

Phoned Mr. Dig
on 10/20.

EVANS & DIXON

ATTORNEYS AT LAW

16TH FLOOR MARQUETTE BUILDING

314 NORTH BROADWAY

ST. LOUIS, MISSOURI 63102

(314) 621-7755

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1897-1964

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October 19, 1981

CONFIDENTIAL

George Roush, Jr., M.D. SUBJECT TO PROTECTIVE ORDER.
Director

Dept. of Medicine & Environmental Health
Monsanto Chemical Company
800 North Lindbergh Blvd
(Mailing Station A2SA) - G2WG
St. Louis, Missouri 63166

Re: Piatt - Missouri Horse Arena Cases

Dear Dr. Roush:

I appreciate very much your having copied and forwarding to me the enclosed article which is one of the best we have seen on the Missouri Horse Arena episode which we are involved in, as you know.

As discussed with you today, I would appreciate it very much if you could give me the full reference and the journal from which this came as we desire to have the entire article copied. Also, on Page 166, in brackets, you will see a reference to a Dr. Beale who apparently wrote a letter to the editor of Lancet (referred to in Footnote 24) along with a Dr. W. T. Shearer, M. M. Karl and A. M. Robinson in 1977, with reference to these Missouri Horse Arena cases. It is very interesting to us and will be immensely helpful if we can find out where we can reach Dr. Beale, because you will notice that he apparently examined one of these girls and the mother and other sister about 1972 or 1973 after this incident, and then he says he has now re-examined one of the two girls and can find no disability of a permanent nature. He concludes "Our experience demonstrates that people exposed to dioxin can recover completely with no apparent sequela from toxin. It remains to be determined whether the exposure to dioxin in these children will result in abnormal pregnancies or affect their offspring".

His conclusions in this letter to Lancet obviously support our position entirely and since he is a neutral physician here it would be very helpful if we can find him and arrange to take his deposition. If you have any index or means of finding out who this man is and where he can be located, I would certainly appreciate your letting us know so that we can contact him and arrange to get his testimony in this case.

C03695

George Roush, Jr., M.D.

Re: Piatt - Missouri Horse Arena Cases

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Third, and last, the client that we represent in these cases certainly expects you to bill us as a consultant. I, personally, would feel very bad if you did not, because the help that you have given us has been extremely important to us, and we certainly do not want to take advantage of your friendship in situations like this. I believe that we told you from the first meeting that we expected you to bill us in this, and we certainly do. This should be on a personal basis, and we will handle it in any way you want us to. Please think this over and call me so that we can discuss this further. I will even come out and write the bill for you if necessary.

With kindest personal regards, I remain

Sincerely,



John R. Dixon

JRD:rm

Enclosure

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and Allen (132) published a note on herbicides and spina bifida. They examined all the children referred to in the television program and found one case of an open neural tube defect (spina bifida cystica) while the other children were normal in every respect. It was possible that these apparently "normal" children had spina bifida occulta, however, in none of them had radiography been done and it was probable that the children had nothing more than sacral dimples.

As a final note in relation to this episode, the following brief article appeared in the *New Zealand Medical Journal* (9):

Publicity on certain chemicals as causation of malformations of the human fetus has been widespread. Some of the publicity has been sensation mongering and not all the remarks from the profession have been in keeping with a balanced assessment of scientific evidence. It is proper that there should be intelligent public awareness of the various environmental hazards that may come from the use of chemicals...in farming...however, those who would write of their experiences in medical journals must remember that disasters are the staple of the sensation mongers in the news media industry.

Until recent publicity there had been no suggestion that 2,4,5-T, which has been used for over 20 years in New Zealand, was responsible for congenital malfunctions either in man or in farm animals. It is the duty of the physicians (and scientists) who have any concern for science to attempt to make valid observations that can be repeated. In the problem at issue, fetal malformations are nature's common mistakes which we have no desire to perpetrate or to increase, although they are the inevitable price that is paid for our place on the evolutionary scale. There are extensive gaps in our knowledge but they will be filled only by patient work. Unresolved problems of fetotoxicity can only be solved by accurate record keeping at all stages of pregnancy.

