

REVIEW ARTICLE

Lung Cancer Risk in Workers in the Meat and Poultry Industries – A Review

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Impacts

- Humans are commonly exposed to viruses that cause cancer in poultry, cattle and sheep. These viruses infect and transform normal human cells into cancer cells in the laboratory. It is not known whether they cause human cancer in real life.
- This paper reviews all the scientific evidence available to date from 60 studies, for lung cancer occurrence in persons with very high exposure to these viruses.
- The overwhelming evidence indicates that persons highly exposed to these viruses do have excess occurrence of lung cancer that is not explained by tobacco smoking and likely due to these viruses.

Keywords:

Oncogenic viruses; chickens; meat; live animal; slaughter; frying meat; smoking meat; curing meat

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Summary

Laboratory and *in vivo* studies in primates, and serological evidence in humans, indicate that food animal oncogenic viruses show potential for causing cancer in humans. However, until fairly recently, supporting analytic epidemiologic studies have been lacking and have concentrated on lung cancer. We conducted an extensive Medline search and reviewed 60 studies investigating lung cancer risk in highly exposed workers in the meat and poultry industries. The overwhelming majority of studies of different designs (including all the cohort mortality and cancer incidence studies) indicate at least a 30% excess risk of lung cancer in meat and poultry plant workers, even after controlling for smoking. Evidence points to food animal oncogenic microorganisms as one of the main causes. This has important public health implications because the general population is also widely exposed. Studies carried out thus far have not had sufficient statistical power to investigate other potentially carcinogenic exposures within the industries. Thus, large studies that can adequately control for occupational and non-occupational confounding factors are needed, so that the possible role of food animal oncogenic viruses in the occurrence of human lung cancer can be clearly defined.

Background

In 1982/1983, several letters appeared in the literature calling attention to the occurrence of increased risk of lung cancer in workers in the *meat* industry in England and Wales, Denmark, Sweden, Germany and the United States (Doerken and Rehpenning, 1982); Fox et al., 1982; Griffith, 1982; Johnson and Fischman, 1982; Lynge et al., 1983). These studies either were record linkage analysis of national occupational mortality, cancer incidence and

census data or were the results of analysis of limited data, and they did not control for tobacco smoking.

Since then, several more studies reported on lung cancer risk in the meat industry. Kristensen and Lynge (1993) conducted a review of studies published up to the end of 1989, and McLean and Pearce (2004) in another review updated the evidence up to 2004. Both reviews, involving a total of 30 studies altogether, confirmed the excess occurrence of lung cancer in meat industry workers and noted that not all of the excess could be explained by

tobacco smoking. Kristensen and Lynge (1993) suggested that the role of human papilloma viruses and stress in the occurrence of the excess should be further explored, as these are the only work-related likely candidates for an aetiological role. However, in a subsequent study by Al-Ghamdi et al. (1995), no papilloma virus DNA was found in DNA extracted from lung cancer tumours of 40 butchers and 26 controls. Thus, this finding was not supportive of the hypothesis that papilloma viruses were playing a major role in the aetiology of the lung cancer excess in the industry.

McLean and Pearce (2004) in their review found that the excess risk of lung cancer was strongly associated with exposure to animal slaughtering, or freshly slaughtered meat, or to biological material contained in blood and animal faecal matter and was greater than could be attributed to tobacco smoking. They concluded that the findings *in toto* suggest an aetiological role for biological exposure (infectious organisms and their endo- and exotoxins) in the occurrence of the lung cancer excess. Thus, from these two reviews, the body of evidence suggests that workers in the meat industry have some excess risk of lung cancer that may not be due to tobacco smoking, and thus far, biological agents are at least one probable cause of the excess.

The purposes of this paper are to review studies published up to 2004, which were not included in the two previous reviews, and to review new studies of workers in the *meat* and *poultry* industries published until the end of September 2011.

