solved.

In retrospect it would have been much preferred had we notified the U.S. Department of Agriculture, the agency that has statutory authority for the registration.

Senator HART. I would agree. It would seem to me, and as I say, it is easier second guessing, that it would have been more appropriate and foremost to notify the agency that registers the product. But what about the 2,4,5-T that you learned in June of 1964 had this contaminant? Is it a practice to make an effort to remove the contaminated product from the shelves? What about the product in the houses and retail channels? What retrieval effort is made? What call back?

Dr. JOHNSON. Senator Hart, according to the procedures we were using at the time we did not produce or sell contaminated 2,4,5-T within the limits of sensitivity we had available for measure.

Senator HART. What was it you were notifying people about in 1964?

Dr. JOHNSON. This was the chloracne problem.

May I add a comment?

Senator HART. Yes.

Dr. JOHNSON. As indicated in the formal testimony, the manufacture of 2,4,5-T, when pushed by temperature or heat, will produce this contaminant; it builds up as a caustic insoluble oil. This problem produced the chloracne which initiated the actions we took.

Senator HART. What percentage of dioxin was in the 2,4,5-T that you produced prior to the correction made at this time?

Dr. JOHNSON. It was—now you are asking about the 2,4,5-T?

Senator HART. I beg your pardon?

Dr. JOHNSON. You are asking about the 2,4,5-T. At the time there was an undetectable amount using the rabbit ear test as an indicator.

It might be important to point out that chromatographic procedures for analysis were developed during the late 1950's and early 1960's and applied with increasing sensitivity. This is a changing background of analytical capability. At the time we were using the rabbit ear test and we did not know that dioxin was present, if any.

Senator HART. As of now, do you believe that the earlier 2,4,5-T that you were producing was safe or unsafe?

Dr. JOHNSON. Safe, because we were monitoring the intermediate 2,4,5-T-chlorophenol and similar products since 1941.

Senator HART. But you really do not know how much dioxin was in it. How can you say that?

Dr. JOHNSON. It was, according to our ability to determine dioxin, at that time, we thought zero.

Senator HART. But you know better now, don't you?

Dr. JOHNSON. We know better now because we have more sensitive methods.

Senator HART. How can you say it was safe earlier when we know now it was not?

Dr. JOHNSON. In our firm, Mr. Chairman, the matter of safety is considered to be related to the dosage. The product as we sold it and monitored it; and, as it was used, according to the label, we are convinced it was safe. There was not sufficient exposure to the tetrachlorodibenzo-p-dioxin, even if it had been there in the amounts known today, one part per million or a half part per million. We are convinced it was safe.

Senator HART. Did you feel any requirement at any time to engage others in making the judgment which you just made about the earlier formula?

Dr. JOHNSON. The answer is no.

Senator HART. Now, do you agree with the position that has been taken, as announced this morning by the three Secretaries?

Dr. JOHNSON. In a matter of practical hazard, an an imminent hazard to health, I do not agree. Under the climate of pressure today, it was a wise decision.

Senator HART. That sounds like you are planning to run for reelection, but you do not want to announce it.

I am reminded that the action taken today was to cancel, not to suspend the nonliquid 2,4,5-T and that means, as I understood the Surgeon General's testimony this morning, the Secretaries do not regard that form of 2,4,5-T as imminently hazardous to health.

Do you want to rephrase your answer so as to respond specifically to the finding on the nonliquid?

Dr. JOHNSON. The nonliquid form I consider to be safe under labeling registrations.

Senator HART. I think the Food and Drug Committee finds it has potential hazard to health and therefore cancels rather than suspends it. Do you agree with that?

Dr. JOHNSON. I do not agree that cancellation is necessary.

Senator HART. Is it your intention to appeal the action?

Dr. JOHNSON. This must be considered. I cannot answer at this time. We have few, if any, products of our own that are nonliquid formulations of 2,4,5-T.

Mr. BICKWIT. Do you have any evidence on the degradeability of 2,4,5-T?

Dr. JOHNSON. Yes. Just one moment, please. The evidence is present in the literature published by the land grant colleges and the U.S. Department of Agriculture, predominantly. A publication by Dr. P. C. Kearney, E. A. Woolson, J. R. Plimmer, and A. R. Isensee, reviews the subject of degradation in a chapter entitled "Decontamination of Pesticides in Soils."

Page 139 indicates the persistence of 2,4,5-T to last 5 months. There are additional references and review articles that, if you like, I could submit for the record. It would take quite a bit of time to read these, but I could do so, Mr. Chairman, if you like.

Senator HART. They will be received.

(The material follows.)

List of References on Degradation of
phenoxy herbicides, including 2,4,5-T

The Dow Chemical Company
April 15, 1970

Audus, L. J. (1960) Microbial Breakdown of Herbicides in Soils, p. 1-19 in Herbicides and the Soil, edited by E. K.Woodford and G. R. Sagar, Blackwell Scientific Publications, Oxford. (45 references)

Sheets, T. J. and L. L. Danielson (1960). Herbicides in Soils, p. 170-181 in The Nature and Fate of Chemicals Applied to Soils, Plants, and Animals, ARS 20-9, USDA (62 references)

Thiegs, B. J. (1962). Microbial Decomposition of Herbicides, Down to Earth, Fall 1962. (31 references)

Freed, W. H. and M. L. Montgomery (1963). The Metabolism of Herbicides in Plants and Soils, p. 1-18 in Vol. 3 of Residue Reviews, edited by F. Gunther, Springer-Verlag, Inc., New York. (115 references).

Kearney, P. C. (1966). Metabolism of Herbicides in Soils, p. 250-262 in Organic Pesticides in the Environment, Advances in Chemistry Series 60. (42 references)

Kearney, P. C., E. A. Woolson, J. R. Plimmer, and A. R. Isensee (1969). Decontamination of Pesticides in Soils, p. 137-149 in Vol. 29, Residue Reviews, edited by F. Gunther, Springer-Verlag, New York.

Loos, M. A. (1969). Phenoxyalkanoic Acids, p. 1-50 in Degradation of Herbicides, edited by P. C. Kearney and D. D. Kaufman, Marcel Dekker, Inc., New York. (166 references)

Midwest Research Institute (1967). Herbicide Residues and Their Persistence, and Some Factors Determining the Fate of Herbicides, p. 208-231 and 232-249 in Assessment of Ecological Effects of Extensive or Repeated Use of Herbicides, final report processed for Defense Documentation Center, Defense Supply Agency, AD 824 314, U. S. Dept. of Commerce.

Alexander, M. and M. I. H. Aleem (1961). Effect of Chemical Structure on Microbial Decomposition of Aromatic Herbicides. J. Agr. Food Chem. 9, 44.

Bell, G. R. (1960). Studies on a Soil Achromobacter which Degrades 2,4-Dichlorophenoxyacetic Acid. Can. J. Microbial. 6, 325.

Bollag, J. -M., C. S. Helling, and M. Alexander (1968a). Enzymatic Hydroxylation of Chlorinated Phenols. J. Agr. Food Chem. 16, 826.

Bollag, J. -M., G. G. Briggs, J. E. Dawson, and M. Alexander (1968b). Enzymatic Degradation of Chlorocatechols. J. Agr. Food Chem. 16, 829.

Tiedje, J. M., J. M. Duxbury, M. Alexander, and J. E. Dawson (1969). 2,4-D Metabolism: Pathway of Degradation of Chlorocatechols by Arthrobacter sp. J. Agr. Food Chem. 17, 1021.

Duxbury, J. M., J. M. Tiedje, M. Alexander, and J. E. Dawson (1970). 2,4-D Metabolism: Enzymatic Conversion of Chloromaleylacetic Acid to Succinic Acid. J. Agr. Food Chem. 18 (2), 199.

Rogoff, M. H. (1961). Oxidation of Aromatic Compounds by Bacteria, p. 193 in Volume 3 of Advances in Applied Microbiology, edited by W. W. Umbreit, Academic Press, New York.

Aly, O. M. and S. D. Faust (1964). Studies on the Fate of 2,4-D and Ester Derivatives in Natural Surface Waters. J. Agr. Food Chem. 12, 541.