The Missouri Horse Arena Episode

Many of the episodes discussed in this chapter involved "suspected" TCDD poisoning; however, the Missouri Horse Arena Episode is one in which TCDD was confirmed to be the causative agent.

In 1972, The Missouri Division of Health and The Center for Disease Control, Atlanta, Georgia (13) reported an investigation of a horse arena in eastern Missouri where 54 of 57 horses exposed to the arena had died of an illness characterized by skin lesions, severe weight loss, and hepatotoxicity. Birds, dogs, cats, insects, and rodents were also found dead in and around the arena, and one 6-year-old girl exposed developed hemorrhagic cystitis (characterized by blood in the urine). Analysis of urine cultures for bacterial and viral pathogens were negative. Immediately prior to the onset of illness, the arena had been sprayed with salvage oil for dust control.

The report (13) also noted that similar horse illnesses and deaths occurred in two other horse arenas in the eastern Missouri area sprayed by the same salvage oil

company. The three arenas had been sprayed within 1 month of each other. Subsequent to investigation, soil from all three arenas was excavated and disposed. No further problems occurred since the excavations.

As with earlier episodes, the report soon received national attention. Unfortunately, some newspapers misquoted the report by implying that the cause of the incident was a result of spraying contaminated 2,4,5-T herbicide (12).

Carter et al. (44) and Kimbrough et al. (122) have published detailed chemical, epidemiological, and pathological data of the episode. The investigations concluded that a hexachlorophene factory in southwestern Missouri had accumulated distillate residues containing 306 to 356 ppm TCDD. It was these distillate residues that were subsequently disposed of via a salvage oil company and sprayed on the horse arenas. Furthermore, as Kimbrough et al. (122) noted, the investigation demonstrated that the improper disposal of toxic chemical wastes may have serious consequences. Companies responsible for the disposal of such wastes should be aware of the toxicity of these chemical waste products and should practice proper methods of disposal.

Commoner and Scott (46) have reviewed the Missouri Horse Arena Episode in an attempt to provide consultative data to the Italian Government in the wake of the Seveso, Italy episode. Their review focused on the human reactions (symptoms) to accidental TCDD exposure and the problem of soil degradation of TCDD. They also provided an excellent chronological account of the episode.

The response of the horses to TCDD in the above episode is of special interest. In 1970, Pinsent and Lane (160) reported on a illness in four horses, and the subsequent death of one, following the spraying of a brushwood killer (2,4-D and 2,4,5-T) to destroy nettles around the margin of a pasture containing the horses. The horse that died had remained on the pasture for 12 days. The postmortem examination revealed extensive lesions in the esophagus and stomach with degenerative changes involving the liver and kidney. The authors concluded that neither the clinical picture nor the postmortem findings supported a plant poisoning syndrome, and thus it was not possible for the possibility of poisoning by the herbicides. In view of the findings by Kimbrough et al. (112), it would appear that the horses may have been exposed to TCDD.

Beale et al. (24) have recently reexamined the young girl who had developed hemorrhagic cystitis following repeated exposure to TCDD in one of the horse arenas sprayed with waste oils (see Ref. 13). In the 5-year interval since exposure, the patient had grown normally, and both her height and weight were above the 75th percentiles. Detailed physical, chemical, and neurological examinations were also conducted and found to be normal. The same studies were done on the patient's sister and mother, exposed simultaneously, but less extensively to dioxin, and the results were also normal. Beale et al. (24) concluded: "Our experience demonstrates that people exposed to dioxin can recover completely with no apparent sequela from the toxin. It remains to be determined whether the

exposure to dioxin in the
-their offspring."

The Seveso, Italy Episode

Perhaps the most public episode in Seveso, Italy, has been a concern. Hundreds of people have been exposed either on-site inspection of this episode. In addition, that its outcome could be

Although the Seveso herbicides, it did, however, synthesis, that is, trichlorophene), this associated with its industrial trichlorophenol production accident?

A voluminous amount has been only 2 years layman oriented, factually humanistic interest. Titles titled "A Deadly Saga over Seveso," and "The drama of this industrial

Parks and Sullam (1) collection of selected September 1976. In the stated:

The social, economic Italy out of that poison long shadow on the burned and disfigured of people for many industrial regulations incident forces the attention

Data on levels of TCDD of human or animal following information

The episode of TCDD small town 40 km north

exposure to dioxin in these children will result in abnormal pregnancies or affect their offspring."

