

Sustainable ruminant production to help feed the planet

Questa è la versione Post print del seguente articolo:

*Original*

Sustainable ruminant production to help feed the planet / Pulina, Giuseppe; Francesconi, Ana Helena Dias; Stefanon, Bruno; Sevi, Agostino; Calamari, Luigi; Lacetera, Nicola; Dell'Orto, Vittorio; Pilla, Fabio; Ajmone Marsan, Paolo; Mele, Marcello; Rossi, Filippo; Bertoni, Giuseppe; Crovetto, Gianni Matteo; Ronchi, Bruno. - In: ITALIAN JOURNAL OF ANIMAL SCIENCE. - ISSN 1828-051X. - 16:1(2016), pp. 140-171. [10.1080/1828051X.2016.1260500]

*Availability:*

This version is available at: 11388/177029 since: 2017-05-26T09:02:47Z

*Publisher:*

*Published*

DOI:10.1080/1828051X.2016.1260500

*Terms of use:*

Chiunque può accedere liberamente al full text dei lavori resi disponibili come "Open Access".

*Publisher copyright*

note finali coverpage

(Article begins on next page)



## Sustainable ruminant production to help feed the planet

Giuseppe Pulina, Ana Helena Dias Francesconi, Bruno Stefanon, Agostino Sevi, Luigi Calamari, Nicola Lacetera, Vittorio Dell'Orto, Fabio Pilla, Paolo Ajmone Marsan, Marcello Mele, Filippo Rossi, Giuseppe Bertoni, Gianni Matteo Crovetto & Bruno Ronchi

To cite this article: Giuseppe Pulina, Ana Helena Dias Francesconi, Bruno Stefanon, Agostino Sevi, Luigi Calamari, Nicola Lacetera, Vittorio Dell'Orto, Fabio Pilla, Paolo Ajmone Marsan, Marcello Mele, Filippo Rossi, Giuseppe Bertoni, Gianni Matteo Crovetto & Bruno Ronchi (2016): Sustainable ruminant production to help feed the planet, Italian Journal of Animal Science, DOI: [10.1080/1828051X.2016.1260500](https://doi.org/10.1080/1828051X.2016.1260500)

To link to this article: <http://dx.doi.org/10.1080/1828051X.2016.1260500>



© 2016 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.



Published online: 29 Nov 2016.



[Submit your article to this journal](#)

















[View related articles](#)



[View Crossmark data](#)

## Sustainable ruminant production to help feed the planet

Giuseppe Pulina<sup>a</sup> , Ana Helena Dias Francesconi<sup>a</sup> , Bruno Stefanon<sup>b</sup> , Agostino Sevi<sup>c</sup> ,  
Luigi Calamari<sup>d</sup> , Nicola Lacetera<sup>e</sup> , Vittorio Dell'Orto<sup>f</sup> , Fabio Pilla<sup>g</sup> , Paolo Ajmone Marsan<sup>d</sup> ,  
Marcello Mele<sup>h</sup> , Filippo Rossi<sup>i</sup> , Giuseppe Bertoni<sup>d</sup> , Gianni Matteo Crovetto<sup>j</sup>  and  
Bruno Ronchi<sup>e</sup> 

<sup>a</sup>Dipartimento di Agraria, University of Sassari, Sassari, Italy; <sup>b</sup>Dipartimento di Scienze Agroalimentari, Ambientali e Animali, University of Udine, Udine, Italy; <sup>c</sup>Dipartimento di Scienze Agrarie, degli Alimenti e dell'Ambiente, University of Foggia, Foggia, Italy; <sup>d</sup>Istituto di Zootecnica, University Cattolica del Sacro Cuore, Piacenza, Italy; <sup>e</sup>Dipartimento di Scienze Agrarie e Forestali, University of Tuscia, Viterbo, Italy; <sup>f</sup>Dipartimento di Scienze Veterinarie per la Salute, la Produzione Animale e la Sicurezza Alimentare, University of Milano, Milan, Italy; <sup>g</sup>Dipartimento di Agricoltura Ambiente Alimenti, University of Molise, Campobasso, Italy; <sup>h</sup>Dipartimento di Scienze Agrarie, Alimentari e Agro-ambientali, University of Pisa, Pisa, Italy; <sup>i</sup>Istituto di Scienze degli Alimenti e della Nutrizione, University Cattolica del Sacro Cuore, Piacenza, Italy; <sup>j</sup>Dipartimento di Scienze Agrarie e Ambientali, University of Milan, Milan, Italy

