LETTER TO THE EDITOR

DEAR EDITOR,

I believe that Hwang *et al*. review of the gonadotoxic effects of DBCP [1] mischaracterized both the science and history of dibromochloropropane's hazards in an agricultural setting.

There is little debate that DBCP is gonadotoxic in men. However, Hwang *et al*.'s interpretation of studies of exposed agricultural workers suggests that exposures in this population pose no important risk. The authors fail to adequately report the findings of the studies they consider, and omit other important scientific information.

Hwang *et al*. discuss Glass *et al*.'s 1979 publication [2]. This study found sperm count depression among "applicators involved in irrigation setup work and in the calibration of equipment", and concluded that "the testicular toxicity of DBCP…may occur in a shorter period that was previously reported, [and]….may be reversible in men with mild sperm count depression". Hwang *et al*. focus on Glass *et al*. characterization of depressed sperm counts as "clinically unimportant". However, this assertion is based on the categorization of four DBCP-exposed men with sperm counts below 10^6 as fertile who, according to the authors, "might have been infertile had they desired more children." Clinical infertility rates, therefore, reflect both the physical effects of the chemical and the social realities of the population studied. Given the diversity of DBCP-exposed populations, one cohort's desire for children can tell us little about the social impact of DBCP-induced sperm count depression in other groups of workers.

More concerning is Hwang *et al*. mischaracterization of Sandifer *et al*. study of "Spermatogenesis in Agricultural Workers Exposed to Dibromochloropropane" [3]. Sandifer found a "significant negative correlation…between sperm count and DBCP use-index", and the authors stated the result as "quite consistent with an occurrence of primary disruption of spermatogenesis at the testicular level for all users who had extensive exposure to the compound". Hwang *et al*. neglected to mention these findings, presenting instead some Sandifer data points without p-values or mention of significance. Hwang authors do stress that Sandifer "found no persons who desired more children but were 'infertile', suggesting that there was no effect on clinical fertility". This selective interpretation again downplays the physical impact of DBCP by stressing its social impact in one particular group of workers.

Finally, Hwang *et al*. discuss Ramírez and Ramírez's 1980 publication, "Male sterility caused by exposure of workers to the nematacide 1,2-dibromo-3-chloropropane" [4]. They note that Ramírez and Ramírez "found a negative correlation between exposure to DBCP and sperm counts", but fail to discuss the data in detail. Ramírez found a significant increase in sperm count depression (10^7 spermatozoids/ml; $p<0.01$) and azoospermia ($p<0.05$) with hours of exposure; but no statistically significant relationship between oligospermia and hours of exposure ($p<0.3$). Hwang *et al*. avoid any nuanced discussion of these findings, focusing instead on the limits of the study, sometimes making errors of interpretation or omission. For example, Hwang *et al*. suggest that Ramírez and Ramirez included no information on the age of study participants, but the article states that all participants were aged between 21-44 years. Hwang *et al*. also suggest Ramírez and Ramírez's exclusion of men with other likely causes of sterility--including those with a gonorrhea diagnosis—weakened the study, when in fact it made it stronger by eliminating possible confounders. In addition, the reviewers gratuitously and without citation imply that high marijuana use among this group of workers may account for the azoospermia and sperm count depression. Ramírez and Ramírez 's results are consistent with other studies' findings that sperm counts decrease with DBCP exposure. Considered together, these studies amply demonstrate that DBCP exposure can affect farmworkers in the same way as it affects industrial workers.

