cies and inconsistencies in the preparation of commercial patch test solutions and the implication for diagnostic patch testing.⁷ Upadhye and Maibach dealt with the importance of area of allergen application.⁶ Data on sensitisation are reviewed that compare the importance of the area of allergen application with, in some cases, solution concentration at the skin surface, and in other cases with mass loading per surface area. The relative importance of solution concentration and mass loading is not considered. Finally, Fischer and Maibach dealt with a comparison between the TRUE-test patch (similar to that used by Nethercott *et al.*) and the Finn chamber used with petrolatum in tests for nickel sensitivity.⁷ The TRUE-test was found to eliminate problems of uneven delivery of allergen that specifically arose from the use of petrolatum. Rather than showing solution concentration to be an invalid measure of potential ACD, this study found that the results from the two methods compared well with each other across a large range of serial dilutions.

A comprehensive model of ACD risk from exposure to contaminated soil has not yet been developed. In the absence of such a model, we think that Nethercott *et al.* are unwarranted in their assertion that mass per surface area provides the only valid predictor of potential ACD from environmental contamination.¹ Furthermore, we think that the analysis in Stern *et al.*, based on numerous studies of solution concentration *v* ACD response, provided a reasonable empirical basis for estimation of ACD risk.²

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- 1 Nethercott J, Paustenbach D, Adams R, Fowler J, Marks J, Morton C, *et al.* A study of chromium induced allergic contact dermatitis with 54 volunteers: implications for environmental risk assessment. *Occup Environ Med* 1994;51:371-80.
- 2 Stern AH, Bagdon RE, Hazen RE, Marzulli FN. Risk assessment of the allergic dermatitis potential of environmental exposure to hexavalent chromium. *J Toxicol Environ Health* 1993;40:613-41.
- 3 McKone TE. Dermal uptake of organic chemicals from a soil matrix. *Risk Anal* 1990;10:407-19.
- 4 Wester RC, Maibach HI, Sedik L, Melendres J, DiZio S, Wade M. *In vitro* percutaneous absorption of cadmium from water and soil into human skin. *Fundam Appl Toxicol* 1992;19:1-5.
- 5 Yang JJ, Roy TA, Krueger AJ, Neil W, Mackerer CR. *In vitro* and *in vivo* percutaneous absorption of benzo(a)pyrene from petroleum crude-fortified soil in the rat. *Bull Environ Contam Toxicol* 1989;43:207-14.
- 6 Upadhye MR, Maibach HI. Influence of area of application of allergens on sensitization in contact dermatitis. *Contact Dermatitis* 1992;27:281-6.
- 7 Fischer TI, Maibach HI. The thin layer rapid use epicutaneous test (TRUE-Test), a new patch test method with high accuracy. *Br J Dermatol* 1985;112:63-8.
- 8 Fischer TI, Maibach HI. Amount of nickel applied with a standard patch test. *Contact Dermatitis* 1984;11:285-7.
- 9 Anderson KE, Linden C, Harsen J, Volund A. *The degree of nickel allergy and the enhancing effect of multiple reactions evaluated by dose-response testing in allergic patients.* Amsterdam: European Society of Contact Dermatitis, 1992.

Authors's reply—We are pleased to have this opportunity to respond to the letter by Stern and Hazen. Most of their letter is repeated verbatim in another letter to the

editor they recently sent to another journal. In our response to that letter,¹ we presented what we think is a clear and concise definition of the problem and its resolution. We appreciate this opportunity to continue the discussion as it provides us with another opportunity to further describe the factors that predict the risk of elicitation of allergic contact dermatitis (ACD) through dermal contact with Cr(VI) in soils.

The position that we have presented in our paper is that the only valid measure of dermal dose is mass of chemical per unit surface area of skin ($\mu\text{g}/\text{cm}^2$ skin), and that knowing the applied concentration of the chemical (mg/l) without knowing the volume of the contactant applied (l), cannot provide a measure of the mass of chemical contacting the stratum corneum. As simple as the rationale for this concept may seem, Hazen and Stern have provided a lengthy rebuttal that only exemplifies that they do not appreciate the significance of the available data.