Methods

First, we considered studies published up to 2004 on workers in the *meat* industry that were omitted in the previous reviews ($N = 13$). Next, we updated the evidence for new meat industry studies published from 2005 to the end of September 2011 ($N = 10$). We then reviewed all the studies on the meat industry (new and old) to evaluate whether or not the excess lung cancer risk in meat workers is independent of tobacco smoking. Next, we critically evaluated the role of exposure to oncogenic viruses and other potentially carcinogenic exposures in the workplace, in the occurrence of the excess lung cancer risk. This was achieved by conducting a detailed examination of cohort studies of workers in *cattle*, *pigs* and *sheep* slaughtering and processing plants and case-control studies nested within these cohorts. The reason for the focus on cohort studies is because these are the studies that were purposefully put together and designed to investigate disease risk in meat slaughtering and processing plant workers or in butchers and meatcutters. Also, they do not suffer from some of the more troublesome biases

that frequently plague analytic case-control studies. Additionally, they have been the principal studies to have provided some insight as to what occupational exposures may be responsible for the lung cancer excess in meat and poultry workers. Finally, we reviewed the evidence for lung cancer occurrence in workers in the *poultry* industry based on cohort studies ($N = 7$) and a case-cohort study nested within a combined cohort. The evidence for lung cancer occurrence in the poultry industry has not been reviewed before.

A total of 60 studies (30 previously reported on and 30 new) were included in this review. Fifty-three were from the meat industry (cattle, pigs, sheep) and seven from the poultry industry (chickens and turkeys). In this review, only studies that specifically identified and provided information on workers in the meat or poultry industries were considered. Key words used to identify studies include meat or livestock workers, meat processors, butchers, slaughterhouse, abattoir, meatpacking plants, chicken slaughtering, chicken processing, meat department of supermarkets, poultry processing, poultry production, meatcutters, meat handlers, meat wrappers and meat production workers. Search terms used for the outcome included lung cancer, bronchogenic carcinoma and lung neoplasms. These titles were searched under Medline for the period 1950–2011. We also searched with key words such as mortality, occupation, industry, cancer incidence, death certificate and case-control studies. Finally, we searched references in published papers to identify additional studies during the same period. Titles such as food producers, wrappers and packers were not considered as they could involve other industries outside the meat and poultry industries. Also, meat and poultry farmers are not considered in this review.

It was decided to do a traditional systematic review and present the results in detail in tables, rather than perform a formal meta-analysis for the following reasons: (i) to permit a clear appreciation of the diverse sources of the evidence; (ii) because the distributions of lung cancer risk and candidate carcinogenic exposures are not uniform within the meat and poultry industries. Risk may be confined to a particular subgroup(s) (e.g. workers in a specific race/sex subgroup, workers in a specific job category) because of exposures unique to such a subgroup(s); (iii) many of the studies reviewed, especially case-control studies of lung cancer, typically provided little more than a summary odds ratio (OR) or relative risk measure in a table for the meat or poultry industry, because the purpose of those studies was to examine the role of a multitude of industries and occupations in the occurrence of lung cancer, and the meat and poultry industries or occupations were just two of many other occupations and industries investigated; (iv) the effect measures used

varied considerably among studies, involving estimation of relative risk, OR, mortality OR, standardized mortality and cancer incidence ratios, proportional mortality ratio (PMR), etc. In addition, some of the studies did not provide confidence intervals or standard deviations.

As a relative risk of 1.3 is the lowest value for which statistical significance on the increased risk has been reported for the association between lung cancer and the meat industry (Coggon et al., 1989; Reif et al., 1989; Johnson et al., 1995a; Boffetta et al., 2000), for this review, we arbitrarily considered a minimum relative risk of 1.3 to be an indicative of excess occurrence of lung cancer.

Results

Table S1 shows the 30 studies that were previously reviewed. As can be seen, 83% (25 of 30) of the studies reported a relative risk of at least 1.3 for lung cancer associated with working in the meat industry. This high rate was maintained irrespective of the study design, with the exception of the three death certificate studies.

