CORRESPONDENCE

Serum Levels of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Phenoxy Herbicide Sprayers

A study reported by Johnson et al. in the Journal in November 1992 is fundamentally flawed (1). In that study, recent serum samples from 37 workers who had sprayed chlorinated phenoxy acid herbicides in the past were analyzed for 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in order to estimate the workers’ TCDD levels at the time of the cessation of spraying and the rate of exposure while spraying. The past levels were estimated from current serum levels using a mathematical model that incorporated the half-life of TCDD in serum, the duration of exposure, and the time since the cessation of spraying.

The current serum levels of TCDD ranged from 2 to 18 parts per trillion (ppt; adjusted for lipid weight) for all but one of the sprayers who had a concentration of 34 ppt. The authors noted that the maximum level of TCDD reported for the general population is 26 ppt.

The workers were divided into three groups according to the period when they were spraying: pre-1965, 1965-1974, and post-1974. The current serum TCDD levels were similar in all three groups of workers. When the mathematical model was used to extrapolate back to the time of cessation of employment, the estimated exposure levels were higher for the earlier years. For example, there was at least one worker in each period with a current serum level of 3 ppt TCDD (i.e., at the lower end of the normal range for unexposed people). This level was extrapolated back to 78 ppt at the time of stopping employment for a pre-1965 sprayer, to 14 ppt for a 1965-1974 sprayer, and remained at 3 ppt for a post-1974 sprayer.

The authors concluded that, “Estimated rates prior to 1965 were more than an order of magnitude higher than those after 1974” and that “...some sprayers may have been exposed to levels comparable with those that produce cancer in laboratory animals.”

The fundamental flaw in the paper is that Johnson et al. did not take the normal background levels of serum TCDD into account when they extrapolated back to estimate serum TCDD levels at the time of exposure. They stated, “These calculations implicitly assume that all levels at the time that blood was drawn represent decayed levels residual from past occupational exposures.” In the Appendix describing their mathematical methods, they stated: “Note that this calculation assumes that exposure from nonoccupational sources is negligible.” This assumption is obviously untenable when the current serum levels detected are indistinguishable from those of the unexposed population. In order to estimate past TCDD levels, one should first subtract the background level to be expected in an unexposed person. Only the residual amount could be regarded as arising from past occupational exposures and used for extrapolating back to the time of employment.

Fingerhut et al. (2) reported a mean concentration of 7 ppt TCDD in serum in 79 unexposed people, with all values less than 20 ppt. The mean concentration of serum TCDD in the workers in the paper by Johnson et al. was 7.8 ppt (calculated using the detection limit value for the nine workers in whom TCDD was not detected). If the upper limit for the general population, namely 26 ppt, was subtracted from each of the current serum levels reported by Johnson et al. to obtain a conservative estimate of the residual TCDD levels, only one worker, with 34 ppt, would have had a positive contribution from past occupational TCDD exposure. This worker's level would be estimated as 77 ppt at the time of cessation employment if the residual TCDD level of 8 ppt was used for extrapolation (compared with 329 ppt at the time of cessation employment calculated by Johnson et al.). All the other workers' residual TCDD levels would be zero and hence not suitable for extrapolation.

The fact that all but one of the workers had current TCDD levels within the normal range completely destroys the justification for the elaborate modeling of estimated past exposure levels and hence the conclusions drawn by Johnson et al. The only valid conclusion that can be drawn from their data is that the level of residual TCDD in the serum of all but one of the herbicide sprayers was too low to be detected above background levels in the general population.

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References


Response

Thank you for giving us the opportunity to respond to Dr. Smith’s letter in this issue of the Journal. In our paper (1), we had reported on the individual serum levels of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in a group of sprayers in the state of Victoria in Australia at the time of blood collection. We also provided a formula for estimating what serum levels were at the time exposure ceased, assuming occupational exposure had occurred. To our knowledge, this was the first time a formula had been presented that took into account both simultaneous body decay and accumulation of TCDD. It would appear that Smith had no problems with these two points.