The issue at hand concerns the appropriate method for setting a soil standard for Cr(VI) that protects against elicitation of ACD in people sensitised to Cr(VI). Stern and Hazen originally took the position that 10 ppm Cr(VI) in soil should be the standard for ACD because of their belief that: (a) 10 ppm Cr(VI) in solution on skin is a threshold for elicitation (based on their interpretation of historic patch test data) and (b) 10 ppm Cr(VI) in soil on skin might generate 10 ppm Cr(VI) in solution on the skin surface.^{2,3} We undertook numerous studies to test the legitimacy of their assumptions. Firstly, we showed that, at sweat:soil ratios that they thought to be representative of environmental exposure conditions, human sweat does not extract sufficient Cr(VI) from the soil to generate 10 ppm Cr(VI) in solution on the skin surface.⁴ In fact, much less than 0.1 ppm is generated even when the concentration of Cr(VI) in soil is above 500 ppm. Once this was established, they abandoned the soil on skin argument in favour of what might be termed the mud puddle hypothesis. That hypothesis suggested that an unlimited reservoir of soil containing 10 ppm Cr(VI) (rather than a thin layer of soil on skin) could generate 10 ppm Cr(VI) in solution in the environment—for example, in the form of puddles after rain. Although this change in reasoning circumvented the soil on skin issue, it still failed to correct the major data gap, namely, the measurement of dose-response with a dose measure that involved mass of Cr(VI) delivered to the skin (applied dose data). Our second major research effort, wherein 54 people sensitised to Cr(VI) were patch tested, corrected this issue. Specifically, we obtained data on the applied dose threshold in people sensitive to Cr(VI).⁵ When these results were presented to Stern and Hazen two years ago, they proceeded to recalculate the applied dose threshold of $0.089 \mu\text{g Cr(VI)}/\text{cm}^2$ by converting the patch test dose (from $\mu\text{g Cr(VI)}/\text{cm}^2$) to patch concentration in ppm (based on some unsubstantiated assumptions about the patch dimensions). Not surprisingly, the recalculated threshold was once again 10 ppm Cr(VI). In short, although Stern and Hazen's technical bases and reasoning have changed as their assumptions are challenged, the Cr(VI) soil standard has remained unchanged.

In their letter to this *Journal*, Stern and Hazen continue to side step the critical dis-

inction between applied concentration (ppm) and applied dose ($\mu\text{g Cr(VI)}/\text{cm}^2$ skin). We think it is clear that applied dose not applied concentration dictates elicitation.^{5,6} In our paper we identified the threshold dose for people sensitised to Cr(VI) (the dose below which elicitation is unlikely to occur) as approximately $0.089 \mu\text{g Cr(VI)}/\text{cm}^2$ skin, with little or no response occurring at lower doses. A typical dose-response curve was shown at successively higher doses. Stern and Hazen continue to assert that an understanding of applied dose is not necessary, and that applied concentration provides sufficient information to predict response. To evaluate the legitimacy of their position, consider an analogous situation with a volume of water containing one part per thousand arsenic. One cannot conclude whether ingestion of the solution would cause death unless there is some understanding of the volume to be ingested—that is, the dose. The outcome depends on whether the ingested dose is above or below the lethal dose. Regardless of the outcome, however, the ingested concentration would remain constant. Similarly, one cannot predict the effects of the application of a cutaneous allergen when *only* the allergen concentration is known; there must be some understanding of the *applied dose*.

As shown in the figure, the validity of applied dose as the correct dose measure holds true for elicitation of ACD. As described in our paper, we tested nine people sensitised to Cr(VI) with patches of one Cr(VI) concentration (175 ppm) but different applied doses (0.13 *v* $0.88 \mu\text{g Cr(VI)}/\text{cm}^2$) (the patches were made from the same material but one patch was 1/7 the thickness of the other). Six of the nine participants developed ACD upon exposure to the $0.88 \mu\text{g Cr(VI)}/\text{cm}^2$ dose, but none responded to $0.13 \mu\text{g Cr(VI)}/\text{cm}^2$. Hence, it is clear that applied dose, not applied concentration, governs elicitation. Further, these results alone refute the claim of Stern and Hazen that 10 ppm Cr(VI) is the elicitation threshold as a 175 ppm Cr(VI) patch did not elicit a response.