### ABSTRACT

Ruminant production has been an essential part of human activities worldwide since ancient times. The expected increase in world population and per capita income, with an increase in the amount and prevalence of animal products in human diet, urbanisation, with a concentration of population in urban areas and an increase in losses in the supply chain, and the growing concern over the environmental impact of animal farming require a long-term global strategy for a more intensive and sustainable ruminant production. Therefore, solutions to increase the supply of high-quality products of ruminant origin, without harming human health, animal welfare, and environment, should consider the following interconnected issues discussed in this review: (a) effects of meat, milk and dairy products consumption on human health, focussing on the imbalance caused by their insufficient consumption, and the alleged increased incidence of certain diseases due to their consumption; (b) importance of the sustainable intensification of ruminant production systems (e.g. better feed conversion and higher production output per unit of input introduced into the farming system); (c) environmental impact of ruminant production; (d) improvement of animal performance by improving animal welfare; (e) adaptation of ruminants to climate change; (f) sustainable ruminant feeding (e.g. precision feeding techniques, optimisation of grazing systems, and use of unconventional feeds); (g) challenges posed by production intensification to animal breeding and conservation of animal biodiversity; and (h) strategies to increase ruminant production in developing countries, thus achieving food security in vast areas of the planet affected by fast growth of human population.

### ARTICLE HISTORY

Received 27 April 2016  
Revised 8 October 2016  
Accepted 11 October 2016

### KEYWORDS

Animal products; food safety and security; sustainability; climate change; precision farming

## Introduction

In the history of mankind, animal products have been the basis of the diet of people with different ages, health conditions, and secular and religious beliefs. The estimated increase in world population, which is expected to reach more than 9 billion people in 2050 (UN 2015), the expected increase in both per capita income and prevalence of animal products in human diets (Bruinsma 2003; FAO 2011), the urbanisation phenomenon, which will lead to a high concentration of people living in urban areas and higher losses in the supply chain (Herrero et al. 2015), and the growing concern over environmental impacts of animal farming require a long-term global

strategy to develop more intensive and sustainable animal production worldwide. This global issue is connected with the crucial statement of the World Exposition Milan 2015, Italy (Expo 2015): 'Feeding the planet, energy for life'.

By the year 2030, the annual production of milk, meat and eggs is expected to be approximately 900 billion tons, 400 million tons and 100 million tons, respectively. Meat production will come mainly from chicken, followed by swine, and to a lesser but growing extent, ruminants (cattle, sheep and goats) (FAO 2011). Ruminant livestock are extremely important not only for the production of the highest quantity of animal protein (milk and meat) in human diets, but

**CONTACT** Dr Ana Helena Dias Francesconi  france@uniss.it  Dipartimento di Agraria, University di Sassari, viale Italia 39, 07100 Sassari, Italy

