Investigating the troublesome relationship between the cow milk and human health

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The cow milk and dairy products, which have been long considered fundamental components of the human diet, are nowadays in the centre of a scientific dispute, as they are claimed to be health threatening for human consumers. This dispute sometimes becomes pseudoscientific due to the huge number of dedicated sites in the web, which deliver incomplete, if not false, information to the consumers. Indeed, in some cases the cow milk is described as a harmful food, rich in hormones and antibiotics, obtained from animals reared under poor welfare conditions, too high in protein content and, for these reasons, not suitable for human consumption. These assertions are well beyond the usual food safety concerns related to the potential microbiological and toxicological risks, and the occurrence of food allergies. In the “One Health” context, veterinary scientists can give a substantial contribution to this dispute in at least three sectors.

The first and more obvious contribution is in the sector of microbiology, food hygiene, and animal health. In the EU, the marketing of milk and dairy products requires the achievement of safety standards in accordance with the provisions of the Reg. EC/853/2004 and Reg. EC/2073/2005. Nevertheless, in the last decade numerous cases of food poisoning caused by the consumption of dairy products produced with either raw or pasteurized milk have been reported. This has important consequences by social, economic and trustworthiness point of views. Important goals have been reached over the past 50 years in the eradication of certain zoonoses carried by milk and dairy products (tuberculosis and brucellosis). In addition, the technological innovation in milking systems and an adequate training of the operators have led to a significant reduction in the total milk bacterial load, to a quality improvement with important consequences for both drinking milk and dairy sectors. However, the biological risks is still preeminent and, in some ways, more unpredictable. It can be identified in the presence of pathogenic microorganisms such as *E. coli*, *Listeria monocytogenes*, *Salmonella*, *Staphylococcus aureus* and *Campylobacter* species among others, and requires a deal of scientific attention in the next future.

Even if rare, *Listeria* contamination of dairy products can cause serious illness. It can grow in refrigeration temperatures (4 °C) reaching dangerous charges for humans. Generally, it is devitalized by pasteurization but, due to its persistence in the environment, a post-pasteurization contamination is not rare (Baek et al., 2000). There is evidence that the bacteria grow less in raw milk than in the processed one, probably for the competing microflora effect (Mathew and Ryser, 2002). Challenge tests suggested that some strains displayed improved virulence when incubated in pasteurized milk.

Salmonella is one of the most important aetiological agent of zoonoses in Europe. Among others, unpasteurized milk and, specially, cheeses made with raw milk can be risk foods. Surveys conducted among European countries showed a very low prevalence of salmonella in dairy foods made from raw milk. Despite this, the outbreaks and human cases in which *Salmonella* is the pathogenic agent are numerically important, both in Europe as in North America (Verraes et al., 2015). It can survive during the production of hard cheeses, whereas it can grow during the production of semi-hard cheeses. This pathogen can cause illness also if present in low numbers in foods (EFSA, 2013).

Staphylococcus aureus is an important cause of bovine mastitis and one of the most cost-intensive diseases in the dairy industry (Dufour et al., 2012). Antibiotic treatment is nowadays still the elective approach for treating clinical or subclinical mastitis (mainly beta-lactams). Anyway, a different approach is strongly desired, more preventive based improving a good stockmanship, biosecurity and good milking hygiene, which are corroborant in preventing mastitis (De Briyne et al., 2014), whereas the use of antibiotics should be limited to control clinical mastitis after bacterial isolation and sensitivity testing. Among other causes, cows with subclinical mastitis can be considered as a reservoir for this hazard causing the contamination of the dairy production and processing chains (Kümmel et al., 2016). The contamination of dairy foods made with raw milk pose a serious risk for the consumers since staphylococcal enterotoxins is denatured neither by thermal processes nor by human gastrointestinal proteases (Balaban and Rasooly, 2000).

Escherichia coli is generally considered an indicator of faecal contamination (Ghafir et al., 2008). Raw milk can be contaminated with Shiga toxin-producing E. coli (STEC) from animals harbouring it also without any appearance of illness (Miszczycha et al., 2013). The human outbreaks are almost exclusively associated with the consumption of raw milk cheeses rather than pasteurized milk cheese (Baylis, 2009). The five major pathogenic serotypes isolated from raw milk cheeses are O26, O103, O111, O145 and O157. In Italy O26 is an emerging serotype. Rapid acidification and long ripening are processing able to avoid STEC growth,

although it must be kept in mind that the O26 strain can survive under extreme acidic environments such as in the stomach (Miszczycha et al., 2013).

Mycobacterium avium subsp. *paratuberculosis* (MAP) causes paratuberculosis (Johne's disease, JD), a chronic and progressive granulomatous enteritis affecting ruminants and several others domestic and wildlife species (Kennedy and Benedictus, 2001). MAP prevalence in dairy herds has been estimated to be higher than 50% (Nielsen and Toft, 2009). MAP could be a zoonotic risk, according to clinical and pathological lesion similarities between JD and human Crohn's. From a public health viewpoint, one of the most important ways for human infection by MAP is through the consumption of contaminated milk and dairy products (Gill et al., 2011). MAP was found in raw bulk milk (Hanifian et al., 2013), and can survive thermization as well as pasteurization processing (Van Brandt et al., 2011). Viable MAP has been also found in retail pasteurized milk (Carvalho et al., 2012).