Hwang *et al*. fail to include some material that further demonstrates the risk DBCP posed to farmworkers [5]. In 1978, the US EPA concluded there was a clear and dose-dependent relationship between DBCP exposure and depressed sperm counts in these workers, and that DBCP also posed an alarming cancer risk to farmworkers, especially through dermal contact. Ample evidence from corporate documents also shows that Dow and Shell, the first DBCP producers, were concerned with agricultural exposures early on. In 1958, Dow had determined that DBCP application through a sprinkler irrigation system could cause air concentrations at about half the levels found to cause serious health effects in lab animals, and also posed an important risk of skin contact. In 1960, Dow advised Florida officials against the overhead sprinkler application of DBCP to protect workers from health hazards. The same year, Shell found exposures among citrus grove applicators to range from 0.83 ppm to 3.31 ppm, up to more than three times higher than the 1ppm level suggested by Torkelson. In 1963, tests from Hawaiian pineapple fields showed air concentrations ranging between 6.2 and 11.0 ppm [5].

Dow and Shell's backpedalling on DBCP toxicity, protections and warnings came in tandem with increasingly strict regulation on nematicides, which prior to 1961 had not fallen under the Federal Insecticide Fungicide and Rodenticide Act. When regulators became concerned about the human health effect suggested by animal testing, Dow and Shell worked together to convince regulators that DBCP could be safely formulated and used. They claimed that because there had been no adverse reports of human health problems with DBCP, the health effects noted in experimental animals were not generalizable to humans. However, there is no evidence that Shell or Dow tested

1874-303X/15

workers' sperm counts or reproductive outcomes while making claims to a history of safe use [5].

It is not, as Hwang *et al*. claim, "startling" that the problems originally found in animals were eventually evident in humans. The entire premise of toxicology is that animal results presage human health harms. Hwang *et al*. imply that Torkelson's admittedly "arbitrary" concentration limit reflected an understanding of "species specificity and the comparatively low impact of DBCP on human DNA" [1]. However, the studies they cite on these topics were not published until decades after Torkelson settled on his number. In fact, toxicological testing conducted by the two chemical companies showed similar effects across a number of animal species including monkeys, rats, guinea pigs and rabbits [5].

For each study they consider, Hwang *et al*. seem to emphasize the findings or limitations that suggest DBCP does not cause statistically significant gonadotoxic effects in agricultural workers. Is there an underlying agenda here? Usually a conflict of interest disclosure will help readers make their own determination about authorial intent and motivation. In this case, the conflict of interest statement claims "The authors confirm that this article content has no conflict of interest". Unmentioned is that at least one of the authors (Larry Lipshultz) has served as a highly-paid expert witness for the defense in litigation involving agricultural workers with DBCP sterility claims. This oversight appears to violate journal policy that "Financial contributions to the work being reported should be clearly acknowledged, as should any potential conflict of interest". *Open Urology & Nephrology* editors should publish a correction with a full and detailed disclosure of conflict of interest, or retract this flawed review.

Susanna Bohme
Corporate Accountability International, USA
E-mail: sbohme@stopcorporateabuse.org

CONFLICT OF INTEREST

The author performed some paid consulting work for attorneys representing farmworkers with DBCP claims, over five years ago. Currently, she is listed as an expert witness in at least one DBCP case.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

[1] Hwang K, Eisenberg, ML, Walters RC, Lipshultz LI. Gonadotoxic effects of DBCP: a historical review and current concepts. Open Urol Nephrol J 2013; 6: 26-30.

[2] Glass RI, Lyness RN, Mengle DC, Powell KE, Kahn E. Sperm count depression in pesticide applicators exposed to dibromochloropropane. Am J Epidemiol 1979; 109(3): 346-51.

[3] Sandifer SH, Wilkins RT, Loadholt CB, Lane LG, Eldridge JC. Spermatogenesis in agricultural workers exposed to dibromochloropropane (DBCP). Bull Environ Contam Toxicol 1979; 23(4-5): 703-10.

[4] Ramírez R, Ana L, Ramírez M, Carlos M. Esterilidad masculina causado por la exposicion laboral al nematicida 1,2-dibromo-3-chloropropane. Acta Medica Costarric 1980; 23(2): 219-22.

[5] Bohme SR. Toxic injustice: a transnational history of exposure and struggle. Oakland, California: University of California Press 2014; p. 360.

Received: December 15, 2014 Revised: March 2, 2015 Accepted: April 8, 2015