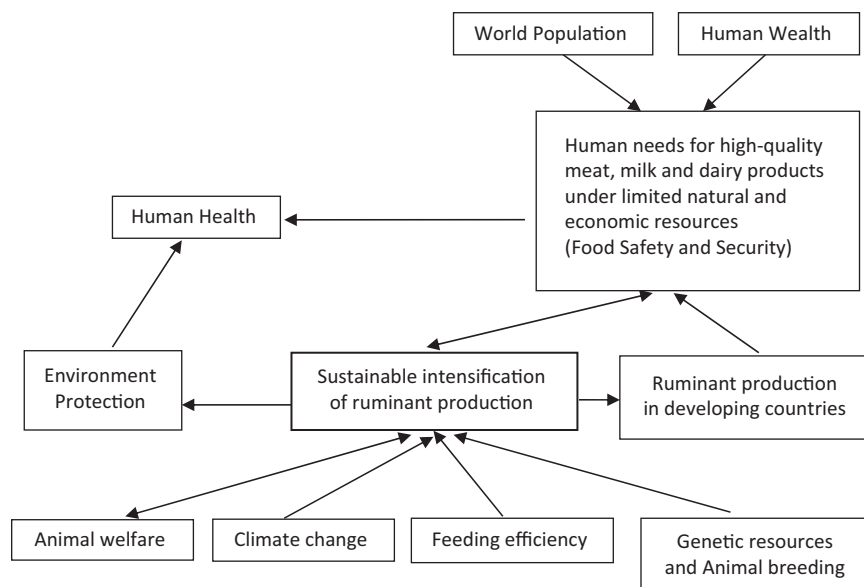
© 2016 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

also for their ability to feed on fibrous feeds that cannot be used as human food (Eisler et al. 2014). Furthermore, ruminants occupy the largest area of land worldwide compared with other livestock species, and constitute one of the principal food sources for people living in developing countries affected by scarce soil fertility or desertification. On the other hand, a considerable part of the animal impact on environment, especially greenhouse gas (GHG) emissions, is attributed to ruminants (Knapp et al. 2014), and a large part of ruminant livestock is affected by welfare problems (Goldberg 2016). Animal welfare issues could also be aggravated by the absence or lack of respect of welfare regulations, especially in developing countries, and by ongoing climate change, which might impact negatively the productive and reproductive performance of ruminants reared on pasture and, to a lower degree, in intensive conditions where mitigation practices are more feasible.

This review focuses on the sustainable intensification of ruminant production by looking at several components that are interconnected (Figure 1). In brief, the continuous rise in world population and human wealth has increased and will continue to increase human demand for high-quality animal products, including meat, milk and dairy products. The sustainable intensification of ruminant production, under limited natural and economic resources, could satisfy food safety and security, thus improving human health while protecting the environment. All these components belong to the main loop of the diagram. Food safety and security will rely in large part on the sustainable intensification of ruminant production in developing countries, where the major increase in

human population in the next 30 years is expected to occur and where large agricultural areas should be better exploited (secondary loop). Finally, the sustainable intensification of ruminant production should respect welfare regulations (where they exist) and ensure animal welfare and performance under climate change scenarios, in order to achieve a low impact of ruminant production on environment by relying on the following: (a) feeding techniques that increase feed efficiency and can be adapted to different scenarios, (b) traditional and innovative methods of animal breeding, including new technologies of gene editing that enable the rational use of genetic resources, and (c) maintenance and enhancement of animal biodiversity. In order to deal with these interconnected issues, this review is divided into the following topics: (a) the relationship between the consumption of meat, milk and dairy products and human health, with particular reference to the imbalance caused by insufficient consumption of these animal products, especially in members of the populations most at risk (children, elderly and sick people), and to the alleged increased incidence of certain diseases (cancer, cardiovascular disorders and metabolic syndrome) resulting from their consumption; (b) the importance of sustainable intensification of ruminant production systems (e.g. better feed conversion and higher production output per unit of input into the farming system); (c) the environmental impact of ruminant production; (d) the compatibility between animal welfare and production efficiency, with an analysis of the possibility of improving the performance of ruminants by achieving better



**Figure 1.** Diagram of factors involved in the process of sustainable ruminant production to feed the planet.

health, nutritional and breeding conditions; (e) the adaptation of farming systems to climate change, by evaluating the possibilities of physio-climatological adjustments of the ruminants to changing conditions; (f) the new prospects for ruminant feeding, with attention to the use of precision feeding, the optimisation of grazing systems and the use of unconventional feed ingredients to replace carbohydrate and protein sources used in human diets; (g) the challenge posed by production intensification for animal breeding and conservation of animal biodiversity; and (h) the ruminant production in developing countries, with an analysis of the strategies needed to fill the production gap between their local farming systems and those of developed countries – a crucial issue to achieve food security in vast areas of the planet currently affected by fast growth of human population.