New studies in meat industry

Table S2 lists 23 new studies that were not previously reviewed. Of these, 17 (74%) reported an association between lung cancer and the meat industry and the other six did not (Blair et al., 1985; Olsen and Jensen, 1987; Schoenberg et al., 1987; Jahn et al., 1999; Besson et al., 2006; Consonni et al., 2010).

Thus, the overwhelming majority of studies in the meat industry conducted to date, that is, 42 of 53 (79%), have reported a minimum relative risk of 1.3 for the disease in meat industry workers or for meat-related occupational exposures such as butchers and meatcutters. Assuming the findings from all these studies are valid, one important question is to be posited: to what extent tobacco smoking may account for the excess occurrence of lung cancer in these workers. This is particularly relevant for meat workers having high rates of tobacco smoking. In one national survey in the United States, butchers and meatcutters smoked the second highest amount of cigarettes per day among all occupational groups (Leigh, 1996).

Role of tobacco smoking

Of the 30 studies previously reviewed, only five controlled for tobacco smoking (Vena et al., 1982; Gustavsson et al., 1987; Johnson, 1991; Siemiatycki, 1991; Jockel et al., 1998). With the exception of the study by Vena et al. (1982), four of the five studies (80%) reported excess risk of lung cancer in meat workers. The study by Vena et al.

(1982) had potential for serious misclassification of exposure as they used the Standard Industrial Classification (SIC) codes, and occupations in the meat industry are defined as follows: having worked as an operative, labourer, inspector, packer or wrapper, foreman, farm service labourer, meatcutter, in any of six industries that include (i) meatpacking (SIC 2011), (ii) sausage and other prepared meat products (SIC 2013), (iii) medical and hospital equipments (SIC 5047), (iv) kitchen and restaurant equipments (SIC 5049), (v) and (vi) food stores (SIC 54). These occupational and industrial codes used in their study for defining meat industry are too broad and obviously included non-meat industries and occupations. Also, farming exposure is well known to be associated with decreased lung cancer risk, and the term 'Packer' can refer to packing produce or packing items outside the food industry. Thus, this study should not qualify for investigating this issue.

Of the 23 new studies updated in the present review, 13 (i.e. all of the case-control studies) adjusted for tobacco smoking or were in non-smokers. Ten of the 13 (77%) reported an excess of lung cancer in meat workers, and the remaining three did not (Schoenberg et al., 1987; Jahn et al., 1999; Consonni et al., 2010).

Of the total of four studies altogether that adjusted for smoking but did not find an association for lung cancer and meat workers, the study by Vena et al. (1982), as mentioned above, suffered from severe misclassification and was not a valid study of meat workers. The case-control study by Jahn et al. (1999) considered only 10 women with lung cancer who were butchers and meat workers and the one by Schoenberg et al. (1987) also involved only 12 lung cancer deaths among butchers, hence of low statistical power. Thus, all three of the four studies that controlled for tobacco smoking and did not observe a significant risk of lung cancer for meat workers were inadequate either in exposure classification or in statistical power, while the overwhelming number of studies that adjusted for tobacco smoke, 14 of 18 (78%), reported an excess of lung cancer in meat workers.

Role of occupational carcinogenic exposures

Given that it has been established from the evidence above that there is excess occurrence of lung cancer in the meat industry independent of tobacco smoking, the major question becomes what exposures in the meat industry are responsible. Possible candidates include oncogenic viruses, fumes emitted from the wrapping machine, smoke emitted from smokehouses during the smoking of meat, aerosols emitted during frying/cooking of meat, and nitrosamines and other chemicals present in spices, or formed or used during curing of meat.

Oncogenic viruses

Candidate oncogenic viruses present in food animals and their products include bovine leukosis virus (BLV) that causes leukaemia and lymphosarcoma in cattle (Burny and Mammerickx, 1987), human and animal papilloma viruses that cause benign and malignant tumours in humans and animals (Jablonska et al., 1985; Campo, 1987; Anhang et al., 2004) and Jaagsiekte sheep retrovirus that causes lung cancer in sheep (Palmarini and Fan, 2001; Wootton et al., 2005).