Stern and Hazen's suggestion that ACD may not always follow a clear dose-response relation runs counter to the fact that in our study and numerous other patch test studies there is a clear dose-response relation between applied Cr(VI) dose and elicitation of ACD. Furthermore, Stern and Hazen's basis for a 10 ppm Cr(VI) response threshold rests entirely on a dose-response relation they have generated from a variety of disparate studies, some of which are more than 30 years old. Hence, to suggest that ACD may not follow a classic dose-response paradigm is not consistent with their own published analysis. Stern and Hazen mischaracterise our referencing of four papers that support the applied dose concept. We did not claim that these papers state that mass loading per skin surface area is the *only* valid measure; these papers were cited because they acknowledge the importance of the applied dose concept. Rather than be diverted into a lengthy rebuttal as to why these papers are relevant, we direct Stern and Hazen once again to the most recent and incontrovertible evidence to date: the figure shows the results. Although these data have been presented to Stern and Hazen numerous times in the past two years, they have never offered an explanation as to how their position can be valid in the face of these results. Indeed, they have

Response of patch tests of nine Cr(VI) sensitised people. The patches contain identical concentrations but differing applied doses.

avoided acknowledging these data and their implications in both versions of their letter.

Stern and Hazen make several statements about the dynamics of soil adherence to skin. Firstly, they suggest that soil loading on skin is highly variable thereby implying that any soil standard that incorporates a soil adherence factor might be questionable. This is certainly inconsistent with current United States Environmental Protection Agency (USEPA) guidance,⁷ which suggests a very narrow range for soil adherence rates (0.1–1.0 mg soil/cm² skin) in risk assessment. The USEPA's suggested range is taken from the results of over 10 studies that measured soil adherence under a variety of exposure scenarios, including purposive contact under laboratory conditions. The recent work of Kissel *et al.*⁸ which was funded by USEPA, supports this position. Kissel *et al.* measured soil adherence after soil and mud contact under numerous exposure conditions, including gardening, rugby, etc. As noted by Kissel *et al.* "Routine soil loadings on skin are likely to be substantially lower than the current EPA default (upper-bound) estimate of 1 mg/cm²".

Secondly, as we noted in our previous response to this letter,⁷ McKone makes no claims as to the validity of assuming continuous replenishment of soil on skin, it is simply an assumption in his dermal absorption

model. An alternative version of his model assumes a single deposition. Thirdly, we are surprised that Stern and Hazen would offer the paper of Wester *et al.* to support their position.⁹ As they noted, Wester *et al.* found that cadmium moved from soil to the skin surface as a function of cadmium loading (mg Cd/cm² skin) and was independent of cadmium concentration in soil (ppm Cd). This is identical to the findings presented in the figure and further supports our position that applied dose, and not applied concentration, is relevant.

Fourthly, we agree that Yang *et al.* have shown that percutaneous absorption of a chemical in soil may be driven by a soil monolayer rather than the total mass of contaminant applied over a given area of skin.¹⁰ This is irrelevant to the applied dose *v* applied concentration argument, but it suggests that the USEPA soil adherence estimates are conservative. In other forums, Hazen has suggested that his own unpublished observations, wherein he applied soil to his own arm and measured adherence, suggest the USEPA's estimates are not sufficiently conservative. We think that a soil standard should be based on a more rigorous scientific database than Hazen's personal experiments.

As well as ignoring the dose-response principle, Stern and Hazen's position requires numerous leaps of faith regarding:

(a) the quality and consistency of the 30 year old patch test data, (b) the accuracy of any threshold derived from these data, (c) the likelihood that 10 ppm Cr(VI) in soil will generate 10 ppm in solution and, (d) the similarity of patch test conditions to those of contact with soil or water in the environment. Although they assert that "the data relating ACD response to Cr(VI) in solution by patch test methods are numerous and consistent," Paustenbach, *et al.*¹¹ provided an extensive review of the patch test data originally evaluated by Stern,² and they concluded that it was difficult to develop a credible response threshold from these data.

