

## SHORT REPORT

## Can salivary lead be used for biological monitoring of lead exposed individuals?

D Koh, V Ng, L H Chua, Y Yang, H Y Ong, S E Chia

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**Background:** Measurement of blood lead (BPb) is the usual method for biomonitoring of persons exposed to inorganic lead.

**Aim:** To explore the use of salivary lead (SPb) as an alternative.

**Methods:** BPb and SPb levels were measured in a group of 82 lead exposed adults.

**Results:** The mean BPb of the workers was 26.6 µg/dl (SD 8.6, range 10–48) and the mean SPb level 0.77 µg/dl, or 3% of the BPb level. As the SPb distribution was skewed, logarithmic transformation was performed to normalise the distribution. A bivariate scattergram of BPb and logSPb ( $r = 0.41$ ,  $p = 0.00$ ) had a line of best fit expressed as  $BPb = 29.7 + 8.95 \log SPb$ . The relation of logSPb and BPb was stronger among non-smokers ( $r = 0.42$ ) compared to smokers ( $r = 0.3$ ); and among those without a medical condition ( $r = 0.44$ ). Multiple linear regression analysis (fitting smoking and medical condition into the model) yielded an  $R$  of 0.54, and an adjusted  $R^2$  of 0.26.

**Conclusion:** The study findings do not support the use of SPb for biomonitoring at BPb levels ranging from 10 to 50 µg/dl.

## Main messages

- Salivary lead (SPb) was previously reported to be highly correlated with blood lead (BPb) among adults with high BPb, but not among children, or adults with low BPb. There was no standardised method of collecting saliva in the various studies.
- This study of adults with BPb 10–50 µg/dl showed a poor correlation between SPb and BPb ( $r = 0.4$ ).
- Using a multivariate model, SPb, smoking status, and medical condition of the subject could only explain 26% of the variation in BPb.

## Policy implication

- While the idea of using SPb to monitor individuals exposed to Pb is attractive, our findings do not support its use for this purpose at BPb levels between 10 and 50 µg/dl.

Many toxins and their metabolites are excreted in saliva, and salivary levels can reflect levels in the other body compartments.<sup>1</sup> Previously, Pan<sup>2</sup> showed a good correlation between salivary and blood lead ( $r = 0.72$ ) among adult males. The subjects were divided into four groups of 88, 114, 31, and 33, with increasing group mean values of blood lead (BPb) (18, 27, 67, and 82 µg/dl). At BPb levels >50 µg/dl, salivary lead (SPb) levels increased almost exponentially. The correlation coefficient ( $r$ ) for blood and log salivary lead was 0.8. The  $r$  for BPb and SPb within each of the four groups were unreported.

At low levels of BPb, the relation with SPb is less clear. A study<sup>3</sup> of 24 normal subjects with BPb levels of 6–14 µg/dl showed a poor and negative correlation with SPb levels ( $r = -0.186$ ). Another study of nine children with BPb levels of 20–60 µg/dl, also showed a weak correlation ( $r = 0.07$ ) between BPb and SPb.<sup>4</sup> Lead levels in parotid saliva among 10 adults with BPb levels of 16–33 µg/dl showed poor correlation ( $r = 0.137$ ) with BPb.<sup>5</sup>

In view of these inconsistent results, we studied the relation between BPb and SPb in 82 adult lead exposed workers with BPb levels of 10–50 µg/dl.