Coxiella burnetii is an intracellular pathogenic bacterium with great importance in ruminants, which is the cause of the worldwide zoonotic disease Q fever. Human infections occur mainly by airborne transmission, even if *C. burnetii* was detected in raw milk, raw-milk cheese and butter prepared from raw milk (Hilbert et al., 2015). Stringency of milk pasteurization has been established on requirements for *C. burnetii* as being the most heat-resistant organisms of public health significance (Cerf and Condron, 2006). The diffusion of the pathogen across dairy herds is quite high. It was detected in 62.5% of the bulk milk samples and up to 60% in individual milk samples (Hilbert et al., 2015).

The interaction between the cow feeding, in terms of management and feed composition, and the hygienic conditions and microbial quality of milk is of primary importance and can have an immediate feedback. It is the case, for example, of the total or partial substitution of silage with fodder and concentrates, which leads to significant reduction of those strains of clostridia causative of late blowing of hard and semi-hard cheeses. This obviates the need to add preservatives in hard or semi-hard cheese manufacturing, which nowadays meets the expectation of a growing part of consumers.

The second contribution of the veterinary sector to this debate may come from the use of animal models in research in comparative nutrition physiology. The classical approach to nutrition, which considered each nutrient individually, is outdated and novel research conducted in a great deal in animals have revealed that foods are complex matrices able to affect the animal's physiology in a holistic way.

Most of the recent scientific evidence supports the concept that milk and dairy product consumption help meeting the nutrient recommendations and may protect against several chronic diseases (Kongerslev Thorning et al., 2016), although a shadow still exists on the association between milk intake and prostate cancer (Harrison et al., 2017). Then, colostrum and milk are not a mere source of nutrients but contain a plethora of hormones and growth factors, which fulfil several physiological functions in the mammary gland, but affect also the newborn physiology, in particular the development and maturation of the gastro-intestinal system (Blum and Baumrucker, 2002). In addition, the observation that proteolytic cleavage of milk proteins gives rise to cryptic peptides with bioactivities often unpredicted and distinct to the parent protein increased the interest of researchers in the milk as a “healthy food”, even representing new opportunities for protein-based therapeutics (Autelitano et al., 2006).

Conversely, other studies indicated the cow milk as a health threatening food for the consumer and associate consume of cow milk to a number of pathologies spanning from acne to several kinds of cancer, and from cardiovascular diseases to Alzheimer's disease and low fertility. Several arguments adverse to cow milk consumption by humans have been raised, such as the different composition between human and cow milk, and the content of sophisticated chemical messengers controlled by the mammalian lactation genome (e.g.: Branched Chain Amino Acids of milk proteins and exosomal miRNAs produced by the mammary gland) able to activate the mTORC1 signalling system. The activated mTORC1, if persistently augmented, is claimed to be one of the fundamental driving force for the development of diseases of civilization (Melnik et al., 2013). Another interesting aspect, although not well defined, is the idea that cross-species consumption of milk beyond infancy may trigger adverse long-term biological consequences (Wiley, 2012).

Most research about the effects of milk consumption consists in observational studies or randomised controlled trials, which are not appropriate to understand the cause-effect relationships between milk consumption and the consumer's health. Therefore, more research is needed in the near future to elucidate the causative mechanisms linking the consumption of the cow milk to human health. Feed/food effects on the host are mediated by their interactions with the intestinal microbiota, direct nutrient signalling, nutrient/gene interactions, interactions with the endocrine system, and cross talk with the immune system (Bradford et al., 2016). A number of experimental data support the hypothesis that feed/food can affect animal physiology by shaping the intestinal microbiota (Leulier et al., 2017), and this is probably true for milk and dairy products as well. Consequently, the new frontier of nutritional research will be the understanding of this “feed/food-microbiota-host physiology” axis, by moving decisively from a descriptive/correlational to a causal approach.

The use of model organisms have played and will play a decisive role in providing complementary physiological information useful for the human being, and the piglet is one of the elective models for the human intestine (Leulier et al., 2017). Therefore, veterinary research could give a crucial contribution in understanding how the nutritional environment, in particular the milk and dairy products, can affect the intestinal microbiota and how the food/microbiota interaction can affect the animal health, even considering the long-term effects in a life history perspective.

The value of this new knowledge would be absolutely none, if not appropriately delivered to the public. Indeed, the third contribution of scientists working in the veterinary sector should be the engagement with the public to disseminate scientific knowledge in a precise but simple language. In addition, scientists should help the government bodies in developing appropriate health claims for the product labels. These are most important tools to allow consumers to make informed purchase decisions based on science and not on marketing claims or poor trustworthy information available in the web.

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