Using this formula, we then went further and provided an estimate of what levels would have been at the time occupational exposure to TCDD ceased for these workers. To do this, we explicitly made the assumption that exposure from nonoccupational sources in Victoria is negligible. Smith acknowledged that we clearly stated this assumption; however, she finds this assumption untenable and flawed. At
issue, therefore, is whether this was a reasonable assumption or not. The best way to test this assumption is to measure TCDD levels in the general population in the state of Victoria in Australia. We had procured such serum specimens at the same time we collected the case samples. However, because of the high cost of the assay, a decision was made to postpone testing these control samples until further funds were available. Nevertheless, other evidence supports our assumption:

1) Our review examined 31 consecutive international reports published in Chemosphere on TCDD levels in biological samples (serum, adipose tissue, milk) collected from subjects in the general population who supposedly had no known exposure to TCDD (subjects were not questioned about whether they had any occupational exposure). In this review, we noted that 18 reports provided information on the range of observed values. Ten of these 18 reports (i.e., >50%) reported no measurable TCDD in some of the subjects representing a sample of the general population. Moreover, in two of these studies, one in Vietnam and one in Thailand, no TCDD was present in any of the samples tested.

2) In more than one third (13 of 31) of the reports, the mean sample levels were 4 parts per trillion (ppt) or less; in 90% of the studies (28 of 31), the mean TCDD was 10 ppt or less. Levels seemed to differ by country — in Sweden, for example, a TCDD concentration of 10 ppt or more in serum, milk, or adipose tissue taken from a member of the general population has never been reported in published studies. There seemed to be variation in mean levels within the same country, which could be attributed to sample variation. Thus, a mean TCDD level of 1.6 ppt (range, <1-9.8 ppt) in adipose tissue from Munich, Germany, was reported in one study, while in Hamburg, Germany, adipose tissue levels were between 1.5 and 18 ppt.

3) It should be noted that, in many of the published reports, samples from the so-called general population were collected without inquiring whether there was opportunity for occupational exposure to have occurred (e.g., adipose tissue samples from surgical patients or from cadavers). For example, in a study of 57 subjects from an apparently general population in Missouri without known exposure to TCDD, one had a serum TCDD level of 20.2 ppt. This rather high value subsequently prompted closer questioning which revealed that the subject was a nurse who scrubbed her hands at the hospital with an antiseptic lotion that may have been contaminated with TCDD.

To our knowledge, large-scale studies that have specifically ruled out obvious occupational or known TCDD exposure among subjects defined as unexposed have not reported serum or adipose tissue TCDD levels above 20 ppt (2, J). As Smith pointed out in the NIOSH study (2), all of the unexposed subjects had TCDD levels of less than 20 ppt. Similarly, in the Centers for Disease Control Veterans Health Studies in the United States, the mean serum TCDD level in 646 Vietnam veterans was 4.2 ppt with 95% of the values falling below 7.9 ppt; in the control group of 97 non-Vietnam veterans, the mean was also 4.1 ppt with 95% of the values falling below 9.3 ppt; the highest value in the control was 15 ppt (3).

In the U.S. Environmental Protection Agency NHATS study (4) of 46 tissue samples prepared as composites from over 900 specimens representing the nine U.S. census divisions, the mean adipose tissue TCDD concentration was 5.0 ppt, with a range of undetected at 1 ppt to 10 ppt. Thus, the presence of levels in the general population of greater than 20 ppt should be regarded as extreme and should be viewed as more than likely indicating greater than background exposure.

