

Investigation into a possible cancer cluster in Patient Support Staff at Royal Perth Hospital and other possible health consequences of their exposure to phenol-based cleaners at work: An independent, expert perspective

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Background

In December 2009 Royal Perth Hospital (RPH) management asked me to give external and independent expert advice on an investigation of concerns that RPH staff members had expressed about the frequency of cancer in people who had worked with phenol-based cleaners in the hospital, at both Wellington St and Shenton Park.

I visited RPH on 10th December 2009 where I was briefed by Dr Paul Mark, the Hospital's Acting Executive Director, met with the Lead Organiser of the Liquor, Hospitality and Miscellaneous Union at RPH and other members of the Hospital staff, and met with Dr Mark and Hospital and Department of Health WA experts in occupational health and epidemiology to discuss the investigation required to address staff concerns.

In addition to detailing their concerns about the frequency of cancer in Patient Support Staff (PSS) members, the RPH staff members expressed concern about other health problems they associated with phenol-based cleaners, including headaches, nose bleeds, sore throats, respiratory problems and skin allergies.

The use of phenol-based cleaners at RPH stopped in 2009 after Hospital management was informed of staff members' concerns about the frequency of cancer in those exposed to them while working at the Hospital.

The investigation

It was agreed at the meeting on 10th December 2009 that Hospital and Health Department experts would undertake an investigation into the health of PSS members who were or may have been exposed to phenol-based cleaners while working at RPH. The investigation included:

1. Measurement of the rates of cancer and death in PSS staff members and their comparison with contemporary rates in all residents of the Perth Metropolitan Area of similar age and sex distribution to the PSS staff.
2. A survey of as high a proportion of PSS staff as possible to document the extent of their exposure to phenol-based cleaners and their history of health problems possibly linked to this exposure, compare the frequency of these problems with that in other residents of the Perth Metropolitan Area (when comparable data were available), and relate this frequency to the extent of reported exposure.
3. The history of use of Phenol-based cleaners at RPH and the toxicology of phenolic and other compounds contained in them.

A protocol for this work was completed before the end of 2009 and detailed methods developed in early 2010. I participated in protocol and methods development by email and endorsed the final documents. Thereafter the necessary work was done in Perth largely without my involvement.

I received the first full draft of a report on the investigation on 26th November 2010. It was entitled *Impact of phenol-based cleaners at Royal Perth Hospital* and had been prepared by the Department of Health's Epidemiology Branch. I reviewed this draft and gave my initial comments and advice on 7th January 2011. After further review and comment on new or revised draft material for the report, I endorsed the final draft version on 19th February 2011. At that time I recommended that a further expert review be obtained for the final draft and this perspective on it, and that Professor Nicholas de Klerk of the Telethon Institute for Child Health Research be asked to be the reviewer. This recommendation was accepted, Professor de Klerk was approached, he agreed to do the review, and he provided a report of his review on 25th April 2011. As a result of Professor de Klerk's review, some changes were made to both the final version of the investigation report, *Impact of phenol-based cleaners at Royal Perth Hospital*, and this perspective, and provided to the Royal Perth Hospital on 28th April 2011 and 6th May 2011 respectively.

The report

The report, *Impact of phenol-based cleaners at Royal Perth Hospital*, speaks for itself and I will not summarise it here. Rather, I will offer answers to a set of questions that I judge to be important to RPH staff and management and that are addressed by the investigation and the report. These questions are:

1. Has there been a cluster of cancers in Patient Services Staff at RPH, the Hospital staff members considered to have been most exposed to phenol-based cleaners?
2. Is there other evidence to suggest that risk of cancer is increased in RPH staff members who were exposed to phenol-based cleaners?
3. Is there evidence that exposure to phenol-based cleaners at RPH has increased the risk of any disease other than cancer in exposed staff members?
4. Do any of the report's findings suggest that further investigation into the health of RPH staff members exposed to phenol-based cleaners is necessary?

Has there been a cluster of cancers in Patient Services Staff at RPH, the Hospital staff members considered to have been most exposed to phenol-based cleaners?

No. The overall incidence of cancer in PSS staff was no higher than that in other residents of Perth in the period from 1983 to 2008. The cancer incidence in PSS staff was observed to be 11% less than in comparable Perth residents; the standardised incidence ratio (SIR) was 0.89, 95% confidence interval (CI) 0.78-1.01. There was also no increase in cancer incidence in the most recent period analysed, 2000 to 2008: SIR 0.81, 95% CI 0.68-0.96 (Report Table 5, page 30).

Is there other evidence to suggest that risk of cancer is increased in RPH staff members who were exposed to phenol-based cleaners?