### Meat, milk and dairy food consumption and human health

This section focuses on the main characteristics of meat, milk and dairy products that influence human health, noting that their consumption has many beneficial effects on humans, despite the massive media campaign claiming that these products are detrimental for human well-being. In the subsequent sections, we will describe how different factors – especially animal welfare, feeding techniques and animal breeding – can affect the production and quality of meat, milk and dairy foods from a sustainable ruminant production perspective (Figures 1 and 2).

### Meat consumption and human health

Meat is a dietary source of heme-iron, vitamin B12, zinc and high biological value proteins that are highly digestible and contain all essential amino acids. These nutrients are generally present in all kinds of meat, but the amount of some may vary according to intrinsic characteristics of the animal species considered and the farming system adopted (Mele et al. 2016). The common definition of red meats includes beef, pork, lamb, mutton and horse meat, whereas white meat includes chicken, rabbit and turkey. However, as a general rule, the nutritional composition of meat is not strongly related to its colour, which is only due to the amount of myoglobin (Fe-heme) present in the muscle fibres (Mancini 2013) (Table 1). Most of the differences among the types of meat are related to total lipid content that in turn affects the energy content of meat, and to the fatty acid composition of intramuscular fat. Protein content is approximately 20%, regardless of the type of meat considered, being only marginally affected by species (Table 1).

The importance of meat consumption in different life stages having distinct nutritional requirements, and some critical aspects of epidemiological studies of the relationship between meat consumption and colorectal cancer are pointed out herein.

### Meat consumption during childhood

The transition from breast-feeding to a complete diet is crucial to satisfy the nutritional requirements of newborns. According to the guidelines published by

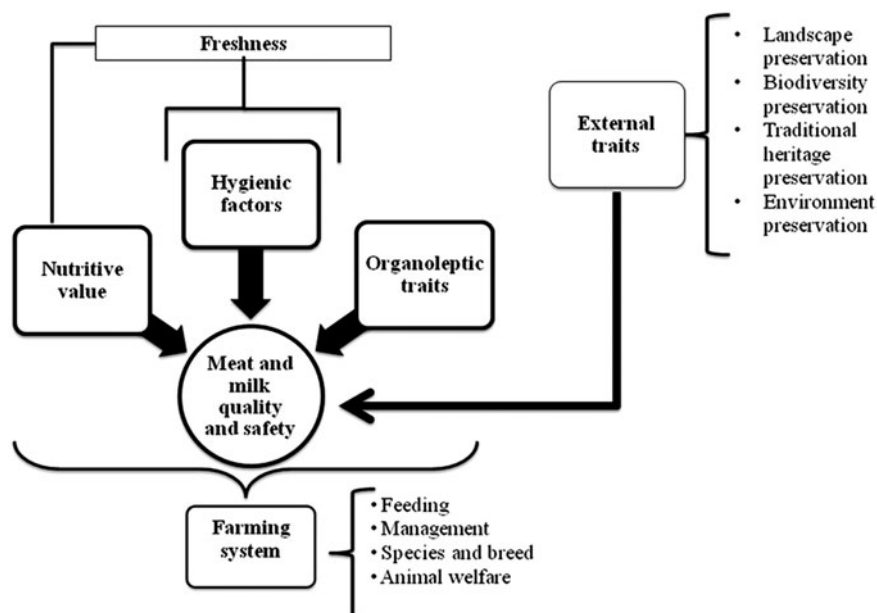


Figure 2. Main components influencing meat and milk quality and safety.