Johnson et al. (1986a,b, 1995a, 2011a), Johnson (1989, 1994, 2011) reported on a cohort of 28 900 members in a meatcutters' union in Baltimore, Maryland. Excess lung cancer risk was observed in all sectors of the industry (abattoirs/slaughtering plants, wholesale processing plants where no killing is carried out, combination of slaughtering and processing plants, and meat and deli departments of supermarkets). Plants where pigs were processed exclusively had the highest risks (Johnson et al., 1995a, 2011a; Johnson, 2011), and lower but definite increased risks were also observed in processing plants that handled beef predominantly, and in abattoirs handling cattle, pigs and sheep (Johnson et al., 1995a; Johnson, 2011).

In a small nested case-control study of lung cancer within the Baltimore cohort (Johnson, 1991), extremely high risks were observed for subjects who worked in stockyards and who brought in live cattle, pigs and sheep into the kill room and who were engaged in slaughtering, when compared with a truly unexposed group of workers outside the meat industry. These are activities possibly associated with one of the highest risks of exposure to transmissible agents. Similarly, butchers who killed had significantly higher risks than meatcutters who did not, and clear and consistent dose-response relations based on duration of exposure were observed for being a butcher or a meatcutter and for exposure to raw meat. These significant risks persisted after controlling for tobacco smoking. The association with working in a stockyard has been also confirmed in a case-cohort study of lung cancer in poultry workers (Felini et al., 2011).

These findings are supported in different ways by several studies: First, Gustavsson et al. (1987) in a similar nested case-control study within a cohort of butchers and slaughterhouse workers examined various exposures within the meat industry. They directly controlled for smoking and obtained elevated ORs for subjects involved in live animal care or had contact with animals. However, in contrast to the nested case-control study by Johnson (1991) in which risks associated with different tasks within the industry were obtained by comparing with a truly unexposed group of workers outside the industry, the whole study population in the study by Gustavsson et al. consisted of butchers and this means the entire popu-

lation was exposed to biological agents. Hence, the OR for each task was a comparison of those who performed the task versus those who did not, but who were also exposed, and thus, the odd ratios were biased towards the null value and though elevated were lower than those obtained in the study by Johnson (1991).

Second, record linkage studies of national data in England and Wales, Sweden and Denmark reported higher risk in slaughterhouse workers than in non-slaughterhouse workers or higher risks in skilled versus unskilled butchers and meatcutters (Fox et al., 1982; Griffith, 1982; Lyngge et al., 1983). Third, in the study by Coggon et al. (1989) of 1610 workers employed in bacon factories, abattoirs and meat distribution centres in England that slaughtered pigs or handled pork, beef and lamb, an increased risk of lung cancer was observed. The risk was higher for workers exposed to warm (freshly slaughtered) meat than for those exposed to chilled meat. The implication is that warm freshly killed meat is associated with a higher exposure to microbial agents. Survival of microbial agents in the environment will begin to deteriorate shortly after slaughter and thus will be significantly reduced in meat that is chilled later in the manufacturing process. Fourth, Guberan et al. (1993) reported on mortality and cancer incidence in 552 self-employed butchers and 310 pork butchers in Geneva, Switzerland. Elevated risk was observed for cancer of the lung in pork butchers, but not in self-employed butchers handling other types of meat or the wives of butchers. As in the study of Coggon et al. (1989), the pork butchers were exposed to freshly killed warm meat, although they were also exposed to curing agents and to smoke during smoking of pork. Thus, these five cohort studies and their nested case-control studies indicate an excess risk of lung cancer in the meat industry particularly associated with high exposure to oncogenic viruses. They also indicate that risks could be particularly higher for those handling pigs than beef. McLean et al. (2004) studied mortality and cancer incidence in a total of 6647 workers in a meat processing plant handling mostly mutton and some beef, and in two plants handling only mutton, in New Zealand. An excess risk of death from cancer of the lung and increased risk of lung cancer incidence were observed. In this instance, it would appear that the excess risk is more largely explained by exposures in sheep plants than in plants handling beef. However, this study did not examine which workplace exposures were possibly responsible for the excess. Fritschi et al. (2003) reported on mortality and cancer incidence in members of the Australasian Meat Industry Employees Union in Australia, which consisted of workers employed in *poultry* processing, abattoirs, boning rooms, retail and supermarket meat rooms, cold storage, and small goods manufacturing. The SMR