4) To our knowledge, there had been no study of serum TCDD levels in the general population in Victoria. Given the discussion above, we were faced with the problem of what to use as background levels. We turned to our data for sprayers first employed after 1974, bearing in mind that it was in the mid-1970s that the Australian government passed regulations to reduce TCDD concentration in herbicides. As can be seen in Table 1 of our paper (1), even though some of these workers would have been significantly exposed to TCDD during the earlier years (1975-1976) and much less so in later years, all 20 individuals with an average duration of exposure of 10.7 years had TCDD levels less than 17 ppt. In fact, the two subjects with the highest levels of 16 ppt and 10 ppt were first employed in 1975 when TCDD exposure was probably still substantial, and they had worked for 12.5 and 14.9 years, respectively. Of the 15 sprayers whose TCDD levels were uncensored, 12 (i.e., 80%) of these occupationally exposed workers had serum TCDD levels of 5 ppt or less. The mean TCDD level for these 15 workers was 5 ppt. Serum TCDD levels in all of these 20 workers would be expected to be higher than background, since they probably continued to be more exposed to TCDD than the general population, in spite of the reduced levels of TCDD in herbicides in later years. These figures on the whole, therefore, suggest to us that background levels in Victoria were probably very low to the point of being negligible (probably 3 ppt or less, on average). We believe this to be a reasonable assumption given the above discussion and that ignoring such low background levels in our back calculations would have negligible effect on our estimates and conclusion. This approach is certainly much less associated with error than that suggested by Smith in which she proposed subtracting 26 ppt from each current level and then using the residual to do the back calculation, which in our view would be inappropriate. Incidentally, we were aware that others have used this procedure. However, we decided against it because background levels vary from area to area, and our data suggest negligible levels on average for Victoria. Even if one should subtract 5 ppt (the mean for the 15 exposed workers first exposed after 1974) from the 34 ppt observed for that one worker Smith referred to, his estimated TCDD level at time of termination of work would have been 280 ppt instead of 329 ppt (a difference of only 15%).

Indirect evidence in two different ways suggest that our calculations were in the correct ball park: 1) as we mentioned in our paper, we tested our estimate of exposure rate using our formula on the New Zealand data (5),
Disclosing Cancer Diagnosis to a Patient

The manner in which a physician discloses to a patient the diagnosis of cancer can, in and of itself, determine whether the patient will die or survive. The physician can instill hope and the desire to try to fight and be part of a winning team or can cause the patient to want to do nothing and wait for the inevitable end. A telephone call by a nurse or even the doctor stating, “You have cancer” can be totally devastating. The patient assumes the worst, realizing the doctor does not want to tell him or her face-to-face.

In a study by two doctors (/) on how disclosure of a cancer diagnosis by a physician is perceived by patients, the conclusion was reached that, “Maximizing hope during the disclosure of a diagnosis is one way clinicians can contribute to psychological adjustment early in the treatment process.” The diagnosis should be in a manner suggesting a high degree of individuality, intimacy, and privacy. Patients want to have some prior connection with the physician who presents the diagnosis (e.g., the family doctor). Further, they welcome the participation of an oncologist who can offer additional information about the prognosis and treatment.

Most patients truly want all the medical information available. They want to be assured their treatments will be the best available, and they want to know what alternatives are possible in case of failure of the initial treatment. It is appropriate to discuss actual cases where individuals have overcome similar ordeals.

Patients favorably view procedures that encourage their participation in the fight. This includes not only the acceptance of the best that medical science has to offer but also the best resources the physician who can offer additional information the patient has to offer but also the best resources the physician who can offer additional information. The physician should nurture and encourage the fighting spirit in those patients who demonstrate a willingness to take control of their situations and to accept some degree of personal responsibility for their healing. Physicians need not endorse activities or unproven techniques used by a patient. Rather, to the extent that such activities or techniques do not interfere with current treatment, they should be encouraged—if for no other reason than to improve the feeling of participating and the quality of life by and for the patient.

The patient’s normal fear of cancer pain and treatments should be clearly addressed when the illness is first diagnosed and disclosed. Increasing the patient’s understanding of what is happening to his or her body and what will be the likely course of the illness enables the patient to feel in control. A growing body of evidence suggests that this increased understanding actually improves the overall clinical picture for such patients. Assurance that the physician will not abandon the patient is extremely important. Offering to be available to answer all questions is tangible evidence of this commitment. A physician’s appropriate physical contact such as holding a hand, a pat on the shoulder, or a hug goes a long way.

Above all, patients need to have the feeling that they are able to talk with their physicians as partners in the fight and as confidants to whom they can relate their feelings.

To many physicians, this is just another patient. Their appointment calendar is full, and they have other things to do and other concerns. For the patient, it is his or her life. The diagnosis of cancer may be one of the most traumatic events in the life of an individual and in the lives of their family members. The way they are told not only can affect the quality of these many lives temporarily, but also can actually possibly influence the results!

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References


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Reference


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Editor's note: Richard Bloch served as a member of the National Cancer Advisory Board from 1982 to 1988.