We think that the mud puddle concern is also untenable because Stern and Hazen have no evidence that 10 ppm Cr(VI) in soil can produce 10 ppm Cr(VI) in solution. Finally, their position requires a belief that patch test conditions represent environmental exposure; this is not the case. In a patch test, the patch remains in contact with the skin for 48 hours. The allergen under the patch is *under occlusion*. It is implausible to expect that 48 hour continuous contact with water will occur under environmental exposure conditions. More importantly, it is well known that 48 hours occlusion results in a substantial increase in the penetration of the allergen due to a decrease in integrity of the skin surface. Hence, it is difficult to think that wearing a patch containing an allergen for 48 hours under occlusion is representative of incidental contact with a mud puddle. Finally, Stern and Hazen make several statements about an equilibrium processes, indeterminate loading, etc, which are unaccompanied by any literature citations and seem to be conjecture.

In summary, we think that it is clear that elicitation thresholds can only be accurately and completely expressed as mass per unit area of skin ($\mu\text{g}/\text{cm}^2$). Concentration alone, which Stern and Hazen continue to suggest is the appropriate measure of dose, provides only the mass per volume (mg/l) that has come into contact with the stratum corneum interface without reference to the mass delivered (mg). This dose measure cannot logically be used without also knowing the volume of the material in solution that has been applied as it does not provide the mass delivered to the skin ($\mu\text{g}/\text{cm}^2$). The patch test experiment that we reported in our paper clearly, and we thought simply, showed that concentration (in terms of mol or ppm) was not a proper dose measure. This should not be treated as a matter of conjecture, as Stern and Hazen suggest. The concept to which we refer is a basic concept in exposure assessment. If Stern and Hazen have data supporting their position, they should provide it.

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1 Paustenbach DJ, Finley BL, Nethercott JR, Fowler J. Response to comments by Stern and Hazen. *J Toxicol Environ Health* 1995; 44:382–3.

2 New Jersey Department of Environmental Protection (NJDEP). Derivation of a risk-based chromium level in soil contaminated with chromite ore processing residue in Hudson County. Trenton, NJDEP, 1990.

- 3 Bagdon RE, Hazen RE. Skin permeation and cutaneous hypersensitivity as a basis for making risk assessments of chromium as a soil contaminant. *Environ Health Perspect* 1991;92:111-9.
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- 5 Nethercott JR, Paustenbach JD, Adams R, Fowler J, Marks J, Morton C, *et al.* A study of chromium induced allergic contact dermatitis with 54 volunteers: implications for environmental risk assessment. *Occup Environ Med* 1994;51:371-80.
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- 7 United States Environmental Protection Agency (USEPA). *Risk assessment guidance for superfund. Vol 1, human health evaluation manual (part A)*. USEPA, 1989. (EPA/540/1-89-002).
- 8 Kissel J, Duff R, Richter K. *Results of field measurement of dermal soil loadings and laboratory investigation of the effect of soil loading on in vitro dermal absorption of organic xenobiotics from soil*. Savannah, Georgia: Society for Risk Analysis, 1993.
- 9 Wester RC, Maibach HI, Sedik L, Melendres J, DiZio S, Wade M. *In vitro* percutaneous absorption of cadmium from water and soil into human skin. *Fundam Appl Toxicol* 1992;19:1-5.
- 10 Yang JJ, Roy TA, Krueger AJ, Neil W, Mackerer CR. *In vitro* and *in vivo* percutaneous absorption of benzo(a)pyrene from petroleum crude-fortified soil in the rat. *Bull Environ Contam Toxicol* 1989;43:207-14.
- 11 Paustenbach DJ, Sheehan PS, Paull JM, Wisser LM, Finley BL. Review of the allergic contact dermatitis hazard posed by chromium-contaminated soil: identifying a safe concentration. *J Toxicol Environ Health* 1992;37:177-207.

and other health professionals involved in giving travel advice would also find this book beneficial.