**Table 1.** Chemical and nutritional characteristics of different types of meat.

Item	Rabbit	Chicken	Turkey	Pork	Beef	Calf	Suckling lamb	Lamb
Dry matter, g/100 g meat	27.1	26.2	26.0	26.2	27.5	25.5	26.5	27.2
Protein, g/100 g meat	22.1	21.1	24.0	19.4	21.0	20.5	20.0	21.5
Lipids, g/100 g meat	4.0	4.2	1.8	5.9	5.4	4.0	4.5	4.4
Kcal, g/100 g meat	124.2	122	106.8	130.9	133.0	118	120.9	125.8
Cholesterol, mg/100 g meat	60.0	81.0	35.0	61.0	70.0	66.0	52.0	48.9
Vit. B12, µg/100 g meat	8.0	0.72	2.0	1.0	2.0	1.2	2.0	2.0
Fe-heme, µg/100 g meat	0.25	0.16	0.32	0.26	1.80	0.71	0.40	1.68

Adapted from Lombardi-Boccia et al. (2002), Williams (2007), Dalle Zotte and Szendrő (2011) and Mele et al. (2016).

the World Health Organisation (WHO 2003), foods of animal origin are recommended starting from six months of age. In contrast, vegan diets cannot completely satisfy the nutritive requirements of infants during the weaning period, especially regarding iron, zinc and vitamin B12 (WHO 2003). Among foods of animal origin, meat plays a very important role, especially as a source of iron. The iron requirements per kg of body mass are the highest in infants compared to other human life stages. Studies suggest that when the diet of infants was deficient in iron as a consequence of low meat intake, their neuro-psychic and cognitive development was negatively affected (Lozoff & Georgieff 2006; Beard et al. 2007). Dietary deficiency in iron and zinc along with protein malnutrition are considered as risk factors for cognitive damage. Research indicates that dietary supplementation with meat protein was more efficient than with plant protein in improving growth and cognitive ability in children (Neumann et al. 2007). Zinc deficiency was also associated with a higher incidence of infectious diseases and mortality in the developing world (Black 2003).

Meat is also the main dietary source of vitamin B12, which is almost absent in vegetables (Montville et al. 2013). Low meat intake during the weaning period was associated with vitamin B12 deficiency in infants, causing negative neurological effects (Garewal et al. 1988), megaloblastic anaemia and skin hyperpigmentation (Higginbottom et al. 1978) as well as other dysfunctions related to liver, intestine and spleen metabolism (Black 2008). In several cases, vitamin B12 deficiency occurred in infants who were breast-fed by vegan mothers or by mothers whose meat consumption was not adequate (Higginbottom et al. 1978; Garewal et al. 1988; von Schenck et al. 1997). Unfortunately, incomplete brain development was also found in infants supplemented with vitamin B12, as a therapy against vitamin B12 deficiency, because the response to this type of supplementation can be highly variable (von Schenck et al. 1997). Overall, the fundamental role of meat consumption during the early stages of life was also confirmed by studies

carried out in developing countries, where the lack or scarce intake of meat was the main cause of the poor growth of children, especially during the first year of life (Neumann et al. 2003).

### *Meat consumption and the immune system*

Protein deficiency reduces the responses of the immune system in humans (Castaneda et al. 1995). In general, animal proteins are considered more efficient than plant proteins in sustaining the growing process and the immune system. Some clinical trials showed the positive role of specific amino acids such as arginine and glutamine, in improving cellular immunity and the overall responses to infection and inflammation processes (Coëffier & Déchelotte 2005; Daly et al. 1990).

Glutamine is the most abundant amino acid in the human body and can be endogenously synthesised. This amino acid is the main source of energy for enterocytes, lymphocytes and macrophages (Newsholme 2001; Andrews & Griffiths 2002). However, glutamine requirements during inflammation or infection processes are higher than what the human organism is able to synthesise. As a consequence, a dietary supply of glutamine is fundamental to properly sustain the immune response. Meat is the main dietary source of glutamic acid, containing more than 4 mg of glutamic acid per 100 g of meat. On the other hand, meat also contains some components considered pro-inflammatory, such as Fe-heme, which may induce the production of free radicals. Hence, excessive meat consumption may induce higher inflammation risk, especially if the diet is poor in fibre and antioxidants from fresh fruit and vegetables (Fung et al. 2004; Lopez-Garcia et al. 2004). The critical role of the overall diet composition in human health was confirmed by Hodgson et al. (2007), who studied the effect of the substitution of carbohydrates with proteins from lean red meat on the inflammation response in humans. The results of this study suggested that partial replacement of dietary carbohydrate with protein from lean red meat did not elevate oxidative stress or inflammation, indicating that oxidative stress depends on the



overall balance between pro-inflammatory and anti-inflammatory substances.