(standardized mortality ratio) for respiratory disease was 1.5 in women and 0.8 in men. For high exposure to animal viruses, the non-malignant respiratory diseases OR was 2.0 (95% CI, 0.94–8.16); for high exposure to blood, it was 2.2 (95% CI, 0.5–9.0). No mention of lung cancer mortality was made because of the small sample size. However, the standardized incidence ratio (SIR) for lung cancer overall in men was 1.6 (95% CI, 0.97–2.59) and 0.4 ($n = 1$) in women. Another cohort study showed an association between lung cancer risk and butchers when compared with bakers (Doerken and Rehpenning, 1982), but this study was not well described, and so was not considered further, although listed in the Table S1.

Overall then, these data strongly suggest that a high risk of lung cancer within the meat industry occurs in workers who have contact with live animals while working in stockyards, or in workers who kill and dress cattle, pigs or sheep, or in those who come into contact with freshly killed or warm meat. Because these activities are expected to have the highest exposures to oncogenic viruses present in the animals and they are also not associated with any other known carcinogenic exposures, these data strongly implicate exposure to oncogenic viruses as an important candidate to explain the excess occurrence of lung cancer within the meat industry.

Curing and smoking of meat

Carcinogenic exposures during the smoking and curing of meat include polycyclic aromatic hydrocarbon (PAH) present in smoke (International Agency for Research on Cancer, 1973, 1987), nitrosamines present in spices used for curing or formed during curing (Sen et al., 1973; Jakszyn et al., 2004) and possibly butylated hydroxyanisole and butylated hydroxytoluene used as preservatives (Ito et al., 1983; Williams et al., 1983). The higher risk observed in pig handlers than in other meat workers (Guberan et al., 1993; Johnson et al., 1995a, 2011a; Johnson, 2011) can be partly attributed to their being *additionally* exposed to higher levels of carcinogens during curing and smoking of meat than workers handling cattle and sheep. This is supported by the findings of excess lung cancer risk in workers in plants or butchers handling pigs and pig products (Griffith, 1982; Coggon et al., 1989; Guberan et al., 1993), and the relative risk of 1.4 for curing reported by Gustavsson et al. (1987). However, usually <5% of workers in meat or poultry processing plants would be expected to be engaged in curing or smoking meat. Thus, while these two exposures can contribute to the lung cancer risk, it is unlikely that they are the principal causes of the excess lung cancer observed in published mixed cohorts of cattle, pigs and sheep workers. Also, the pig cohorts are much smaller than the mixed cattle, pigs and sheep cohorts. Hence, the role of carcinogenic expo-

sure associated with curing and smoking of meat has not been adequately investigated, and much larger studies are needed to do so.

