"There will be no more!": the legacy of the Toowong breast cancer cluster

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ABSTRACT

- During 1994–2006, 10 cases of invasive breast cancer were diagnosed among 550 women employed for some time at a broadcast media site in Brisbane, Queensland.
- These cases represented a more than sixfold increase in risk compared with the female population of Queensland.
- After an initial unsatisfactory inquiry, an independent assessment was successful when the investigation addressed environmental factors of concern to the employees, as well as agents that may have accounted for the cluster.
- The perceptions of the women affected were documented in the television program *Australian Story*.
- No specific cause of the cluster was identified, but staff concerns were allayed by relocation from the site.
- The outcome suggests a specific duty of care involving adequate attention being paid to community needs in such situations.

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Cancer clusters are common, but only a small proportion are reported. Investigations may confirm anecdotal reports of a higher than expected incidence of disease, and will focus on circumstances that would account for the cluster. A few cancer clusters can be related to point sources of specific potent carcinogens, particularly those inducing less common tumours, but more often, they are attributed to chance.[1,2]

The events surrounding investigations into a cluster of breast cancers among broadcast media workers in Brisbane, Queensland suggest that this approach to cluster investigation is inadequate. The cluster involved women employed by the Australian Broadcasting Corporation (ABC) at a site in the outer Brisbane suburb of Toowong. An initial investigation culminated in the appointment of an Independent Review and Scientific Investigation Panel.[3] An account of the events was shown in the "human interest" television series *Australian Story*. Availability of both a scientific analysis and the documented perceptions of those affected affords insight.

Outrage

"There will be no more!" was the cry of a woman responding to another case of breast cancer among ABC employees at Toowong during the episode of *Australian Story* broadcast on 12 March 2007. The new case had occurred in the face of apparent inaction to prevent such a development.

The Toowong cluster of 10 verified cases was shown to constitute a sixfold increase in risk for women working at the site compared with the general female population of Queensland (Box 1). Following the Third Progress Report from the Independent Review and Scientific Investigation Panel, it was agreed by all concerned — the investigators, the staff and ABC management — that an adequate investigation had now been undertaken. *Australian Story* focused on the battle that the affected women had to undertake to achieve this outcome, which only occurred after rejection of an initial investigation that, although perhaps properly grounded in science, could never alleviate the anxiety experienced by the ABC staff. The issue here is the difference between investigating factors that would account for the cluster and investigating factors that are unlikely to be causative but are weighing on the minds of the people in the cluster. Exactly which carcinogens should be assessed when a cluster is confirmed?

Causes of breast cancer

Each known carcinogen targets a particular organ or organs:[4] asbestos causes lung cancer and mesothelioma; 2-naphthylamine causes bladder cancer; benzene causes leukaemia; and so on. However, no carcinogen is established (equated here with IARC [International Agency for Research on Cancer] Evaluations Group 1;[5] see Box 2) as causing breast cancer following occupational exposure. No occupation has been consistently associated with increased breast cancer risk.[6-8] Following a large prospective study, Calle et al concluded that:

> These results offer little support for an association between occupation and breast cancer mortality in general or for particular occupational titles, including teachers and nurses.[9]

The few established causes of breast cancer have emerged in non-occupational contexts.[5] Cancers among survivors of the Nagasaki and Hiroshima atomic bombs established that ionising radiation causes breast cancer. Iatrogenic studies of breast cancer and endometrial cancer provide evidence for the Group 1 status of postmenopausal oestrogen therapy.[5] Drinking alcohol causes breast cancer (and other tumour types).[5] Beyond these agents, exogenous causes of breast cancer in humans remain to be proven. Not surprisingly, none of the clusters of breast cancer reported in the medical literature are attributable to specific carcinogens.[10-12]

A wide range of hormonal and reproductive risk factors have been established for breast cancer.[13] Increased risk is correlated with early menarche and late menopause, and risk increases at its highest rate with age during menstrual life. Nulliparous women have about a 40% higher risk than parous women, and the earlier a woman's first birth, the lower the risk. Risk of breast cancer falls with increasing parity, independent of age at first birth, and risk is decreased in women who breastfeed. Breast cancer risk is increased two- or threefold in women who have one or more first-degree relatives with breast cancer. A minority of heritable risk is attributable to *BRCA* genes.[14]

Circumstances that would explain the cluster

A high level of exposure of the ABC staff to an agent known to cause breast cancer would account for the cluster in Toowong. Ionising radiation was therefore suspected, but not for long. The possibility that a bank of improperly shielded linear accelerators or x-ray machines was located onsite could be dismissed as easily as Toowong having been the site of a thermonuclear war. There appeared to be no credible sources of sufficient ionising radiation.