Crosby, D. G. and H. Tutass (1966). Photodecomposition of 2,4-Dichlorophenoxyacetic Acid. J. Agr. Food Chem. 14, 596.

Crosby, D. G. and M. -Y. Li (1969). Herbicide Photodecomposition, p. 321-363 in Degradation of Herbicides, edited by P. C. Kearney and D. D. Kaufman, Marcel Dekker, Inc., New York. (102 references)

Brown, E. and Nishioka, Y. A. (1967). Pesticides in Water. Pesticides Monitoring J. 1(2), 38-46.

Norris, L. A. (1968). Stream Contamination by Herbicides after Fall Rains on Forest Land. Western Society of Weed Science Research Progress Report, p. 33-34.

Montgomery, M. L. and L. A. Norris (1970). A Preliminary Evaluation of the Hazards of 2,4,5-T in the Forest Environment, USDA Forest Service Research Note PNW-116.

Sheets, T. J. and J. F. Lutz (1969). Movement of Herbicides in Runoff Water. Presented at the Dec. 1969 meeting of the American Society of Agricultural Engineers, Chicago, Illinois.

Bailey, G. W., J. D. Pope, Jr., and D. R. Cochrane (1968). The Degradation, Kinetics, and Persistence of Silvex Under Impound Conditions. Abstracts p. 43, WSSA Meeting, New Orleans, Louisiana, February 1968.

Residue Reviews, Volume 29 (1969), Edited by F. Gunther,
Springer-Verlag, New York

Decontamination of pesticides in soils

By

P. C. Kearney,* E. A. Woolson,* J. R. Plimmer,* and A. R. Isensee*

I. Introduction

The soil, as a medium for decontamination, offers a large number of processes by which organic substances can be destroyed. As such, progressive accumulation of organic pesticides would appear to be unlikely. Unfortunately, the chemical and physical properties of certain insecticides and herbicides afford them a degree of stability against the natural destructive processes in soils. The stability of these compounds is best illustrated in a recent summary of persistence data on 12 major classes of pesticides in a number of soil types (Fig. 1) (Kearney *et al.* 1969). Persistence values are expressed in months and each bar represents one or more classes of herbicide or insecticide. Each open space in the bar represents an individual pesticide falling within the larger chemical class of compounds. The length of each bar depicts the time for each class of pesticide to decrease 75 to 100 percent of the amount applied. These values are based on normal rates of application. As anticipated, the organochlorine insecticides are the most persistent pesticides. The organic herbicides persist for a few days or for more than 12 months depending on their respective properties. Only the

* U.S. Department of Agriculture, ARS, CR, Beltsville, Md. Specific mention of trademark instruments does not constitute an endorsement by the U.S. Department of Agriculture over others designed to give similar performances.

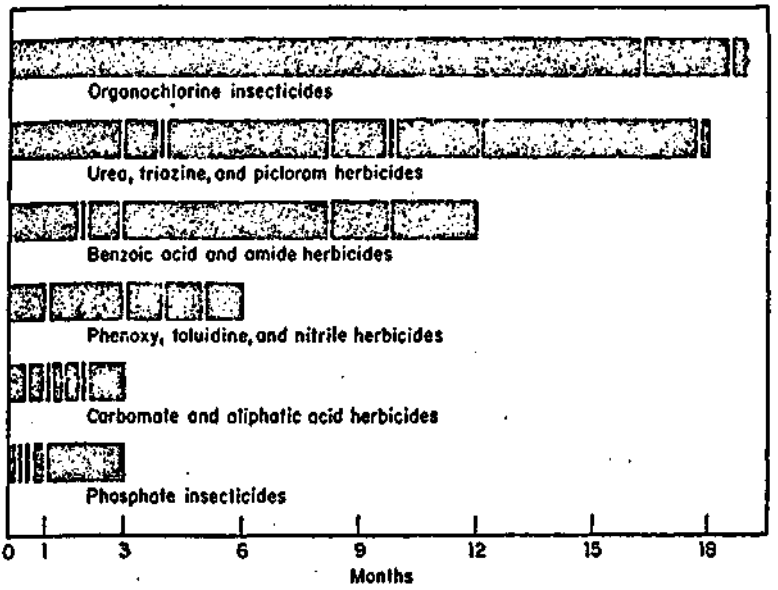


Fig. 1. Persistence of pesticides in soils

major herbicides that persist for a month or longer are shown in Figure 1. The phosphate insecticides do not persist for long periods in most soils. A more detailed picture of organochlorine pesticide persistence is shown in Figure 2. Chlordane and DDT usually persist for several years while heptachlor and aldrin extend their activity through the formation of their respective metabolites, *i.e.*, heptachlor epoxide and dieldrin.

Why are we concerned about pesticide residues in soils? Their effects would appear to be very subtle and not directly related to man or his environment. The need for pure water is obvious, for man directly consumes processed water. Not so with soil, and therefore, why is there concern over soil contamination?

There now exists unequivocal evidence that most plants can absorb and translocate residual pesticides from contaminated soils (Nash 1968). Uptake and translocation have been demonstrated with radiolabeled pesticides incorporated directly into the soil and then seeded with several agronomic crops. Many of the soil variables that influence this uptake process have been studied. For example, increasing the concentration of dieldrin and DDT in soil causes a corresponding increase in the amount of insecticide recovered by the wheat plant. The plant is apparently indiscriminate in its ability to absorb most substances from soils. Therefore a link exists between residual pesticides in soils and man's food chain. In addition, residual pesticides are potential pollutants of water and air.

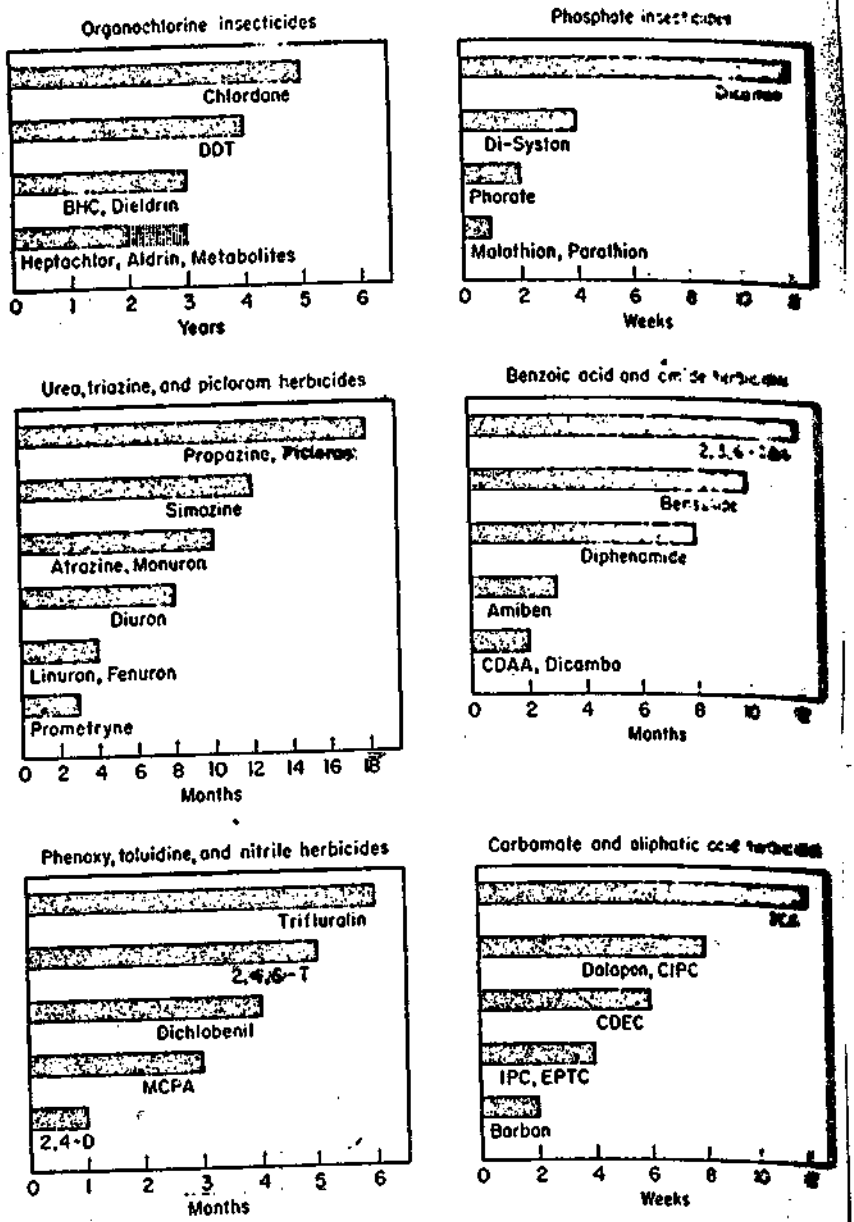


Fig. 2. Persistence of individual pesticides in soils

Now that we have defined the problem and the need for decontamination in soils, what methods are available for removing persistent pesticides? The fate of a pesticide in soils is determined by a number of processes which come under the general heading of physical, biological, and chemical (Fig. 3). Under physical, they include phase