Exposure to fumes during wrapping meat

In the Baltimore cohort study, a high increased risk of death from lung cancer was observed in women working in meat processing plants, supermarkets and poultry plants (Johnson et al., 1986b). These lung cancer deaths were unique in their occurrence because (i) risks were high in the younger ages (up to 12-fold increased risk in female workers in meat processing plants). At the initial follow-up in meat processing plants, 67% of the lung cancer deaths were in women aged between 35 and 49 years; for women working in the meat and deli departments of supermarkets, 36% of the women with lung cancer died when they were <50 years old; and in chicken slaughtering plants, all three women who died of lung cancer (100%) died at ages <50 years old (the risk for these ages was increased between 8- and 50-fold; (ii) the duration of employment was unusually short for these lung cancer deaths (in meat processing plants, 67% of the female lung cancer deaths had worked for <5 years, and similarly, in supermarkets and chicken slaughtering plants, the figures were 71% and 100%, respectively); (iii) no dose–response by duration of employment was evident, in contrast to lung cancer deaths associated with exposure to oncogenic viruses. At the second follow-up (Johnson et al., 1995a), women in abattoirs/slaughterhouses had also begun to show significantly increased risk of the lung cancer also as in the other sectors described. Thus, this unique presentation was seen in women in all sectors of the meat and poultry industries in the Baltimore cohort. Because of this unusual presentation, and the fact that a major activity women carried out in the meat industry was wrapping meat (e.g. in supermarkets this is the *only* activity they carried out), we postulated that these lung cancer deaths in women had an origin different from exposure to oncogenic viruses. We hypothesized that these deaths could be caused by fumes emitted from the wrapping machine that contained PAH, benzene and phthalates (Smith et al., 1983; Johnson et al., 1999). These fumes also contain hydrogen chloride, a powerful irritant that could significantly enhance the carcinogenicity of these chemicals.

Re-enforcing this hypothesis was the observation that women in the meat and deli departments of supermarkets also had excess risk of deaths from tumours of myeloid stem cell origin, while the men who worked side by side with the women in the same room as meatcutters showed no increased risk of death from either lung cancer or tumours of myeloid stem cell origin (Johnson, 1994; Metayer et al., 1998). Later updates of the Baltimore cohort observed decreasing lung cancer risk over time in

supermarket and poultry workers (Johnson, 1994; Johnson et al., 1997), and this observation further supported the wrapping fumes hypothesis, because exposure to these fumes decreased significantly after 1975. Thus, the reduction in lung cancer risk in these women could be chronologically linked with a reduction in exposure to these fumes that occurred after 1975 (Johnson, 1994). The only other study to examine risk in relation to these fumes reported a non-significant OR of 1.5 for exposure to plastic pyrolysis products (Fritschi et al., 2003). Thus, exposure to fumes emitted by the wrapping machine that contain PAHs, benzene and phthalates is a candidate exposure that should be considered for explaining lung cancer risk, especially in women in the meat industry.

Exposure to fumes or aerosols during cooking/frying meat

It is well known that carcinogenic heterocyclic amines are formed during cooking or frying of meat and are found in the air breathed by workers performing these tasks (Jakszyn et al., 2004). To date, no study has provided reliable information on or a thorough assessment of lung cancer risk associated with this exposure in the meat industry.

Workers in poultry slaughtering and processing plants

Candidate occupational exposures that could explain lung cancer excess occurrence in poultry workers also include the same groups listed for cattle, pigs and sheep, viz. first, oncogenic viruses (poultry) like the avian leukosis/sarcoma viruses (ALSV) that cause a wide variety of tumours in chickens and turkeys including lung cancer (Payne, 1987), reticuloendotheliosis viruses (REV) that cause lymphoid leukosis in chickens and turkeys (Witter, 1984), and Marek's disease virus that causes leukosis in chickens (Payne, 1985); second, fumes from the wrapping machine (Smith et al., 1983; Johnson et al., 1999), smoke during smoking of poultry (International Agency for Research on Cancer, 1973; Nordholm et al., 1986), aerosols emitted during frying/cooking of poultry (Vainiotalo and Matveinen, 1993) and carcinogenic chemicals associated with curing of poultry (Sen et al., 1973; Jakszyn et al., 2004).