It is not uncommon to find lower rates of cancer and death when rates in groups of people identified by their employment are compared with rates in the general population within which they live. This

observation is commonly referred to as “the healthy worker effect”. It is usual, therefore, to do two additional kinds of analysis to see whether, in spite of these lower rates, there may still be an increased rate of cancer or death in the initially employed population. The first such analysis seeks to determine whether the rate of cancer is higher in people who were or have been employed for a long time in the occupation of industry than in those who have been employed for a short time. The second seeks to determine if the rate of cancer is higher in those who were first employed in the occupation or industry a long time ago than in those who were first employed in it more recently. The Report contains such analyses of the cancer incidence rates (Report Table 6, page 31).

Cancer incidence rates

Those who worked in PSS for five or more years had a somewhat higher rate of cancer than those who worked in PSS for less than a year: hazard ratio (or relative risk) 1.23, 95% CI 0.88-1.73. That is, those who had worked for 5+ years were about 23% more likely to develop cancer, although statistical uncertainty means that they could have been as much as 12% less likely or 73% more likely. Those in the middle category of time since first employment, 9-18 years, had a higher incidence of cancer than those with the shortest time since first employment (0-8 years) or those with the longest time (19+ years). This is an unusual pattern and not easily explained; although it could occur if cancers caused by some agent in the hospital workplace were not to appear until some 10 years after first exposure and there were few people with that exposure who had begun working at the hospital 20 or more years in the past.

In addition to comparing rates of all cancers together in PSS employees with those in the general population of Perth, rates of the commoner types of cancer were also compared (Report Table 7, page 31). Relatively small numbers of each of the compared types of cancer make the SIRs uncertain but one group of cancers stands out, those of unknown primary site: SIR 2.98, 95% CI 1.54-5.20. These cancers are not clearly associated with a specific organ or tissue of the body and are generally quite advanced when they are diagnosed. They are thought to be either advanced common cancers that have been poorly characterised or, perhaps, a unique kind of cancer with a different origin from other kinds of cancer. While the lack of evidence that other common cancers are increased in incidence in PSS staff suggests that this might just be a chance increase, the fact that the rate of unknown primary cancers increased with both duration of employment and time since first employment (Report Table 8, page 33) suggests that it is real.

Cancer death rates

Overall, the cancer death rate was a little higher in PSS staff members than the Perth population: standardised mortality ratio (SMR) 1.15, 95% CI 0.90-1.45 (Report Table 11, page 35). Cancer death rates were more strongly related to duration of employment in PSS (Report Table 12, page 36) than were cancer incidence rates. Compared with people employed for less than one year in PSS, those employed for 5+ years were a little more than twice as likely to have died from cancer: Hazard ratio 2.19, 95% CI 1.15-4.20. Chance is an unlikely explanation for this difference. Like cancer incidence, the rate of death from cancer was higher in the middle category of time since first employment than the shortest or the longest.

Cancer related to reported exposure to phenol-based cleaners

Two other analyses examined the risk of cancer in PSS employees (Report Tables 22 and 23, page 47). They were based on a small sub-group of present and former PSS staff who responded to a mailed questionnaire about their health and exposure to phenol-based cleaners while working in PSS, and provided complete exposure information. They were a highly selected group of people; but comparisons *between* members of this group could provide unbiased information. Eighteen of 227 people in the group who also gave permission to link their surveys to Cancer Registry records were found to have a cancer registered in the WA Cancer Registry; 44 of the whole group (233 people) said a doctor had told them they had cancer. When reported hours of exposure to phenol-based cleaners in those with a registered cancer or, separately, those who said a doctor had told them they had cancer were compared with hours of exposure in those who did not have a cancer, there was weak evidence that the odds of having a cancer increased with increasing hours of exposure. The odds ratio (the ratio of the odds of having a cancer if in a higher exposure group to the odds of having one if in the lowest exposure group) for a registered cancer in the highest exposure group was 1.39, 95% CI 0.37-5.18, and for a reported cancer 1.57, 95% CI 0.65-3.84. Chance is a possible explanation for these increased odds ratios.

Conclusions

Overall, there is little evidence to suggest that RPH staff members exposed to phenol-based cleaners have an increased risk of cancer as a whole, or that their risk of cancer as a whole is related to their amount of exposure to phenol-based cleaners. It is possible however that RPH staff members exposed to phenol-based cleaners have an increased risk of cancers of unknown primary site. This finding was unexpected. In the course of normal scientific inquiry, findings such as this would be treated as uncertain until they have been confirmed in other, similar exposure circumstances.