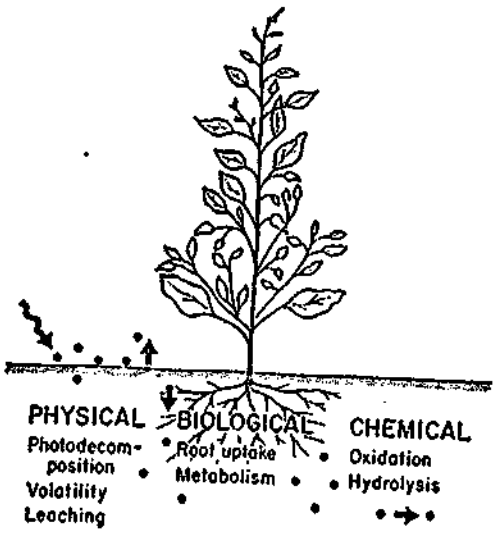


Fig. 3. Processes that determine fate of a pesticide in soil

decomposition, volatility, leaching, and adsorption. Under biological, they include root uptake and microbial metabolism and under chemical they include oxidation, reduction, and hydrolysis. Several of these are responsible for decomposing pesticides. For example, soil enrichment techniques for the proliferation of specific microorganisms effective in metabolizing foreign substances have been a favorite method for microbiologists. It is conceivable that "catch plants" or plants with a high affinity for certain pesticides could be grown on contaminated soils and then removed after taking up some part of the residual pesticides. It is possible that a combination or several of these methods could be employed to reduce pesticide concentrations in soils.

If each of these processes were active on a pesticide, then soil residues would not exist. If soil microorganisms could be induced to rapidly metabolize DDT to the level of carbon dioxide, then soils would be an ideal medium for decontamination. They don't, and herein lies the problem of reducing soil residues. The work to be reported today deals with two approaches to reducing pesticide residues. The first concerns the use of light to decompose transported pesticides in water and hence its application to irrigation waters and soils. The second concerns the decontamination of field soils containing DDT by flooding and inoculation with microorganisms.

II. Pesticide decontamination in water

A major source of environmental contamination is caused by the movement of materials from their site of application. Pesticides move primarily in the liquid or vapor phase. Pollution of water by organic

compounds is undesirable, contamination by biologically active compounds is potentially dangerous. Two particular situations in which pesticides in water cause concern relate to the waste problem encountered in static or lagoon operations and to irrigation systems. The danger of the latter situation is best illustrated with the water-soluble, mobile herbicide picloram (4-amino-3,5,6-trichloropicolinic acid). Minute amounts of this potent herbicide irrigated on sensitive crops could have disastrous results. Concentrations as little as 10 p.p.b. in soils have a lethal effect on such sensitive crops as soybeans.

What methods are available for removing pesticides in water? The use of energetic radiation (ultraviolet or gamma ray) has been suggested (MARCUS *et al.* 1962) for fragmentation or destruction of organics in water. This method should be effective on a large number of pesticides especially in dilute aqueous solutions. Unfortunately, the technology has developed little beyond the experimental stage. Large scale ultraviolet and gamma irradiation techniques are in early technological stages and wider industrial application is the needed stimulus for further development.

We have determined the periods of exposure required to destroy the biological activity of a number of herbicide solutions in a small-scale ultraviolet irradiator. The method may be applicable as a pretreatment for waste waters or as a treatment for contaminated irrigation systems.

The reaction system is a borosilicate glass vessel and holds 250 ml. of the solution to be irradiated (Fig. 4). A quartz, water-cooled, double-walled tube is fitted into this well and is immersed in the solution. A 450 watt Hanovia lamp is suspended in the well. The quartz well transmits a large part of the available energy down to the shortest wavelengths emitted by the lamp.

Solutions of herbicides in water were irradiated (250 ml. at a time) for periods of 5, 10, and 15 minutes. Picloram, 2,4,5-T, bromacil, diphenamid, and 2,3,6-TBA were the herbicides used in the initial experiments. These compounds were chosen because their solubility and persistence are sufficiently high for them to be potential contaminants in irrigation water. Oats were used to bioassay picloram, 2,4,5-T, and diphenamid and cucumber was used for bromacil and 2,3,6-TBA. The treatments consisted of zero, 5, 10, or 15 minute irradiations of the solutions at 1, 5, or 10 p.p.m. concentrations and a control in which no herbicide was added. The time required to destroy the five herbicides is shown in Figure 5 (PLIMMER 1968).

A five-minute irradiation greatly reduced the phytotoxicity of picloram and 2,4,5-T at five and 10 p.p.m. and bromacil at one p.p.m. Diphenamid and 2,3,6-TBA required a 10-minute exposure. These initial results indicate that five minutes or less exposure to ultraviolet irradiation of solutions in the range of one p.p.m. would significantly lower their phytotoxicity to plants. More pesticides, under conditions

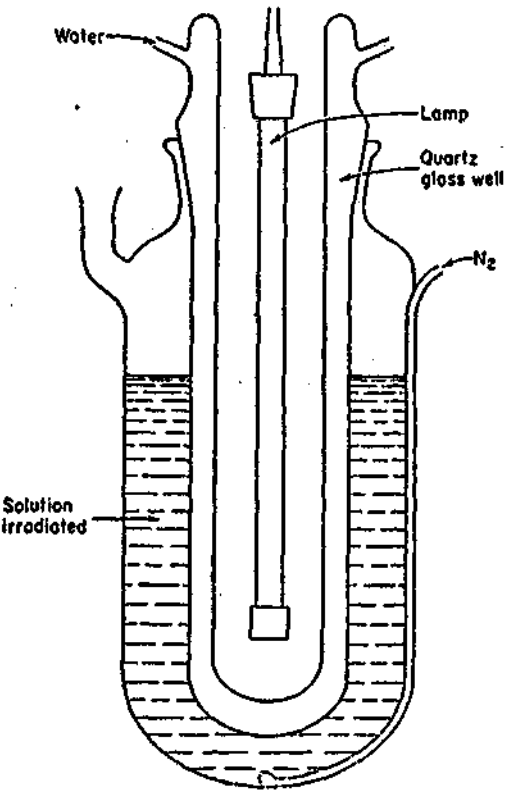


Fig. 4. Photochemical reaction vessel

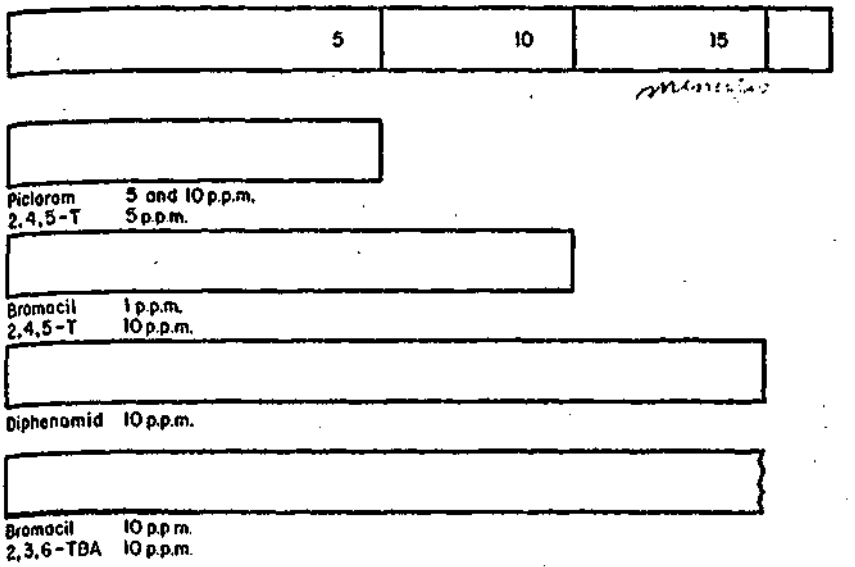


Fig. 5. Times required to destroy herbicidal activity by irradiation

approaching large volumes of water on flow systems need to be investigated before wide application to pesticide decontamination is attempted.