There has been a total of four separate cohorts of workers in the *poultry* industry (Table S3): (i) a study of poultry workers in a Baltimore Meatcutters Union (Johnson et al., 1986a,b, 1997, 2010a); (ii) a study of poultry workers in a Missouri Poultry Union (Netto and Johnson, 2003; Johnson et al., 2011b); (iii) a study by Fritschi et al. (2003); and (iv) a study of poultry workers belonging to a Pension Fund by Johnson et al. (2010b). The study by Fritschi et al. (2003) included poultry workers together with other workers in the meat industry in their main results. Like the Baltimore, Missouri and Pen-

sion Fund cohorts, it also observed some excess of lung cancer for those that were exposed to poultry and for those exposed to fumes from the wrapping machine. As mentioned above, Johnson et al. (1986b) initially found a 4-fold risk of death from lung cancer overall in female poultry workers in the Baltimore cohort (based on three deaths). All three had duration of employment of <5 years and all died before the age of 50 years, and the SMRs for these ages were very high (up to 50-fold). Like the meat industry, these data suggested that the risk might be related not only to oncogenic viruses, but also to exposure to fumes given off from the plastic used to wrap poultry. In the meat industry, it was known that this exposure was significantly reduced after 1975, and it was shown that this decrease in exposure was accompanied by a progressive decrease in lung cancer occurrence over time in women in supermarkets (Johnson, 1994). It is likely that a similar pattern of events also occurred in the Baltimore poultry slaughtering and processing plants, because the initially overall 4-fold risk of lung cancer risk observed in the first follow-up to 1980 (Johnson et al., 1986b), progressively declined to 1.8-fold in the second follow-up up to 1989 (Johnson et al., 1997) and to 1.4-fold in the latest update of this cohort up to 2003 (Johnson et al., 2010a). However, not all of the lung cancer occurrence in poultry workers even in the Baltimore cohort can be attributed to fumes from the wrapping machine or oncogenic viruses at this time, as, for example, in the Missouri poultry study in which an excess of lung cancer deaths was also recorded, it is known that some of the plants cured and cooked chickens or turkeys (Netto and Johnson, 2003; Johnson et al., 2011b). Hence, exposures to carcinogenic nitrosamines, PAHs and heterocyclic amines during curing, smoking and cooking of meat and poultry are all likely candidates that still need to be considered to explain lung cancer occurrence in workers in poultry slaughtering and processing plants.

In a most recent case-cohort study of lung cancer nested within the combined Baltimore, Missouri and Pension Fund poultry cohorts of over 30 000 poultry workers and controls (Felini et al., 2011), the main occupational risk factors identified *after adjusting for tobacco smoking* were for working in a stockyard (RR = 12.2); working in the deli department of supermarkets (RR = 4.1); killing chickens at work (RR = 2.5); working in a commercial poultry farm (RR = 2.2); working in the meat department of supermarkets (RR = 2.0); and working as a butcher (RR = 2.0). These findings like those from nested case-control studies in the meat industry also seem to implicate exposure to oncogenic viruses and fumes from the wrapping machine.

Thus, studies of these nine cohorts (five meat and four poultry) and their nested case-control studies from differ-

ent countries around the world are remarkably consistent with each other. They provide strong confirmatory evidence of the excess occurrence of lung cancer in the meat and poultry industries initially reported from record linkage, PMR and case-control studies. They also indicate that it is not explained by tobacco smoking.

The available evidence, though not unanimous, indicates that humans have antibodies in their blood to poultry oncogenic retroviruses (Johnson et al., 1995b,c; Choudat et al., 1996; Tsang et al., 1999) and to bovine leukaemia virus (Buehring et al., 2003). Also, as mentioned above, meat and poultry workers in addition to having high exposures to these viruses are also exposed to benzene, PAHs and phthalates from the wrapping machine (Smith et al., 1983; Johnson et al., 1999). Therefore, exposure to oncogenic viruses (which include bovine, ovine and poultry retroviruses, Marek's disease virus, and papilloma viruses) and exposure to fumes from the wrapping machine are the two important exposures that the evidence so far suggests may be responsible for this excess. It is particularly noteworthy that lung cancer in sheep is caused by the Jaagsiekte sheep retrovirus (Palmarini and Fan, 2001; Wootton et al., 2005), and avian leukosis/sarcoma retroviruses cause lung tumours in chickens among a wide variety of other cancers (Payne, 1987). It should be pointed out also that it has been shown that the presence of a wound can act as a tumour promoter in the occurrence of cancer induced by Rous sarcoma virus (a type of ALSVs) through the release of transforming growth factor-beta (TGF-beta) (Sieweke et al., 1990). Also, workers in the meat and poultry industries have high rates of lacerations and deaths from various infections (Cai et al., 2005; Johnson and Zhou, 2007; Johnson et al., 2007). Hence, even if some of these transmissible agents are not directly oncogenic in humans by themselves, they could still be partially responsible for the excess occurrence of cancer in these workers, in combination with the high frequency of wounds, infection and injury to the skin and other parts of the body that occur in workers in these two industries. It is to be noted that injuries from knives and bone splinters can occur during the handling of raw meat at home.