The prospect of endogenous factors accounting for the cluster cannot be as readily dismissed. Although unlikely, a significant

1 Details and confirmation of the cluster

The cluster of breast cancer cases at ABC Toowong initially involved 13 women — invasive breast cancer was confirmed in 11, one had mucoid carcinoma and was also included, while one case of ductal carcinoma-in-situ was excluded. The investigation was restricted to women diagnosed while employed at ABC Toowong during 1 January 1994 – 30 June 2006, excluding two of the cases and leaving 10 as the focus of investigation. Five of the women were < 40 years old when diagnosed, four were 40–49 years, and one was over 50 years. They had worked at ABC Toowong for 6–18 years (median, 11 years). A total of 550 women were employed at Toowong at any time during the period in question, for an average of 3.3 years. Most of the women were aged in their 20s (47%) or 30s (28%) when they entered the relevant time period; 3% were 18–19 years, 15% were in their 40s and 7% were 50 years or older.

A Queensland Health investigation found that, although a statistical excess of cases was likely, epidemiological techniques could not definitively establish the expected number of cases in light of the available data.[3] It was concluded that any excess was most likely due to coincidence and that workplace-related factors were an unlikely explanation. The results of this investigation did not allay concern — a staff walkout ensued, and the ABC convened an Independent Review and Scientific Investigation Panel, whose Third Progress Report[3] was made public in December 2006.

This report indicated that, given the age of this workforce and the incidence of breast cancer in Queensland, 1.6 cases of breast cancer would be expected, and the 10 cases corresponded to a standardised incidence ratio of 6.25 ($P = 0.000001$). This represents a 1 in 1 000 000 probability of a group of breast cancer cases this large or larger occurring by chance at the site, assuming the women had the same incidence of breast cancer as women in the rest of Queensland. The relationship of risk to duration of employment was indicated by a relative hazard of 1.12 (a 12% rise in risk of breast cancer per year of employment), with a P value of 0.022 indicating a 1 in 45 chance that the increased risk with longer employment was just a chance finding.[3]

On 13 July 2007, another former Toowong journalist was reported as being diagnosed with breast cancer. This event does not immediately contribute further understanding, but may do if the cluster criteria are expanded to include it, with commensurate alteration in the number of expected cases. ◆

2 IARC Evaluations of Carcinogenic Risks to Humans

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans[5] concern chemicals, complex mixtures, occupational exposures, lifestyle factors, and physical and biological agents for which there is at least some positive evidence of carcinogenicity. Epidemiological and experimental evidence are separately evaluated as providing *sufficient*, *limited*, or *inadequate* evidence or *suggesting lack of carcinogenicity* of the agent in humans or animals, respectively. *Sufficient evidence* is indicative of causation, *limited evidence* falls short of that confidence, and *inadequate evidence* indicates that positive evidence of carcinogenicity is restricted in amount and/or inconsistent, and does not allow either of the former findings to be made.

The *Overall Evaluation* of carcinogenicity is made by taking account of both the epidemiological and experimental data, as well as other data, specifically including that indicating mechanism(s) of action. The *Overall Evaluation* is categorised by whether the agent is *carcinogenic for humans* (Group 1), *probably* (Group 2A) or *possibly* (Group 2B) *carcinogenic for humans*, or *not classifiable as to carcinogenicity to humans* (Group 3). These evaluations are made in general terms (eg, static electric and magnetic fields and extremely low-frequency electric fields are *not classifiable as to their carcinogenicity to humans*) without reference to any particular tumour type or mode of exposure (unless the whole monograph is restricted to a particular mode of exposure).

IARC = International Agency for Research on Cancer. ◆

number of the affected women could have been *BRCA* carriers. An unusual preponderance of childless women, together with women who had a first birth late in life or who were using certain oral contraceptives, could at least partially explain the cluster.

The investigations

In May 2005, concerned ABC staff members asked Queensland Health to investigate whether there were more breast cancer cases in their workforce than would be expected and whether the working environment might be responsible (Box 1). As related in *Australian Story*, this investigation included ascertaining a detailed history for each woman affected. The consequences of this line of enquiry were disastrous. The women expected environmental monitoring and quantitation of pollutants in response to their notification of a cluster. What they got was intimate questioning about when their periods started, whether they breastfed, and if they were using oral contraceptives. Such an investigation failed to address the women's anxiety, and its execution held no prospect of preventing further instances of cancer. The women were outraged; cooperation was refused.