III. DDT decontamination

Turning our attention to field soils, one of the most serious residue problems occurs with organochlorine insecticides. As previously mentioned, DDT persists for several years in most agricultural soils. Complete removal of these residues may be impossible. However, lowering existing residues below some arbitrary threshold level may result in minimal plant residues. Our objective, then, was to find some agent in nature that could attack the DDT molecule. This agent did not necessarily have to cause complete destruction of DDT, but perhaps alter it to a more biodegradable or labile form. Obviously, organisms indigenous to most soils do not possess this agent. Intestinal microorganisms in the rat, however, are able to alter DDT extensively.

Whole cells or cell-free extracts of *Aerobacter aerogenes* catalyze the degradation of DDT *in vitro* to at least seven metabolites (Wedemeyer 1966), previously reported from rats given DDT orally (Peterson and Robison 1964). These reactions proceed by dechlorination, elimination, oxidation, and finally decarboxylation to yield dichlorobenzophenone. Therefore, it occurred to us soils inoculated with *A. aerogenes* may be capable of metabolizing residual DDT.

To test this hypothesis, three soil types were amended with zero, 5, 10, and 20 p.p.m. of DDT. The soils were Lakeland sandy loam, Hagerstown silty clay loam, and Sharkey clay. Four-hundred g. of soil were weighed into pots and DDT was applied in chloroform solution. Since metabolism of DDT by *A. aerogenes* appears to occur most rapidly in still cultures or under partially anaerobic conditions, two-thirds of the soils were flooded to simulate partial anaerobiosis. The water covered the soils to a depth of approximately one inch. One-third of the DDT-treated soils was maintained at field capacity, one-third was flooded, and one-third was flooded and inoculated with *A. aerogenes*.

Cells of *A. aerogenes* from slants obtained from the American Type Culture (ATC 13048) were mass cultured in three percent trypticase soy broth at 36° C. for eight hours. The cells were harvested by high-speed centrifugation, washed, and resuspended in the original volume of fresh broth solution. The cells were incubated for three days in still cultures, harvested again, washed, and concentrated 10-fold in a one percent yeast-extract solution. Aliquots (10 ml.) were added to the flooded soils and mixed into the surface layers. All soils were sampled at weekly intervals. Residual DDT and products were measured by electron-capture gas chromatography. Moist soil samples were extracted with a 3:1 mixture of hexane:isopropanol and injected on to a

column of five percent SE 30 on 100/120 mesh DMCS-treated Chromosorb W. Column temperature was 210° C. with a flow rate of 120 ml./minute. Detector temperature was 215° C.

A total of 18 different parameters could be examined considering there are possible three soils, three concentrations, and two treatments with *A. aerogenes*. Of primary interest is the effect of flooding with and without inoculation. Therefore, let us examine the disappearance of only DDT at the highest rates of application in the three soil types (Fig. 6). Two general trends are apparent. First DDT

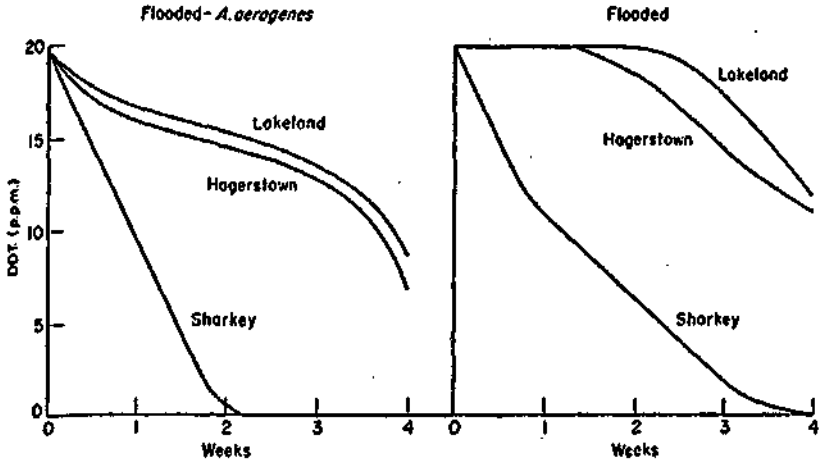


Fig. 6. DDT decomposition in three soils (see text)

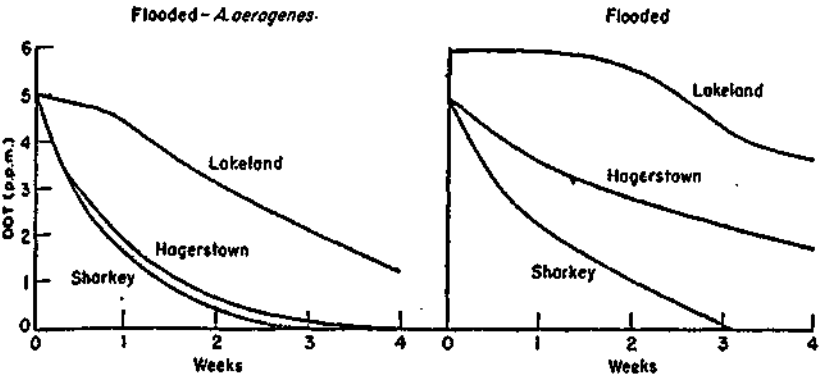


Fig. 7. DDT decomposition in three soils (see text)

disappeared more rapidly in the inoculated soils. Second, complete loss occurred in the Sharkey clay, while lesser amounts were lost from Lakeland and Hagerstown in both flooded series. DDD (TDE) was observed to occur in most soils, but its appearance did not parallel

losses in DDT. In other words, there was a net loss of DDT-DDD in this system and no other products were detected by gas chromatography. Somewhat the same picture is encountered at five p.p.m. of DDT (Fig. 7), with complete loss in the Sharkey clay, more accelerated disappearance in the inoculated soils, and a general trend for total loss of DDT-DDD with time. Recovery values for DDT during the early sampling periods on Lakeland were high and explain the values obtained above five p.p.m. in the flooded soils.

Additional studies were initiated to determine the fate of the DDT in these systems. The experiment using Lakeland soil at five p.p.m. plus DDT-^{14}C was set up in a closed glass system for trapping $^{14}CO_2$. Nitrogen was bubbled through the system and any gaseous carbon dioxide was trapped in base. Samples of the carbon dioxide trapping solution were removed periodically and analyzed for radioactivity. Less than one percent of the total added activity was released in volatile components. This would be in general agreement with results previously reported (Guenzi and Beard 1967).

Therefore, several other alternatives are available to explain the disappearance of the DDT from these soils. A polar metabolite could be present in the aqueous phase and not removed by the hexane:isopropanol extraction, or a metabolite is absorbed on some soil component and not recovered. It is also possible that a volatile metabolite is formed which escapes from the system with time. The presence of a polar metabolite can apparently be ruled out, since only 7 to 28 percent of the added DDT-^{14}C could be detected in the aqueous phase. Subsequent research with ^{14}C-DDT in a similar type of experiment indicated that up to 20 percent of the ^{14}C could not be extracted from flooded soils after a four-week incubation period. The radioactivity is apparently tightly bound to soil particles in some form not recoverable with hot hexane:acetone, ethyl acetate, or ethanol (Kearney and Woolson 1969). Therefore, we must conclude the loss is real and reproducible, although the mechanism is not fully understood.

