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Review

Carcinogenicity of consumption of red meat and processed meat: A review of scientific news since the IARC decision

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ABSTRACT

In October 2015, the International Agency for Research on Cancer (IARC) issued a press release on the results of the evaluation of the carcinogenicity of red and processed meat. Based on the accumulated scientific literature, the consumption of red meat was classified as "probably carcinogenic to humans" and processed meat as "carcinogenic to humans". Given the importance of this topic, this review was aimed at revising the current state-of-the-art on the carcinogenicity of red and processed meat, some time after the IARC decision. Some new epidemiological studies and new reviews clearly supporting the IARC decision have been published during these months. However, a number of gaps still exist. It is basic to establish the mechanisms leading to the increased risk of colorectal cancer (CRC) and other cancers arising from red and processed meat consumption. Another important pending issue is to establish the role of known/suspected carcinogens contained in uncooked or unprocessed meats, as well as the influence of cooking. Finally, it would be highly recommended to conduct new epidemiological studies to elucidate whether the consumption of white meat, such as pork and/or poultry, are -positively or inversely-associated with an increased risk of CRC and other types of cancer.

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1. Introduction

In October 26, 2015, the International Agency for Research on Cancer (IARC), an Agency of the World Health Organization (WHO), issued the press release No. 240. (IARC, 2015), which summarized the results of an evaluation by that Agency on the potential carcinogenicity of consumption of red and processed meat. Red meat refers to meat of beef, veal, pork, lamb, horse, goat and mutton. In turn, processed meat is considered as products usually made of red meat that are cured, salted or smoked (e.g., bacon or ham), and often containing high quantities of minced fatty tissues (e.g., sausages). Based on data of the scientific literature, the consumption of red meat was classified as "probably carcinogenic to humans" (Group 2A), while processed meat was classified as "carcinogenic to humans" (Group 1). Details on this decision were published in the Lancet Oncology (Bouvard et al., 2015), as an advance of a monograph of the IARC, whose publication (volume 114) is estimated for summer of 2017.

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With respect to the possible mechanisms involved in the potential carcinogenicity of red and processed meat, Bouvard et al. (2015) highlighted the presence of well known/suspected carcinogenic compounds such as N-nitroso-compounds (NOCs), polycyclic aromatic hydrocarbons (PAHs) and heterocyclic aromatic amines (HAAs). These compounds may appear in some meat processing procedures, such as curing and smoking (e.g., NOCs, PAHs), or when meat is heated at high temperatures (e.g., HAAs). After the press release No. 240 of the IARC, we proceeded to carefully revise the scientific literature on the possible mechanisms/reasons of that carcinogenicity, which were not contemplated in the decision of the IARC (Bouvard et al., 2015). Our revision was basically focused on the presence of a number of chemical compounds that are already present in raw or unprocessed meats (Domingo and Nadal, 2016). We concluded that NOCs, PAHs and HAAs would not the only chemicals potentially responsible of the carcinogenicity of red and processed meat. Taking into account the results of a case-study (Catalonia, Spain) conducted in our laboratory, we noted that environmental pollutants with known carcinogenic potential such as some heavy metals, polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs), dioxin-like polychlorinated biphenyls (PCBs), and other persistent organic contaminants, are present -in greater or lesser quantities-in raw/unprocessed meats. We revised the potential role that the presence of arsenic, cadmium, mercury, lead, PCDD/Fs, PCBs, polybrominated diphenyl ethers (PBDEs), hexachlorobenzene (HCB), polychlorinated naphthalenes (PCNs), polychlorinated diphenyl ethers (PCDEs), PAHs and perfluoro alkyl substances (PFASs) in raw/unprocessed meats, could mean for the carcinogenicity of the consumption of red and processed meats. Moreover, the results of our own studies (Aznar-Alemany et al., 2016; Jogsten et al., 2009; Perelló et al., 2008, 2009, 2010), as well as those from other researchers, suggest that certain cooking processes can modify (decreasing or increasing) the levels of environmental pollutants in foods in general, and in meats in particular. However, concentration changes would depend on not only the particular cooking process, but even more their original contents in each specific food item. As most of these environmental pollutants are organic, cooking procedures releasing or removing fat from the meat should tend to reduce the total concentrations of the contaminants in meat (Domingo, 2011; Perelló et al., 2009, 2010). On the other hand, in our studies we also observed that white meats, such as chicken, contained usually less organic contaminants than red meats. This would be an indicator of the importance with respect the potential carcinogenicity of the content of environmental pollutants in meats, before they are cooked or processed (Domingo and Nadal, 2016).