Conclusion

In summary, we found that 79% (42 of 53) of studies of workers in the *meat* industry reported at least a 1.3-fold excess of lung cancer, including all five cohort studies. Of the 18 studies that controlled for tobacco smoking, 14 (78%) reported this association. All seven (100%) cohort studies of workers in *poultry* plants reported the association. These data *in toto* establish that there is a definite excess of lung cancer occurrence in meat and poultry

workers. The evidence thus far indicates that exposure to oncogenic transmissible agents that infect food animals and exposure to fumes from the wrapping machine are almost certainly involved in this occurrence. This is supported by the fact that food animal oncogenic viruses are known to infect and/transform human cells *in vitro* (Stenkvist and Ponten, 1964; Koo et al., 1991; Johnson and Griswold, 1996), to cause cancer in primates experimentally (McClure et al., 1974), and poultry workers and subjects in the general population have antibodies to these viruses in their blood (Johnson et al., 1995b,c; Choudat et al., 1996; Buehring et al., 2003).

The role of exposure to smoke or aerosols during smoking or cooking of meat and poultry that contain carcinogenic PAHs and heterocyclic amines or to nitrosamines during curing of poultry has not been adequately investigated *in any study to date* and still remains to be assessed. This needs to be done if workers in these industries are to be fully protected from carcinogenic exposures at the workplace and if the association of lung cancer with oncogenic viruses is to be definitively assessed. This may be quite a challenge, as typically only a handful of workers in a plant are involved in smoking and curing of meat.

Large epidemiologic studies are needed now that can control adequately for occupational and non-occupational confounding factors and elucidate further the role of transmissible agents as well as that of the other specific carcinogenic exposures in the meat and poultry industries that may also be contributory. Case-control studies nested within large occupational cohorts would be most suitable for this type of investigation and would play a critical role in this endeavour and are urgently needed. Also, studies that will obtain laboratory evidence of human infection using serological and molecular assays such as polymerase chain reaction (PCR) assays are needed. In the meantime, there is sufficient evidence for employers and unions to begin to take steps to reduce potentially carcinogenic exposures in the meat and poultry industries.

Finally, it should be recognized that the findings of excess cancer occurrence (particularly lung cancer) among workers in the meat and poultry industries are relevant for other occupational groups that have potential for exposure to these viruses, such as veterinarians, farmers, meat and poultry inspectors, cooks, laboratory workers. The findings also have profound public health implications, as the general population is also exposed to various food animal oncogenic viruses, through direct contact with live animals or their raw products, ingestion of raw or inadequately cooked meat, eggs or milk, and inoculation with vaccines grown in eggs, such as measles, mumps and yellow fever vaccines (Johnson et al., 1995b,c; Choudat et al.,

1996; Tsang et al., 1999; Buehring et al., 2003; Hussain et al., 2003). This issue then is potentially of great importance.

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Conflict of interests

There are no competing interests.

Ethics approval

This study was conducted with approval of the University of North Texas Health Science Center Institutional Review Board for the conduct of research in human subjects.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Studies prior to 2004 previously reviewed ($N = 30$).

Table S2. New studies prior to, and after 2004 in the meat industry ($n = 23$).

Table S3. Cohort studies of workers in poultry slaughtering and processing plants ($N = 7$).

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