IV. Conclusions

Radiation as a method for preventing the spread of pesticides in water systems deserves further consideration. Ultraviolet radiation for sterilization processes is in commercial use. High energy radiation has similar applications and its use in food processing has been studied. Ultraviolet radiation has been used for the complete removal of organic materials from sea water samples on a laboratory scale (Armstrong *et al.* 1966). A pebble-bed type of reactor has been described, but not further developed, which appears suitable for continuous ultraviolet irradiation of solutions. A radioactive material is incorporated into impervious ceramic "pebbles" together with a suitable phosphor which emits ultraviolet radiation. A flow system is envisaged

with the pesticide in dilute solution flowing over the ceramic pebbles. In addition to thermal methods of destruction, we suggest that radiation methods be further explored as a simple means of removing pesticides in situations where applicable.

Removal of pesticides from soils is a far more complex process, since the system is static and not conducive to flow-through operations. Several methods have been suggested for reducing residues. The use of calcium polyphosphate on the residual chloro-*s*-triazines has not been successful under field conditions (HARRIS *et al.* 1968). The use of absorbents (charcoal) for removing toxic materials in replanting certain nursery stock has been successful; extention of this technique to field conditions for atrazine and organochlorine residues has been attempted (LICHTENSTEIN *et al.* 1968). In these situations, however, the cure may be worse than the sickness, since a new and far less understood variable is now being introduced into the soil. Such may be the case with microbial decontamination of DDT by *A. aerogenes*. Many experimental variables would have to be studied before large-scale field studies would be justified.

In the final analysis any decontamination method would have to be economically feasible before it would be acceptable to the farmer. The most promising and yet still unexplored method for reducing soil pesticide residues lies at the molecular level. A thorough understanding of the electronic and steric factors that render a pesticide molecule susceptible to the natural biological degradation pathways is still in early developmental stages. This approach would appear to offer the most challenging chemical method for reducing residues on a continuing basis.

Table I. *Common and chemical names of pesticides mentioned in text*

Bromacil	5-bromo-3-*sec*-butyl-6-methyluracil
DDD	1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane
DDT	1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane
Diphenamid	*N,N*-dimethyl-2,2-diphenylacetamide
Picloram	4-amino-3,5,6-trichloropicolinic acid
2,4,5-T	2,4,5-trichlorophenoxyacetic acid
2,3,6-TBA	2,3,6-trichlorobenzoic acid

Summary

A limited number of methods are available for decontaminating soils and water. Complete destruction of organic herbicides in water may be effected by exposure to intensive high-energy radiation. Measurement of the rates of photodecomposition of picloram, diphenamid, bromacil, 2,3,6-TBA and 2,4,5-T by bioassay techniques is in progress. Experiments with model continuous flow cells indicate rapid destruction of organic dyes. No picloram could be detected in a solution of initial concentration of 1 p.p.m. after 30 minutes or less exposure to high intensity UV irradiation. Where complete removal is not feasible, reduction of existing residues below a level in soils where the

significance of plant uptake becomes minimal may be desirable. Biological alteration of a persistent pesticide to a more degradable form is another method of reducing residues. DDT residues in three soils (Sharkey clay, Hagerstown silty clay loam, and Lakeland sandy loam at rates of 5, 10, and 20 p.p.m.) were reduced in flooded soils and flooded, enriched soils inoculated with *Aerobacter aerogenes*. Losses were most rapid in the inoculated Sharkey and Hagerstown soils receiving the lowest rate of DDT application during the first week. Parallel experiments conducted with ring labeled DDT-^{14}C showed no $^{14}CO_2$ evolved from the inoculated soils. Conventional chromatographic and radiometric techniques indicated a conversion of DDT to DDD and a reduction of the total DDT-DDD residue in soils with time.

Résumé *

Décontamination de pesticides dans les sols

On dispose d'un nombre limité de méthodes décontamination des sols et des eaux. On peut effectuer une destruction des herbicides organiques dans l'eau par exposition à des radiations intenses de haute énergie. La mesure des taux de photodécomposition du piclorame, du diphenamide, du bromacile, du 2,3,6-TBA et du 2,4,5-T par bio-essais est en progrès.

Des expériences à l'aide de cellules à courant continu indiquent une destruction rapide des colorants organiques. Aucune trace de piclorame n'a pu être décelée dans une solution qui en contenait initialement 1 p.p.m., après 30 minutes ou moins d'exposition à une irradiation UV de haute intensité. Dans les cas où une élimination complète n'est pas possible, une réduction des résidus présents en dessous d'une certaine limite peut être souhaitable pour les sols où l'importance de l'absorption par les plantes devient minime. La transformation biologique d'un pesticide persistant en une forme plus aisément décomposable est une autre méthode de réduction des résidus. Des résidus de DDT dans trois sols (argile de Sharkey, limon argileux alluvionnaire de Hagerstown et limon sableux de Lakeland aux concentrations de 5, 10 et 15 p.p.m.) ont été réduits dans des sols inondés et des sols inondés enrichis, inoculés avec *Aerobacter aerogenes*. Les pertes ont été plus rapides dans les sols de Sharkey inoculés et les sols de Hagerstown ayant reçu la plus faible concentration en DDT durant la première semaine. Des expériences parallèles avec du DDT marqué ^{14}C n'ont révélé aucun dégagement de $^{14}CO_2$ des sols inoculés. Les techniques chromatographiques et radiométriques conventionnelles ont indiqué une conversion du DDT en DDD et une réduction des résidus totaux de DDT-DDD dans les sols en fonction du temps.

* Traduit par S. Dormal-van den Bruel.

Zusammenfassung *

Dekontamination von Pestiziden im Boden

Eine begrenzte Zahl an Methoden steht zur Verfügung, um Böden und Wasser zu reinigen. Vollständige Zerstörung von organischen Herbiziden in Wasser kann durch Belichtung mit intensiver Strahlung von hoher Energie bewirkt werden. Messungen der Photoabbauraten von Picloram, Diphenamid, Bromacil, 2,3,6-TBA und 2,4,5-T durch Biotesttechniken sind im Fortschreiten begriffen. Experimente mit Modelldurchflusszellen zeigen schnelle Zerstörung von organischen Farben. In einer Lösung mit einer Anfangskonzentration von ein p.p.m. konnte nach 30 Minuten oder weniger Belichtung mit hoch intensiver ultravioletter Strahlung kein Picloram mehr nachgewiesen werden. Da, wo vollständige Entfernung nicht möglich ist, wird die Reduzierung von vorhandenen Rückständen in Böden unter eine Menge, wo die Bedeutung für die Pflanzenaufnahme minimal wird, wünschenswert. Biologische Veränderung eines persistenten Pestizids zu einer abbaufähigeren Form ist eine andere Methode, um Rückstände zu reduzieren. DDT Rückstände in Böden (Sharkey Ton, Hagerstown sandiger Ton-Lehm und Lakeland sandiger Lehm mit Raten von 5, 10 und 20 p.p.m.) wurden in überfluteten Böden reduziert und weggeschwemmt und angereicherte Böden mit *Aerobacter aerogenes* geimpft. Die Verluste waren am schnellsten in den Sharkey und Hagerstown Böden, welche während der ersten Woche die niedrigste Rate von DDT Behandlung erhalten hatten. Parallele Untersuchungen, welche mit ^{14}C-ring-markiertem DDT durchgeführt wurden, zeigten keine $^{14}CO_2$ Entwicklung in den beimpften Böden. Konventionelle chromatographische und radiometrische Techniken deuteten die Umwandlung von DDT zu DDD an und eine Reduktion des Gesamt-DDT-DDD-Rückstandes in Böden mit der Zeit.