The Seveso, Italy Episode

Perhaps the most publicized chemical accident in modern times is the TCDD episode in Seveso, Italy. This episode has attracted worldwide interest and concern. Hundreds of scientists, physicians, and veterinarians have participated in either on-site inspections, conferences, or consultations into the various facets of this episode. In addition, the episode has now acquired such political significance that its outcome could change the political structure of a nation.

Although the Seveso, Italy episode did not involve 2,4,5-T or other phenoxy herbicides, it did, however, involve the potential raw material required for their synthesis, that is, trichlorophenol. Thus, in relation to the phenoxy herbicides (and hexachlorophene), this episode represents to many people an inherent danger associated with its industrial production. Hence, the question: can we do without trichlorophenol products and thus insure our safety from another such industrial accident?

A voluminous amount of literature has been written on this episode, although it has been only 2 years since it occurred. Much of this material has been either layman oriented, factually confused, politically pointed, or limited primarily to humanistic interest. Thus, we have seen in newspapers and magazines, articles titled "A Deadly Saga," "The Graveyard on Milan's Doorstep," "Toxic Cloud over Seveso," and "The Poison That Fell From The Sky." However, the human drama of this industrial accident cannot, and must not, be minimized.

Parks and Sullam (158) have assembled, translated, and reviewed an impressive collection of selected articles from the Italian press for the period 10 July to September 1976. In the introduction to this collection of articles, Parks and Sullam stated:

The social, economic, moral, medical and administrative problems which fell on Italy out of that poisonous cloud are of vast extent and complexity. They cast a very long shadow on the future, involving the rebuilding of shattered lives, the care of burned and disfigured children, health care and the monitoring of health for thousands of people for many years to come, and the shaping of policy decisions regarding industrial regulations and the operations of multinational enterprises to which this incident forces the attention of the Italian Government.

Data on levels of TCDD found, the magnitude of the contamination, or the extent of human or animal illnesses or injuries are still sketchy. Nevertheless, the following information on the episode is available from published documents.

The episode of TCDD poisoning occurred on 10 July 1976 in Seveso, Italy, a small town 40 km north of Milan (95,174). The source of the TCDD was a

TCDD is the dioxin of most concern. It occurs primarily in pesticide made from trichlorophenol, for example, 2,4,5-T and silvex herbicides. Quantitatively it is a very potent teratogen; however, qualitatively the nature of the teratogenic effect of TCDD is far less than many other compounds, such as thalidamide or Vitamin A. The one teratogenic response most commonly associated with TCDD is cleft palate. TCDD tends to cause death of the embryo or fetus rather than a wide range of abnormalities. Present data suggest that in mammals TCDD may be carcinogenic. TCDD tends to accumulate in the liver of rodents, but in nonhuman primates it is associated with tissues having a high lipid content, particularly the skin, muscle, and fat. In man, exposure to TCDD is characterized by the appearance of chloracne and its absence makes it unlikely that systemic disorders present are related to TCDD. Asthenic and vegetative symptoms are often present in overexposure, but are difficult to interpret. They would normally be expected to clear with time. There is no conclusive evidence at this time that TCDD is mutagenic, teratogenic, or carcinogenic in man.

Most TCDD that is applied to the environment during pesticide applications, probably photodegrades within the first 24 hr. It is probably not translocated in plants with the soil then serving as the residual reservoir. The half-life in soil varies from 200-340 days, depending upon soil type and climate. Microbial degradation is probably responsible for the soil disappearance of TCDD. Animals that come in contact with contaminated soil or vegetation, will bioconcentrate TCDD in their liver; however, at present, there are no field data available that indicate that the levels of TCDD found in these animals have a biological effect.

With the current production technology, phenoxy herbicides may be produced containing less than 0.1 ppm TCDD. When these herbicides are properly applied to the environment, TCDD residues are nondetectable. Whether significant bioaccumulation occurs in livestock feeding on herbicide-treated rangeland at sufficient levels to be present in meat consumed by man remains to be determined. On this determination will depend the future use of trichlorophenol-based herbicides.

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