### **Meat consumption in the elderly**

The aging process induces a general loss of muscular mass due to the interaction between chronic energy deficit, malnutrition and decrease in physical activity. The loss rate of muscular mass, named sarcopenia, may vary from 6% to 15% after 65 years of age and may reach 40% after 89 years of age (Melton et al. 2000). The US dietary guidelines recommend a daily intake of protein higher than 0.8g/kg body weight, but that intake should be increased up to 1.6g/kg body weight in elderly in order to counteract sarcopenia (Evans 2004). According to Wolfe (2006), an intake of 15g of essential amino acids at each meal may be sufficient to support body muscular mass in elderly people. These high requirements of dietary protein should be satisfied by food containing protein with high biological value such as meat, milk and eggs. Dietary protein of animal origin (whey protein) can also improve cognitive ability (memory) in elderly people (Kaplan et al. 2001).

### **Meat consumption and cancer**

Consumption of meat and processed meat is often believed to be associated with increased risk of cancer (especially colorectal cancer). This association is mainly due to evidence from epidemiological studies and from *in vitro* and *in vivo* studies on animal models that explored the mechanistic role of meat components in the development of cancer. Based on the current literature, the International Agency for Research on Cancer (IARC) committee recently released an updated list of substances considered as 'carcinogenic to humans' or 'probably carcinogenic to humans', classifying processed meat in the first group and red meat in the second (IARC 2015). In particular, the IARC workgroup considered that red meat contains very important nutrients for human health, but, at the same time, there are indications about the carcinogenicity of processed meat and also red meats, if their consumption exceeds 50 and 100g/d, respectively. The risk assessed was 18% higher in heavy meat consumers (processed and unprocessed meat) compared to vegans. This is a relatively low risk differential, considering that epidemiological studies are usually considered robust when the observed risk is at least 100% higher than in the control. The risk assessment of processed meat was based on 12 positive responses out of a total of 18 epidemiological studies and 6 positive responses out of a total of 9 case-control studies, whereas that

of red meat was based on 7 positive responses out of 14 epidemiological studies and 7 positive responses out of 15 case-control studies (IARC 2015). A linear and positive relationship between red and processed meat intake and cancer risk was obtained by considering the results of a single meta-analysis (Chan et al. 2011). However, a more recent meta-analysis concluded that the relationship between consumption of red and processed meat and cancer risk is inconsistent (Oostindjer et al. 2014). Moreover, a recent European Prospective Investigation into Cancer and Nutrition (EPIC) study highlighted that the association between red meat consumption and mortality from colorectal cancer was not significant in a large cohort of European citizens (Rohrmann et al. 2013). It should be mentioned that the IARC (2015) components unanimously declared that *in vitro* and *in vivo* studies on animal models did not provide definitive evidence to support the putative role of red meat as carcinogenic to humans.

The main suspects for meat carcinogenicity are the Fe-heme contained in red meat, the nitrogen organic compounds (NOCs) that are formed in the intestine as a consequence of the presence of nitrates and nitrites in processed meat and, finally, the polycyclic aromatic compounds (PHCs) that are formed during the cooking of red meat (Bastide et al. 2011). The main concern about Fe-heme regards its tendency to promote the production of heterocyclic amines in the intestine, which, in turn, may promote the beginning of cancer formation. According to Bastide et al. (2011), the relative risk of colon cancer was 1.18 (95% CI: 1.06–1.32) for subjects in the highest category of Fe-heme intake compared with those in the lowest category. However, more recently, Ashmore et al. (2013) reported that the association between intake of Fe-heme and colorectal cancer was significant only for levels of Fe-heme intake higher than 18mg/d. Because the average content of Fe-heme in red meat is lower than 2mg/100g, the overall amount of red meat necessary to reach 18mg/d of Fe-heme exceeds the average level of red meat intake reported by FAO statistical studies (FAO 2013).