## METHODS

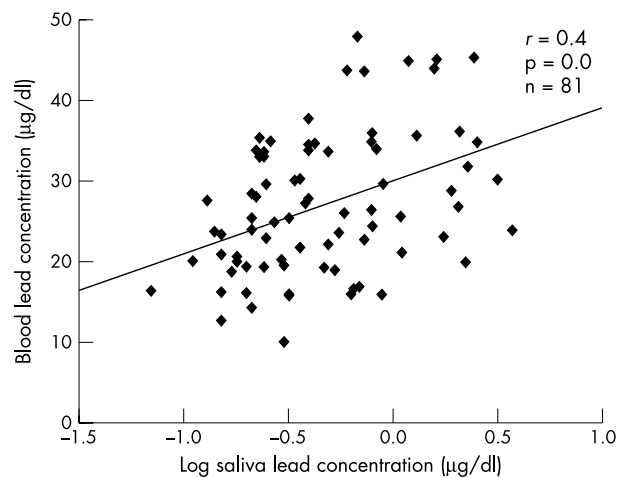
We studied 82 workers employed in a factory manufacturing a lead based polyvinyl chloride stabiliser. Our institutional review board approved the study, and all the workers gave written informed consent to participate. We collected personal information as well as blood and saliva samples during

routine six monthly statutory medical examinations. We advised workers not to smoke, eat, or drink (except water) for one hour prior to saliva collection. After rinsing their mouth with water thoroughly, a single, unstimulated saliva sample accumulated over five minutes was obtained. We used a Varian Spectrac AA-220 Atomic Absorption Spectrophotometer, a graphite furnace, autosampler, and D2 lamp background corrector for quantitative analysis of lead, in triplicate. External quality control for BPb was carried out with the National External Quality Assurance Scheme (UK) and the Inter-Laboratory Comparison Programme (Canada). Data were analysed with SPSS software Base 10.0.<sup>6</sup> The skewed SPb values were transformed (logarithmic transformation) before further statistical analysis. All  $p$  values are two sided and the level of statistical significance is 0.05.

## RESULTS

All workers who had to undergo statutory medical examinations agreed to participate in the study. All 82 workers were male, with a mean age of 35 years, and were mainly Indians (43%), Malays (35%), or Chinese (21%). The duration of employment ranged from three months to 20 years. Most workers (78%) were in the production department; 53% were smokers. Eight workers were hypertensive, two were diabetic, and three had other conditions (neurofibromatosis, hepatitis B carrier, thalassaemia).

**Abbreviations:** BPb, blood lead; SPb, salivary lead



**Figure 1** Bivariate scattergram of blood lead and log salivary lead. Blood lead concentration =  $29.74 + 8.95 \cdot \log \text{salivary lead concentration}$ .

The mean BPb was 26.6 µg/dl (standard deviation 8.55, range 10–48 µg/dl). SPb (range 0.07–7.0 µg/dl) showed a skewed distribution, with one outlier at 7 µg/dl. The outlier value was twice as high as the next value, and is likely to represent a contaminated collection sample. This was excluded from subsequent data analysis. Logarithmic transformation was performed for SPb.

A bivariate scattergram of logSPb and BPb showed a correlation coefficient of 0.41 ( $p = 0.00$ ) (fig 1). The line of best fit is described by the equation:

$$\text{BPb} = 29.74 + 8.95 \cdot \log \text{SPb}$$

The bivariate scattergram of log SPb and BPb were also examined in the following groups: subjects without hypertension ( $n = 73$ ,  $r = 0.45$ ,  $p = 0.00$ ); subjects without recorded illness ( $n = 68$ ,  $r = 0.44$ ,  $p = 0.00$ ), non-smokers ( $n = 38$ ,  $r = 0.42$ ,  $p = 0.008$ ), and smokers ( $n = 43$ ,  $r = 0.30$ ,  $p = 0.05$ ). Multiple linear regression was done, fitting smoking and medical condition into the model ( $R = 0.54$ ,  $R^2 = 0.28$ , adjusted  $R^2 = 0.26$ ).

## DISCUSSION

The idea of using saliva for biomonitoring is attractive. Its collection is less invasive than venepuncture, and likely to be better accepted by individuals, especially for periodic collections. There is also potential for cost savings, as a skilled technician would not be required to perform the collection.

There are also disadvantages of the determination of salivary lead. At present, there is no standardised method for sampling of saliva or determination of SPb, and no available external quality control programme. There are also no biological limit values for SPb in comparison to well evaluated limits for BPb.