References

Armstrong, F. A. J., P. M. Williams, and J. D. H. Strickland: Removal of organic matter from sea water by ultraviolet light. Nature 112, 481 (1966).

Guenzi, W. D., and W. E. Beard: Anaerobic biodegradation of DDT to DDD in soil. Science 156, 1116 (1967).

Harris, C. I., D. D. Kaufman, T. J. Sheets, R. G. Nash, and P. C. Kearney: Behavior and fate of s-triazines in soils. Adv. Pest Control Research 8, 1 (1968).

Kearney, P. C., and E. A. Woolson: Personal communication (1969).

—, R. G. Nash, and A. R. Isensee: Persistence of pesticide residues in soils. In M. W. Miller and G. C. Berg, ed.: Chemical fallout: Current research on persistent pesticides, Chapt. 3, pp. 54-67. Springfield, Ill.: Charles C Thomas (1969).

Lichtenstein, E. P., T. W. Fuhremann, and K. R. Schulz: Use of carbon to

* Übersetzt von A. Schumann.

reduce the uptake of insecticidal soil residues by crop plants. J. Agr. Food Chem. 16, 348 (1968).
MARCUS, R. J., J. A. KENT, and G. O. SCHENCK: Industrial photochemistry. Ind. Eng. Chem. 54, 20 (1962).
NASH, R. G.: Plant adsorption of dieldrin, DDT, and endrin from soils. Agron. J. 60, 217 (1968).
PETERSON, J. E., and W. H. ROBISON: Metabolic products of p,p'-DDT in the rat. Toxicol. Applied Pharmacol. 6, 321 (1964).
PLIMMER, J. R.: Unpublished data (1968).
WEDEMEYER, G.: Dechlorination of DDT by Aerobacter aerogenes. Science 152, 647 (1966).

Mr. BICKWIT. Do you have any evidence on the degradeability of dioxin?

Dr. JOHNSON. In terms of photodegradation, we have some evidence —this is not exhaustive—but nevertheless some evidence that would indicate a half life of—excuse me, I will get that in just a moment. This is the type of experiment run in a laboratory in a solvent. The half life was 2½ hours under a typical type of sun lamp. This is only an indicator type of test. The prognosis is in the presence of light, dioxin will degrade. Degradation in soil we do not have information on. We are diligently, however, preparing carefully labeled—radiochemically labeled—2,3,7,8-tetrachlordibenzo-p-dioxin, and supplying this to the U.S. Department of Agriculture for tests as quickly as possible, because this is the fastest way to get the answer.

Mr. BICKWIT. Do the light conditions you are using exist in nature?

Dr. JOHNSON. Primarily in ranges and pastures, yes. Because 2,4,5-T is intercepted on the upper surfaces of weeds and brush more deposits in exposed than in shaded conditions. The predominance would be exposed to light conditions. Obviously some is going into the shade. Under those conditions of lesser light intensities, I can't reply.

Mr. BICKWIT. Is it ultraviolet light you are using?

Dr. JOHNSON. Yes, with a typical sunlamp.

Mr. BICKWIT. Do I summarize your findings correctly when I say you believe 2,4,5-T is degradeable in a matter of months, and with respect to dioxin there is some evidence it is degradeable, but we do not know whether or not it is?

Dr. JOHNSON. Correct. I should again emphasize if specifications are low, the minute amount presents an extremely small exposure.

Mr. BICKWIT. With regard to the calculations that you offered us earlier, you have assumed that a person who ingests 2,4,5-T is ingesting one part per million dioxin. Isn't it possible——

Dr. JOHNSON. May I clarify the statement for the assumption?

Mr. BICKWIT. Sure.

Dr. JOHNSON. The 0.2 parts per million referred to a hypothetical situation.

Dr. JOHNSON. People do not ingest that much, and that is the total dietary intake, and moreover, 2,4,5-T has not been a residue in food. It is, in effect, zero tolerance.

Mr. BICKWIT. I understood that. What I still understand to be your assumption was that any amount of 2,4,5-T, no matter how small, that was ingested, would have one part per million dioxin in it. That was the basis of your calculation.

Dr. JOHNSON. The specification we have set for our own product is less than one part per million. Actually, it is 0.5. The assumption was to make it easy mathematically, on the high side, and some day I will learn not to draw these mathematical analogies. They never quite make the mark.

Mr. BICKWIT. Well, I hope you learn right now. What I was suggesting as a possibility is, that since 2,4,5-T is degradeable, and since we do not know whether or not dioxin is degradeable, that although your product, when sprayed, has 0.5 parts per million of

dioxin, by the time that is ingested it may have one part per thousand, one part per hundred. It may in fact have more dioxin than 2,4,5-T.

Dr. JOHNSON. I am sorry. I don't understand your logic for this escalation of the dioxin in foods.

Mr. BICKWIT. If we have a compound which contains another compound, and the larger compound breaks down, while the smaller compound does not, the smaller compound becomes a greater and greater percentage of the large compound.

Dr. JOHNSON. Well, Dr. Blair has some information that may be useful in this rather hypothetical situation. May he answer?

Senator HART. Yes.

Dr. BLAIR. Actually, in regard to the question the way you phrased it, if there was a degradation of the 2,4,5-T, there would not be a corresponding increase in that amount of dioxin.

Mr. BICKWIT. Certainly not.

Mr. BLAIR. So your question as phrased has no meaning as I tried to interpret it. Unless you mean that possibly as 2,4,5-T degrades, that it would degrade through dioxin, or into a dioxin product. Then, while the percentage would go up, the exact concentration has not gone up.

Mr. BICKWIT. What I am saying is that your calculations are based on the view that the hypothetical view—that we would allow a 0.5 parts per million tolerance for 2,4,5-T. You then conclude, if 0.2 parts per million of 2,4,5-T were ingested, that an extremely minute amount of dioxin would be ingested.

What I am questioning is whether the conclusion follows from that premise?

Dr. BLAIR. Yes, it would be an extremely small amount, and it would not increase with time.

Mr. BICKWIT. What I am suggesting is that the 2,4,5-T could break down so that it complies with the 0.2 parts per million tolerance. In fact, it might even disappear. Yet, we would be ingesting a good deal of dioxin for which there would be no tolerance.

Dr. BLAIR. It is not possible.

Mr. BICKWIT. I don't understand why not.

Dr. BLAIR. How could you ingest 2,4,5-T that contained a tenth of a part per million——

Mr. BICKWIT. It contained that much when it was sprayed.

Dr. BLAIR. Yes, and with time the concentration of dioxin in that environment has not increased one iota.

Mr. BICKWIT. That's right. The amount has not increased.

Dr. BLAIR. But is not possible to ingest more than what is there. It doesn't make sense.

Dr. JOHNSON. Mr. Chairman, could I make a comment?

Senator HART. I wish I could be helpful. I would like to see if a rephasing of the question might not elicit the point that bothers Mr. Bickwit.

Dr. JOHNSON. Do you want to comment first, or have the question rephrased first?

Senator HART. Make your comment.

Dr. JOHNSON. I think Mr. Bickwit is talking about the possibility of the 2,4,5-T degrading in the food consumed, whereas the degradation question only applies to environment.

Mr. BICKWIT. No, I am not.

Senator HART. Try it again.

Mr. BICKWIT. You are assuming that the maximum amount that we would ingest would be 0.2 parts per million in every amount of food, in every iota of food, that we eat. From that you conclude that the amount of dioxin in that food would be one-millionth of 0.2 parts a million, which I admit is an extremely small amount. I am questioning your assumption of whether the amount of dioxin, compared to the amount of 2,4,5-T that is ingested, would be one-millionth merely because dioxin is one-millionth of the 2,4,5-T amount when it is sprayed?

What I am suggesting is that the dioxin consumed may actually be more than the amount of 2,4,5-T consumed, even if it is only one part per million when sprayed.

Dr. JOHNSON. Is the situation that you have in mind that the 2,4,5-T is sprayed?

Mr. BICKWIT. Yes.

Dr. JOHNSON. The 2,4,5-T is sprayed into the environment. This contains one part per million. Then the 2,4,5-T degrades. The dioxin does not. And over a period of time, is there is a buildup of dioxin? Is this the problem?