The book shows the increased interest and awareness of health problems of travel, and reflects modern, up to date opinions. It is easy to read, concise, with useful summaries and reference lists at the end of each chapter. As well as covering the more commonly debated topics of malaria and traveller's diarrhoea, there are also chapters on less prominent, but equally important issues such as health in ethnic minority travellers and expatriates. As in all branches of medicine; some travel related problems have no ideal answers, or have answers that continue to be matter of opinion or subject to controversy, and this book attempts to consider this and encourages further debate.

In conclusion this book is a clear synopsis of various subjects in travel medicine; it contains up to date medical information, and would be of interest to a wide variety of health professionals, but perhaps would not be suitable for people from a non-medical background. Although slightly overpriced, it would certainly make a good library addition.

DIPTI PATEL

NOTICES

BOOK REVIEW

Travel Associated Disease. Edited by GORDON COOK (Pp 179, £15). 1995. London: RCP. ISBN 1860160123.

The hazards associated with travel have been well documented over the years. In the past, emphasis has been on infectious diseases, but with the rapid growth of travel medicine as a speciality, it has become increasingly obvious that these are not the only hazards encountered by the modern traveller.

This book covers various issues in travel medicine ranging from disease prevention to jet lag. It does not contain exhaustive information on all aspects of the speciality, but concentrates on various "hot topics" that would be useful for physicians in the travel medicine, tropical medicine, and other related fields. General practitioners

The Second International Conference on the Health of Miners. November 11-13, 1995. Pittsburgh, Pennsylvania USA.

The second international conference on the health of miners will be held November 11-13, 1995 in Pittsburgh, Pennsylvania, USA at the Pittsburgh Hyatt. The mining committee of the American Conference of Governmental Industrial Hygienists (ACGIH) is acting as co-sponsor along with the National Institute for Occupational Safety and Health, the Mine Safety and Health Administration, Bureau of Mines, the International Labour Office, the United Steel Workers Union and such corporate sponsors as BHP Minerals and the National Mining Association. Proceedings from the conference will be published in a single peer reviewed edition.

For further information contact: Dr Michael McCawley, Division of Respiratory Disease Studies, 1095 Willowdale Road, Morgantown, WV 26505-2845, USA. Tel: (304) 285-5749; Fax: (304) 285-5861.

IOSH '95 Health and safety conference and exhibition. The route to excellence—a safe journey. 4-6 December 1995. Harrogate, Yorkshire.

The United Kingdom's leading professional health and safety organisation's prestigious annual conference and exhibition is once more being held at the Harrogate International Centre, the Institution of Occupational Safety and Health's conference takes as its theme this year: *the route to excellence—a safe journey*.

A strong line up of high calibre speakers is now being finalised for IOSH '95. The keynote address will be delivered by Sir Neville Purvis, chief executive of the British Standards Institution. Presentations will be given by other senior figures such as David Giachardi, a director of Courtaulds plc, who will discuss competency in the profession, and Stansted Airport's managing director, Terry Morgan, who will talk about how the average health and safety practitioner influences his or her company's decisions.

Speakers will focus on a comprehensive range of subjects in both formal presentations and a series of concurrent workshop sessions. Topics will include:

- the recently announced NVQs/SVQs for occupational health and safety practice and the maintenance of competency standards
- the environment and the effects of packaging
- construction, design and management: the new regulations
- proactive planning for crisis management
- Leyland Truck case study: practical management of risk assessment
- advocacy skills for safety practitioners

For further details contact: Deborah Fisher, IOSH, The Grange, Highfield Drive, Wigston, Leicestershire LE18 1NN, UK.

BRITISH OCCUPATIONAL HYGIENE SOCIETY

Occupational Hygiene 96: Promoting A Healthy Working Environment. 22-26 April 1996. University of Keele, Staffordshire.

Final call for papers. Send title and one-page outline of material you wish to present, indicating if it is for:

- scientific session (10-40 minutes)
- professional development session (60-75 minutes)
- poster display

Students are particularly encouraged to offer papers, that may be presented in special sessions, or posters of their work.

Proposals must be sent by 29 September to Jerry Sherwood, Chairman of the 1996 Conference Committee, c/o BOHS, Suite 2, Georgian House, Great Northern Road, Derby DE1 1LT, UK. UK Fax: 01 332 298 099. International Fax: 441 332 298 099.