The staff wanted the cluster to be investigated with reference to the presence of agents they believed were possible causes of breast cancer: electromagnetic fields, pesticides, heavy metals, environmental tobacco smoke, and asbestos. These factors were systematically addressed by the subsequently appointed Independent Review and Scientific Investigation Panel, resulting in the women's active cooperation with this Panel. *Australian Story* implied that once the women understood that the external factors about which they had concerns were to be comprehensively investigated, they agreed to provide details of their personal histories. Accordingly, the Panel was able to establish that the group of 10 women could not be distinguished from women of a similar age in the Queensland population in the same time period, in relation to family history of breast cancer, body height and weight, exercise, alcohol drinking, menarche, menopause, childbearing, oral contraceptive use, and breastfeeding.[3] Endogenous and relevant behavioural factors were ruled out as contributing to the cluster.

Agents causing concern

It was clear from *Australian Story* that the factor weighing most heavily on the women's minds was electromagnetic fields; given their concern, the available data warrant consideration. Low-frequency electromagnetic fields cannot be dismissed as a trivial consideration due to several studies indicating that risk of childhood leukaemia is related to the strength of these fields. These data, categorised as *limited epidemiological evidence* of carcinogenicity (Box 2), are not complemented by experimental evidence of carcinogenicity.[5] Apart from childhood leukaemia, there is no consistent positive evidence of carcinogenicity. Studies suggest that mobile phone use is not associated with glioma,[15] nor is relevant occupational exposure.[16] Evidence for causation of breast cancer by electromagnetic fields has been sought, but not found.[17]

However, electromagnetic fields cannot be set aside. The issue is not that insufficient data exist to attribute a breast cancer cluster to electromagnetic fields, but that there is sufficient information to

suggest the cluster may be a consequence of electromagnetic fields — especially in the minds of those affected. This was investigated, but measurements at the site did not distinguish it on the basis of field strength and provided no credible inference of causation.[3]

Though few carcinogens are known to cause breast cancer, many are suspected. Certain insecticides, though not known to cause breast cancer, are characterised as xenoestrogens. However, a study prompted by a higher than expected incidence of breast cancer among residents of Long Island, New York failed to implicate insecticides.[18] Various tumour types are implicated in relation to solvents (and proven in the case of benzene), but not breast cancer.[19] Metals are linked to cancers at multiple sites, depending on the particular metal and the mode of exposure; breast cancer is not involved.[20] Asbestos is not known to cause breast cancer. Active smoking has been discounted as a cause of breast cancer, and corresponding data involving environmental tobacco smoke are inconsistent.[5] No marked exposure to any of these agents was evident, and they were excluded as contributing to the cluster.

Shift work is associated with increased risk of breast cancer. In one study, women who reported more than 20 years of rotating shift work were found to have an elevated relative risk.[21] Disturbances of circadian melatonin rhythmicity could be functionally involved with elevated cancer risks.[22] The Panel reported an unusually high level of shift work in the staff diagnosed with breast cancer.[3] Individual risk attributable to shift work may be comparable to that arising from reproductive and hormonal factors.

The most reasonable explanation for the cluster would therefore appear to be a slight risk attributable to shift work, with the remaining and major risk attributable to chance. It is unlikely that new insight regarding breast cancer aetiology will arise as a result of this cluster.

The Toowong legacy

In response to the Panel's report, the ABC promptly relocated staff from Toowong. All parties recognised that evacuation was the correct decision, despite also recognising that a specific cause of the cluster was not apparent.

"There will be no more!" In parallel with staff relocation, what action is warranted in relation to the Toowong cluster? This question must be answered with reference both to medicoscientific criteria for cancer prevention and equally to the needs of the community (ie, the ABC employees) affected. Relocation of staff from the Toowong site was not mandated by identification of a hazard, but met the needs of the people affected, and may represent a duty of care of the employer. Staying in the same building would present the prospect of a further case of breast cancer (one woman in eight is affected), and the cluster being seen to continue.

Neither the available scientific evidence nor the needs of staff appear to warrant ongoing monitoring of any of the agents addressed in the Panel's report in the new or other ABC workplaces. Screening for breast cancer in staff at a level above population-based mammography is also not warranted by the scientific evidence, but may be a duty of care of the employer in these circumstances. That duty requires that staff be adequately informed about such screening, including the limitations of particular procedures.

It has been widely recognised that the needs of the affected community should be addressed during investigation of a cancer cluster.[1,23] However, these needs have been presumed to be met essentially by adequate communication, particularly involving understanding of risk.[24] In contrast, community needs in the Toowong cluster were addressed by altering the direction and content of the investigation. A duty of care was seen to be met when the investigation was extended beyond carcinogens that would account for the cluster to all carcinogens that were worrying those affected. For these carcinogens and circumstances of exposure, the duty is to exclude causation by demonstrating average rather than unusual levels of exposure for those identified as being at risk.

Competing interests

None identified.

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