Specifying the method of saliva collection is important. In earlier studies,<sup>2,3</sup> adults first rinsed their mouths with citric acid solution to stimulate salivary flow, followed by rinsing with deionised water, before collection of salivary drool. The method of saliva collection by Fung and colleagues<sup>4</sup> involved children chewing sugarless gum (which also stimulates salivary flow) prior to collection. In another study,<sup>5</sup> parotid saliva was collected (after reflex stimulation with orange flavoured lozenges) by a modified double lumen Teflon-Lashley cup.

In this study, unstimulated saliva samples were collected. The method of collection was made as simple and

practical as possible under field conditions. Pre-collection instructions—to avoid eating, drinking, or smoking for an hour before collection, and a thorough rinse of the mouth immediately prior to collection—were easily understood and complied with. We carefully supervised each individual saliva collection, as previous reports had suggested that contamination of saliva could be a potential problem. The results showed a fairly uniform distribution of salivary lead among the workers. Only one outlier with an extremely high value was noted. This value is suggestive of contamination during collection, or non-compliance with the pre-collection instructions.

## Blood and salivary lead levels

Plasma lead has two components—protein bound lead and diffusible plasma lead, which is directly excreted into saliva.<sup>2</sup> At BPb <50 µg/dl, the concentration of lead appears to be lower in saliva than in blood. Mean SPb was 31% of the value of mean BPb<sup>4</sup> among nine children with a mean BPb of 42 µg/dl. At a mean BPb of 8.6 µg/dl (range 6–13.6) in 24 adults, SPb was 56%<sup>3</sup> that of BPb. Among 10 normal adults (mean BPb 25 µg/dl),<sup>5</sup> parotid saliva lead was 13% of BPb. In Pan's study,<sup>2</sup> SPb concentration was 31% and 16% of BPb levels in the groups with mean BPb of 18 µg/dl ( $n = 88$ ) and 27 µg/dl ( $n = 114$ ).

In this study, mean BPb was 26.6 µg/dl, while the mean SPb was 0.77 µg/dl, or 2.9% of BPb. This is the lowest percentage of SPb expressed as a percentage of BPb compared to earlier studies, where values ranged from 13% to 56%. One reason for this could be that contamination of saliva during collection in this study is much less compared to the earlier studies. In fact, the authors of an earlier study reported that contamination of saliva during collection could be an important issue.<sup>5</sup> Even Pan<sup>2</sup> acknowledged that lack of better correlation between SPb and BPb could be caused by oral contamination. This made us pay particular attention to proper salivary collection in this study.

At higher BPb levels, >50 µg/dl, SPb concentration was reported to be higher than blood. In Pan's study,<sup>2</sup> the two groups with mean BPb of 67 µg/dl ( $n = 31$ ) and 82 µg/dl ( $n = 33$ ), showed SPb concentrations of 142% and 271% of BPb. This could be caused by increased excretion of lead in saliva at these levels of BPb, or possibly contamination during saliva collection.

The correlation of SPb with BPb in this study is not strong ( $r = 0.4$ ). After adjusting for health condition and smoking habit of subjects, in multivariate analysis,  $R$  increased to 0.54. One reason is that SPb may be proportional to the diffusible component of plasma lead, rather than whole blood lead. Secondly, there may be differential rates of excretion of lead into saliva at different levels of BPb. The  $r = 0.4$  is stronger than what is reported among children<sup>4</sup> and adults<sup>3</sup> with low BPb levels. Collection of saliva from children is more difficult than from adults, and this could have affected the results, in addition to the small sample size ( $n = 9$ ). In the adult study,<sup>3</sup> the mean BPb was 8.6 µg/dl, which is lower than in this study. As such, these populations are not strictly comparable with our study population. Furthermore, these studies did not log transform SPb for statistical analysis, which could have resulted in the weaker  $r$ .

However, the  $r$  in this study was lower than that of Pan ( $r = 0.8$ ),<sup>2</sup> who noted that SPb did not show a parallel increase with BPb. The BPb levels in Pan's study population were higher than this study.

## Conclusion

While the idea of measuring SPb for biological monitoring is attractive, our findings do not support its use for this purpose.

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