Obviously, the important decision of the IARC reached not only the scientific community and other stakeholders (e.g., governments, food safety agencies, etc.), but also the general population through the mass media. To date, comprehensive and reliable international data on potential changes in the consumption habits of red and processed meats by the general population are not available. It is also not possible to predict if some changes on dietary habits are going to occur when the monograph 114 of the IARC is published. However, it seems obvious that social repercussions can be expected, at least initially. As a simple example of this, the Italian newspaper "Il Mattino" published in 2015 (and the article still circulates on Internet) that a single burned steak could be equivalent to smoking 600 cigarettes (http://ilmattino.it/primopiano/cronaca/carne_tumori_esperto-1321148.html). As scientific response, Gallus and Bosetti (2016) recently highlighted in the International Journal of Cancer that *"meat consumption is not tobacco smoking"*, and of course, the mass-media should not publish sensational headlines with messages suggesting that processed read meats can kill as tobacco smoking do it, based on the fact that both are classified by IARC in the Group 1.

The main purpose of the present manuscript was to review the most recent scientific literature specifically focused on the carcinogenicity of the consumption of red meat and processed meat, and whose results have been published after the IARC press release and a few months before the full monograph is published. Therefore, this review covers scientific articles published between October 2015 and February 2017. The scientific literature was reviewed using PubMed (www.ncbi.nlm.nih.gov/pubmed) and Scopus (www.scopus.com/home.url) databases. Both databases were the same that we already used for our previous review-article on the topic with satisfactory results in the search (Domingo and Nadal, 2016). We have again used the following "key terms: carcinogenicity, cancer risks, red meat, processed meat, and dietary intake". Other sources such as Meeting Abstracts, Conference Proceedings, or other potential sources were not included in the present search.

2. Recent epidemiological studies and reviews mainly focused on colorectal cancer (CRC)

This section summarizes the results of the epidemiological studies on the topic here reviewed, which have been published during the assessed period. The main goal of the current review has been to update the available information on the carcinogenicity of red and processed meat published in recent months. It means that only the conclusions of the epidemiological studies here included have been taken into account, without considering the potential relevant confounders the authors have commented in their specific article.

Lippi et al. (2016) performed a critical review of meta-analyses aimed at establishing whether the consumption of total meat and meat subtypes might be associated with human cancer. A convincing association was found between larger intake of red meat and cancer, especially with colorectal, lung, esophageal and gastric malignancies. Increased consumption of processed meat was also found to be associated with colorectal, esophageal, gastric and bladder cancers. In contrast, an enhanced intake of white meat or poultry was found to be negatively associated with some types of cancers. Larger beef consumption was also significantly associated with cancer, while the risk was not increased consuming high amounts of pork. The authors concluded by recommending that consumption of red or processed meat should be limited (i.e., <300 g per week), as already suggested by the World Cancer Research Fund (Demeyer et al., 2008). Lippi et al. (2016) submitted their review in March 2015, but their conclusions are in agreement with the subsequent decision of the IARC (October 2015), as well as with the general recommendations to avoid an increase in the risk of colorectal cancer (CRC) (consumption 50 g per day of processed meat would increase the risk of CRC by approximately 18%). Similarly, Carr et al. (2016a) had already published online (in January 2015, eight months before the press release of the IARC), the results of a systematic review and meta-analysis on meat subtypes and their association with CRC. The main conclusions of the meta-analysis suggested that red meat subtypes differed in their association with risk of CRC and its sub sites, while poultry intake was not associated with risk of CRC or its precursors. Beef and lamb consumption was associated with a moderately increased risk of CRC, while no association was observed with pork consumption. The authors also indicated that additional large scale cohort studies investigating specific meat subtypes were warranted, especially regarding the role of meat pork. In a second study conducted by the same research group (Carr et al., 2016b), the associations of baseline red meat and processed meat with survival outcomes were investigated, and the changes in intake among CRC survivors 5 years