Mr. BICKWIT. I have another way of getting at this, perhaps.

If one gram of 2,4,5-T is sprayed on a blueberry—an unlikely assumption—and the 2,4,5-T degrades so that it complies with the tolerance of 0.2 parts per million, you may still have one microgram of dioxin sitting on that blueberry, without any violation of the tolerance of 2,4,5-T. And that one microgram may well be toxic.

Dr. JOHNSON. I would like to find a degradeable material like that. Theoretically, obviously, if the one gram of degradeable material contained the one microgram or one part per million of nondegradeable material, then the one gram degrades, that one microgram would still be sitting there.

Is that the point you are trying to make?

Mr. BICKWIT. That's right.

Dr. JOHNSON. That's right.

Mr. BICKWIT. Well, how then does a 0.2 parts per million tolerance for 2,4,5-T protect us from dioxin?

Dr. JOHNSON. Because the ratios of those two during the process of growing and supplying the food are going to remain essentially the same.

Mr. BICKWIT. You have no evidence for that statement.

Dr. JOHNSON. I know I don't, but you have no evidence for the hypothetical question, either.

Mr. BICKWIT. I do have some evidence, by your own statement, that dioxin is more likely to be nondegradeable than 2,4,5-T.

Dr. JOHNSON. But these are matters of relative rates. You are suggesting an instantaneous degradation.

Mr. BICKWIT. I am using a hypothetical situation, as you were.

Dr. JOHNSON. My purpose in bringing up what appears to have been a rather foolish example was merely to give a feeling for the magnitude of how much dioxin we are talking about.

Mr. BICKWIT. And my contention is that once the assumption on which the hypothesis was based is removed, then it does not give that feeling.

Dr. JOHNSON. I am sorry. I don't agree.

Senator HART. That is one of the fortunate features of having a reporter here. We can all grab the record in the morning to see if we can count out an understanding and agreement of yesterday.

Mr. BICKWIT. You state in your statement that members of the Mrak Commission had not seen the report prior to Dr. DuBridge's October 29 announcement.

Last week Dr. Kotin of NIEHS told us as work was completed it was promptly passed along to the Commission.

Do you mean to imply that the Bionetics report was not complete until this time?

Dr. JOHNSON. I did not receive a copy of the report of the Panel on Teratology until very late in the deliberations.

Mr. BICKWIT. I think that is unfortunate. I wonder if you have knowledge as to why that was so?

Dr. JOHNSON. No.

Mr. BICKWIT. We have have been told that whenever you burn a polychlorinated phenol, dioxin production is possible, or even likely. Could you enumerate a few of your products that contain such phenols?

Dr. JOHNSON. There's trichlorophenol, tetrachlorophenol and pentachlorophenol, and sodium salts thereof.

Mr. BICKWIT. What is a Dowicide product?

Dr. JOHNSON. The products I just mentioned. Since you related it to the phenols, I assume that is what you are talking about.

Mr. BICKWIT. Yes. I wonder if you could furnish us with a list of all such products——

Dr. JOHNSON. Mr. Rowe clarified a point here that our Dowicide trademark applies not only to chlorophenols, but to other antimicrobials.

Mr. BICKWIT. I wondered if we could have for our files a list of the products which you produce which contain polychlorinated phenols?

Dr. JOHNSON. Yes. I prefer the term chlorophenols. Polychlorinated phenols would indicate a polymer. Chlorophenols.

Senator HART. Now I am getting into something that you don't have to be anything to understand except efficient.

Do you have anything to do with Lake St. Claire?

Dr. JOHNSON. I am not really prepared to discuss that in detail, I don't have any direct responsibility for the Sarnia Plant.

Senator HART. I would be disciplined severely by my outdoor friends if I didn't ask what you are going to do about the mercury that has found its way into Lake St. Claire.

Dr. JOHNSON. I might say this, we intend to exercise responsible action.

Senator HART. That is like the lawyer admitting his client is innocent. But I won't push you if you are not prepared.

Dr. JOHNSON. I am not prepared to say any more.

Senator HART. Thank you very much.

Are there any further items that you have?

Dr. JOHNSON. Yes, if I can take a few more minutes.

Senator HART. Time is not a problem.

Dr. JOHNSON. I would like to make a comment or two, again on dioxin before getting into the last part of my testimony.

There have been questions raised about the decomposition of 2,4,5-T and dioxin. 2,4,5-T is unstable at elevated temperatures. We were able to get degradation when 2,4,5-T or dioxin were burned on paper. We were unable to detect any dioxin residue in the smoke. Now, these are very early bits of information, strictly preliminary but I thought I should mention it at this time.

This morning you asked a question about shortening the time interval between the early indication of some possible difficulties and the learning of sufficient truth about a situation so that we can take appropriate action prior to an imminent hazard to health. Hopefully, if we can improve some of our combined procedures between Government and industry, we can shorten that time.

I have a few remarks to make that apply to the scientific community as well as to this interface with Government. Screening tests, as we have heard, (and I commented on some of my own,) I think are of value. As early indicators. But screening tests alone, without the consideration of quantitative data, can be quite misleading and if necessary——

Senator HART. Can be what?

Dr. JOHNSON. Quite misleading and I think it is necessary to develop understanding in meetings where open reports are published early and where scientific information is submitted to the challenge of other scientists; scientists of the universities; government; industry and professionals so these things can be considered in the caldron of open technical debate.

I think we can operate more quickly to shorten this gap if there is more openness about reports. Moreover, I think another procedure for shortening the time is better to understand test procedures. The screening tests are simple but those tests which are substantive enough to justify intelligent action require, the consideration of scientists outside of the generating laboratory, and the review of appropriate methods.

Test methods for regulatory action are—or for clearance of new products, in particular, require consideration. I don't mean we should lock every clearance procedure into a lock step because the development of techniques is a mutable, changing thing. But the confirmation of tests prior to official acceptance as this relates to public policy is important.

The Association of Official Agricultural Chemists has established a useful procedure. When these gentlemen and this association are considering new tests, the topic is identified, the first scientists to work on the test are identified, collaborators are found to work out objective tests and these tests are run in separate laboratories so that confirming methodology can be established.

As a result the test must be reliable; that is, it must give accurate, precise and reproducible results when used by qualified analysts. It must be practical; simple. It must be available to all analysts and it must be substantial; that is, supported by collaborative study.

Now, I will say these types of tests apply primarily to clearance procedures or to regulatory tests. I am not saying extreme tests are not in order. But those which support the authority of regulatory backup need this type of scientific consideration.

The American Standards Society also has procedures for standardizing tests. These are physical tests. They involve one or more laboratories in the preliminary study and interlaboratory studies, maybe as many as 10, in the more refined studies, and this results in a standard test method which can be used.

The Department of Commerce, National Bureau of Standards, does an excellent job in developing standards. Moreover they have an industrial associates program which permits the access of industry into these laboratories, for a period of time to work, so that industry representatives can better understand the problems of standards and go back to their companies better informed.

Protocols for clearance of new and existing products, I think are important for the Food and Drug Administration to consider seriously. Again I don't mean standard tests would remain forever, but protocols. Industry needs to know where it stands, industry also need to participate; appropriately and at arm's length, to be sure, nevertheless; to participate with specific information.

The period of time between 1966 and now could have been shortened by sharing appropriate information, and I admit we could have assisted by volunteering earlier. But there seems to be some reverse of togetherness and there seems to be great concern that communication between governmental agencies and industry is suspect and would be misused.

I would hope that one valuable result to come of this would be a continuation of developing science fortified by interest in this important matter of communication.

On the point of developing protocols (and I frankly think the whole subject of teratology requires the vigor of scientific debate among professional peers involving industry, university and government) I would hope the National Academy of Sciences could provide such a forum, if not the National Academy perhaps the New York Academy of Sciences and I intend to help encourage this because it is important. It is important that these ideas are traded openly and published.