There is stronger evidence that RPH staff members exposed to phenol-based cleaners have an increased rate of death from cancer than people of the same age and sex in the general population of Perth. This does not necessarily mean that this increased rate is due to their exposure to phenol-based cleaners. There may be other characteristics of PSS staff that put them at higher risk of cancer than people in the general population. Such characteristics could produce increasing death rates from cancer with increasing duration of employment or time since first employment. The healthy worker effect would suppress otherwise higher rates of death from cancer early in employment because people seeking and gaining employment are generally healthier than the average in the community. With passage of time after first employment, however, the true, underlying rates of death from cancer would become evident. The fact that the trends to increasing rates with duration of employment and time since first employment were stronger for cancer death rates than cancer incidence rates supports this possibility. It is probable that the healthy worker effect selects less against employment of people who will soon be diagnosed with cancer than it selects against people who will die soon from cancer.

Is there evidence that exposure to phenol-based cleaners at RPH has increased the risk of any disease other than cancer in exposed staff members?

The investigation addressed this question through analysis of death rates from causes other than cancer in PSS staff members and through the survey of health and exposure to phenol-based cleaners.

Death rates from causes other than cancer

Overall, rates of death from all causes in PSS staff members from 1983 to 2008 were 24% higher than those in the general population of Perth: standardised mortality ratio (SMR) 1.24, 95% CI 1.06-1.43 (Report Table 9, page 33). This higher death rate from all causes was mainly due to a higher death rate in male PSS staff members than men in general in Perth: SMR 1.39, 95% CI 1.14-1.68. The overall higher death rate was more evident in non-cancer deaths – SMR 1.27, 95% CI 1.05-1.54 than in cancer deaths – SMR 1.15, 95% CI 0.90-1.45 (Report Tables 11 and 13, pages 35 and 36). There was little evidence to suggest that death rates in PSS staff had increased or decreased relative to those in Perth over the 26 years covered by the investigation.

Like death rates from cancer, death rates from causes other than cancer were higher in PSS staff members with long employment in PSS than those with very short employment (although this pattern could have been due to chance), and was highest in the middle category of time since first employment (Report Table 14, page 37). The risk for non-cancer death in male PSS employees was substantially higher than that in female employees: hazard ratio 1.78, 95% CI 1.19-2.66. This was not true of cancer deaths.

Other conditions related to reported exposure to phenol-based cleaners

The conditions other than cancer that were asked about in the survey of present and former PSS staff members are listed in Report Tables 15 and 16 (pages 40 and 41). Where possible, PSS staff members' responses were compared with those given by participants in Department of Health WA's Health and Wellbeing Surveillance surveys in 2009. PSS staff members who completed the survey (~20% of those who were sent the questionnaire) reported higher frequencies of all conditions covered by both surveys than did Health and Wellbeing Surveillance survey participants. This pattern suggests that PSS staff members were more likely to participate in the survey if they had a condition that might have been related to exposure to phenol-based cleaners than if they did not. Thus this comparison with the WA's Health and Wellbeing Surveillance survey participants does not assist in determining whether exposure to phenol-based cleaners at RPH had increased risk for any condition. Examining how the frequency of the conditions asked about in the PSS staff members' varies with their reported hours of exposure to phenol-based cleaners is a more reliable approach. Even here, though, there could be some selection of sicker people for participation, since those who provided sufficiently complete information to allow an estimate of hours of exposure reported most conditions more frequently than those who didn't provide complete information (Report Table 19, page 45). Thus, the most valid analyses were considered to be those based on participants' reports of doctor diagnosed conditions: asthma, respiratory conditions other than asthma and skin conditions other than skin cancer.

The results for analyses of doctor diagnosed asthma, respiratory conditions other than asthma and skin conditions other than skin cancer appear in Report Tables 24 to 29 (pages 48 to 51). PSS staff who reported doctor diagnosed asthma had, when compared with those without this history, greater average total hours of exposure to phenol-based cleaners (Report Table 24, page 48) and there were indications that the odds of having doctor diagnosed asthma were higher in those with moderate or high hours of exposure than those with low hours: odds ratios 2.08, 95% CI 0.90-4.82, and 1.74, 95% CI 0.74-4.10, respectively (Report Table 25, page 48). However, on the basis of their p-values, all of these differences could have been due to chance.

There is a rather different picture for doctor diagnosed respiratory disease other than asthma. The difference in mean exposure hours between PSS staff members with and without this history is larger (Report Table 26, page 49) and the trend towards increasing odds of respiratory disease other than asthma with increasing hours of exposure to phenol-based cleaners is stronger: odds ratio for moderate hours 1.73, 95% CI 0.53-5.60, and for high hours 2.75, 95% CI 0.92-8.23 (Report Table 27, page 50). Importantly when the hours of exposure were included as a continuously distributed variable in the statistical model for respiratory disease other than asthma, rather than in three categories, it was estimated that the odds of these conditions increased by 3 in a thousand for each 100 hours of exposure (95% CI 1 to 5 in a thousand). This association is unlikely to be due to chance.