I would mention that the World Health Organization, in a document entitled "Principles for the Testing of Drugs for Teratogenicity," the World Health Organization Technical Report, Serial No. 364 or 1967, has the following to say on test animals for teratology. on the subject of the chick embryo, page 7.

The chick embryo contributes greatly to basic embryological knowledge. However, for the screening of drugs for teratogenicity, its use is not recommended. It is too sensitive to a wide range of agents and affords no parallel with the anatomical and physiological relationship existing between pregnant mammals and her conceptus.

I will support the idea of the use of a chick embryo for screening tests, early indications, but from that point on additional protocols and understanding, I think, are necessary.

Again in the line of helping to shorten this interval, I think strict standards are necessary in defining matters of safety and public health. No question about it. I don't object to tought regulations. But industry needs to know where it stands and the dialogue is important. The dialogue between agencies can help to shorten this time and I am glad to see distinct improvement in communications between the Department of Health, Education, and Welfare and the Department of Agriculture.

Again I would like to say we are not talking about a locked-in procedure that could be used as an excuse to avoid further responsibility for progress.

Another point; millions have been spent on cancer research. Yet to this day, adequate experiments have not been devised or supported on an adequate scale by government to establish thresholds. By that I mean levels below which no response occurs. Without that type of information—there will be continuing public fear as analytical methods become more and more sensitive.

Senator HART. May I interrupt you there?

Dr. JOHNSON. May I finish the point and come back?

With teratogens, mutagens, radioactivity and teratology, this all applies. In other words, if the dose is low enough can any of these effects be avoided. This is the big question today. It is the question which coupled with sensitive analytical methods makes the Delaney clause a difficult thing to live with.

I would like to make the comment that vitamin A, an essential nutrient, is a teratogen at high doses. So this matter of developing test procedures and a big enough experiment with carcinogens, mutagens, teratogens or low levels of radioactivity, needs to be done on a national scale and supported so that some of this public fear can be avoided and so we know where we stand.

Scientists should put limitations on their speculations and preconceptions and get the facts but also realize we have a job in serving the public policy that does not exactly follow the scientific method.

I hope we can work out quicker procedures to go from early indications to reliable decisions by involving some of the procedures I have talked about. After responding to your question, I would like to make that final statement.

Senator HART. I am not sure I need to ask the question now. I agree completely on the desirability of doing that which our best minds can suggest to shorten the time.

The question I intended to interrupt you with I think you did answer. I was going to ask to what extent in developing these thresholds and having broader sampling and more reliable data, to what extent is that the responsibility of the Federal Government?

Dr. JOHNSON. On the matters of carcinogenicity, teratology, radiation. and mutagenesis, where such public concern is involved, and since this involves a wide variety of suspected material, it is my opinion that the Federal Government should play a major role in supporting this research, both in its own laboratories and in extra-

mural research done in universities *and* in industry to help get the diversity of methods and the best thinking of the nation.

Senator HART. All right, then to the extent that the story that we have heard today and heard last week reflects delay and a failure of communication, I would hope that the suggestions you have made and the discussions that we have had all will insure that there will be no delay, there will be no barrier to free communication, and there will be no suspicion attached as agency and producer try to drive through to the answer.

Now, you wanted to remind us of what the Ribicoff committee said.

Dr. JOHNSON. Yes, if I may.

This is read from Report No. 1379 of the 89th Congress, 2d Session "Interagency Environmental Hazards Coordination, Pesticides and Public Policy", a report of the Committee on Government Operations United States Senate, made by its Subcommittee on Reorganization and International Organizations. I will read from page 50. And this puts the scientists on the spot, including me.

The heading of the paragraph is "The Responsibilities of the Scientists" and we are talking about industry scientists, governmental, and university.

"The committee asked the scientific witness for meaningful advice for the Congress, but much of the testimony was inhibited by defense of past positions, employer loyalties, and lack of authority."

Scientists should do as thorough a job of preparing answers on aspects of research administration and planning as they do on the technical details of the work.

The maker of public policy must have alternatives from which to choose. There are always strong vested interests which resist change. Unless the technological situation (in this case, ecology) can be clearly explained and related to public policy issues, the decisionmaker is hardput to recommend any new course. This understanding must be extended also to the citizen. No great social issues have ever been decided until the needs were clear to the man in the street.

Scientists cannot assure that their knowledge will reach the decisionmaker through the normal channels of publication and review in the scientific community. Without shortcutting the classical methods of assessing the truth, there is still an obligation to interpret what is known and replace emotion, rumor, and misconception with a clear explanation of the facts.

The role of the scientist in relation to the legislator is limited to an area somewhere short of the decisionmaking point. Proper use of scientific advice requires considerable effort on both the part of the scientific community and the body politic.

This is the end of my statement.

Senator HART. I am glad you reminded all of us of it.

Doctor, thank you very much.

Do your associates have anything to add in light of the statement?

All right, thank you very much.

Dr. JOHNSON. Thank you.

Senator HART. Next we have Dr. Samuel Epstein, Children's Cancer Research Foundation.

Doctor, we welcome you.

(The following is referred to on p. 376.

ABSTRACT

Teratogenic Study of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in the Rat. G. L. Sparschu, F. L. Dunn and V. K. Rowe, The Dow Chemical Company, Midland, Michigan.

2,3,7,8-Tetrachlorodibenzo-p-dioxin has been found to occur in small amounts as a contaminant in some commercially manufactured samples of 2,4,5-trichlorophenoxy acetic acid. The purpose of this study was to learn whether the presence of this impurity possibly could account for the fetal abnormalities in test animals reported in a recent study (unpublished data: Bionetics Research Laboratories, Bethesda, Maryland).

The dioxin was administered by gavage in 9:1 corn oil-acetone solution in doses of 0 (control), 0.03, 0.125, 0.5, 2.0 and 8.0 micrograms per kilogram body weight per day to groups of 24 (control) and 12 (treatment) pregnant female Sprague-Dawley derived rats on days 6 through 15 of gestation.

On day 20 of gestation, each dam was sacrificed and a cesarean section performed. The number of viable and dead fetuses and early and late resorptions was recorded. Each fetus was examined for any gross abnormalities. Two-thirds of each litter were fixed in Bouin's solution, Wilson sections were examined under the dissection microscope, and tissues were studied for histopathology. One-third of each litter were fixed in alcohol and examined for skeletal abnormalities by alizarin red-S staining.

Presented at the meeting of the Society of Toxicology, Atlanta, Georgia, March 17, 1970.

No differences were observed in the fetuses taken from dams treated at the dosage of 0.03 μg/kg/day and those taken from dams that received the solvent vehicle only. At the 0.125 μg/kg/day dosage, all parameters studies were within normal limits except for a very slight decrease in average weight, and the occurrence of intestinal hemorrhage (18/127) and subcutaneous edema (22/80) in the fetuses from dams that received this treatment. At the 0.5 μg/kg/day level, the number of fetuses was reduced and the number of resorptions and fetal deaths was increased. The average weight of the viable fetuses was very slightly decreased. The incidence of intestinal hemorrhage (36/99) and subcutaneous edema (31/65) was markedly increased over that seen in the 0.125 μg/kg/day treatment.

At the 2.0 μg/kg/day level, only 7 viable fetuses were obtained. These were from 4 of the 11 litters examined. Resorptions were numerous, intestinal hemorrhage was frequent (4/7), and subcutaneous edema was present in all of the 4 fetuses examined by Wilson section. One fetus from this treatment level was found to have a kinked tail and two of its feet were somewhat misshapen. Skeletal examination, however, revealed no evidence of bone abnormalities.

The 8.0 μg/kg/day dosage level proved to be toxic to the dams. There were no viable fetuses in the dams which were examined on day 20 of gestation. All resorptions occurred early and no evidence of fetal tissue was found.

Skeletal examinations revealed delayed ossification of some sternebrae and skull bones. This occurred generally throughout the various groups, including controls, and is not considered to be of practical significance.

The results of this study indicate a high level of maternal and fetal toxicity to be associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Its presence in the sample tested in the Bionetics Laboratories study could well have accounted for the observations reported and attributed to 2,4,5-trichlorophenoxy acetic acid.