The picture for doctor diagnosed skin disease other than skin cancer lies somewhere between those for asthma and respiratory disease other than asthma. Probably the strongest indicator that these conditions might be associated with exposure to phenol-based cleaners is that from the statistical model with hours of exposure included as a continuous variable: the odds of these conditions were estimated to increase by 2 in a thousand for each 100 hours of exposure (95% CI 0-3 in a thousand) (Report Table 29, page 51). This association, however, could have been due to chance.

Conclusions

The higher death rate from causes other than cancer in PSS staff members, relative to that in the general population of Perth, suggests that the underlying risk of death in these staff members is greater than that in the general population.

The higher death rate from all causes (and from cancer and causes other than cancer separately) in men, relative to that in men in the general population of Perth, also suggests there is a higher underlying risk of death in PSS workers, particularly men. This higher death rate in men is unlikely to be an effect of exposure to phenol-based cleaners since female PSS staff members reported some 50% more hours of exposure to these cleaners (average 9,593 hours) than male staff members (6,609) (Report page 43), yet they had less of an increase in risk of death from all causes in male PSS staff members did.

The strong increase in rate of death from other causes in the middle and, although less, longest categories of time from first employment with PSS, with less of an increase in rate of death with increasing duration of employment, could be due to diminution of the healthy worker effect over time.

It is probable that RPH staff members exposed to phenol-based cleaners have an increased risk of doctor diagnosed respiratory disease other than asthma. This may also be the case for skin diseases other than skin cancer.

Do any of the report's findings suggest that further investigation into the health of RPH staff members exposed to phenol-based cleaners is necessary?

Cancers of unknown primary site

While the unexpected increase in incidence of cancers of unknown primary site in PSS staff members might be caused by exposure to phenol-based cleaners, this is by no means certain. Thus it merits further investigation; although the difficulty of further investigation should not be under-estimated.

That risk of these cancers increased quite strongly with duration of employment suggests that risk might be related to amount of exposure to phenol-based cleaners. RPH management should determine whether it is possible to estimate the likely total exposure to phenol-based cleaners of staff members who developed these cancers and compare it with the exposure of a sample of PSS staff members who worked at RPH during similar periods. If those who developed unknown primary site cancers had substantially greater exposure to phenol-based cleaners than their contemporaries, this would provide stronger evidence that this exposure caused these cancers. While such a finding would be of no direct benefit to RPH staff, because the hospital no longer uses phenol-based cleaners, it might encourage reduction in use of these cleaners in other settings and thus improve the health of others.

The health of PSS staff members

The patterns of death rates in PSS staff members, although difficult to interpret due to the healthy worker effect, suggest that they are people at higher risk of illness than the general population of Perth. There a number of reasons why this might be so.

1. People who seek employment in PSS at RPH come from sub-groups within society who, for reason of their social or economic circumstances, or their pattern of health-related behaviours (with which these circumstances are intertwined), are at greater risk of illness than is average for the whole community.
2. People who are or have been sick, but are now well enough to work again, preferentially seek employment in PSS at RPH, or the Hospital gives preference to such people in its employment decision making.
3. There are workplace hazards at RPH, of which phenol-based cleaners may have been one, that cause ill health in PSS staff members.

While phenol-based cleaners probably have made a contribution to illness in PSS staff, at least by increasing risk of lung conditions other than asthma, they are unlikely to be a complete explanation for the findings of this investigation. The great similarity between the results of analyses of rates of death from cancer and rates of death from causes other than cancer, and the lack of substantial variation in relative risks of different kinds of cancers (except those of unknown primary site that are too few to have much effect on the overall results for death from cancer), suggest that whatever is causing greater ill health in PSS staff affects a broad range of diseases, both cancer and non-cancer.

This would tend to rule out any single workplace hazard and favour the first or the second explanation offered above.

Subject to staff agreement, RPH management might consider undertaking a survey of the health (including relevant biochemical and physiological measurements) and health-related behaviours of a sample of its PSS staff members to see how they compare with measurements of these characteristics in the general population. If, as I suspect, such a survey showed an existing higher prevalence of common chronic diseases that limit life and risk factors for these diseases in PSS staff, the Hospital should consider implementing an ongoing program to help these staff members improve their health.

Skin conditions other than skin cancer

Whether or not exposure to phenol-based cleaners has caused skin conditions other than skin cancer may become clearer if expert dermatological examination and assessment of exposure to phenol-based cleaners were to be included in the health survey suggested above.