Nitrogen organic compounds are added to several processed meats to reduce the risk of botulinum toxin and to preserve the red colour of the meat. This is probably the main risk factor for processed meat because high NOCs intake is associated with an increase in colorectal cancer risk in murine animal models (Santarelli et al. 2010). However, it should be taken into consideration that the term 'processed meat' includes a wide range of meat-based foods that may differ for the kind and amount of meat and

preservatives present, and these differences have not been considered in epidemiological studies. Polycyclic aromatic compounds contained in well-cooked red meat, especially fried meat, are considered as a risk factor for colorectal cancer (Santarelli et al. 2008). However, PHCs are not present only in red meat and might occur in any kind of meat, if overcooked. Moreover, several kinds of vegetables and seafood may contain high levels of PHCs as a consequence of environmental pollution (Santamaria 2006; Bansal & Kim 2015). Unfortunately, epidemiological studies have not considered this important aspect, which should be clarified in order to introduce correction factors in the analysis.

To summarise, scientific evidence about the association between red and processed meat and colorectal cancer risk is not conclusive, probably because of the heterogeneity in the composition of red and processed meat, as a consequence of the differences in production systems (Mele et al. 2016). A more conclusive assessment would be possible when epidemiological studies take into consideration the variability in meat products preparation and composition.

### ***Milk and dairy food consumption and human health***

Milk and dairy products are characterised by a high content of calcium (Ca), bioactive compounds and peptides that are beneficial for humans.

### ***Milk and dairy products consumption and bone integrity***

Osteoporosis, which is one of the most relevant diseases in the elderly, is characterised by a reduction in bone mineral density (BMD) and a deterioration in bone structure (Conference Report 1993). The importance of Ca for the preservation of bone integrity is recognised by the European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (EFSA 2009a). Calcium is the most relevant nutrient affecting bone health and Ca requirements increase with aging. Supplements can partially satisfy Ca requirements, but they usually do not contain protein and other minerals, such as Mg, K, Zn and P, which are an essential part of bone structure or fundamental for bone metabolism (Heaney 1996, 2009; Tucker 2009; Weaver 2009). Dairy foods are a good source of Ca and do not contain anti-nutritional factors that reduce mineral digestibility, such as phytates, oxalates or polyphenols that are present in legumes and other crops (Guéguen & Pointillart 2000).

Because the fulfilment of Ca requirements until 20 years of age is positively related to bone mineral density and strength, the consumption of Ca-rich foods like dairy products at a young age is very important to prevent osteoporosis in later years (Lindsay & Nieves 1994; Murray 1996; Heaney 2000; Huth et al. 2006; Straub 2007; Rizzoli et al. 2010). De Smet et al. (2015) found a positive relationship between dairy food consumption and BMD in a group of 306 Belgian children (6–12 years old), and Hawker et al. (2002) reported similar results in young women. In a prospective study in 3251 menopausal non-hispanic women, Kalkwarf et al. (2003) found a link between low BMD and low milk intake during childhood and adolescence, with an 11% lower incidence of osteoporotic fracture in subjects who had previous high milk consumption. Similar results were also reported by Soroko et al. (1994) and Bonjour et al. (2008).

Increased levels of BMD and a reduced risk of osteoporosis can be due to not only high content of bio-available Ca in dairy foods, but also the presence of high biological value protein and vitamin D3 in milk. In particular, protein from casein and whey can prevent bone loss, which frequently happens in elderly people (Rizzoli 2014). A reduction in osteoporosis prevalence, due to an increase in dairy food consumption, would result in reduced expenses of the public health service for the therapy of this pathology (Lötters et al. 2013).

### ***Bioactive compounds from milk that can positively affect bone metabolism***

Calcium is only one of the molecules found in milk that affect bone metabolism. Other milk compounds, such as whey protein and casein-phospho-peptides (CPP), can also increase bone strength. Trials carried out on rats and rabbits suggest that the basic fraction of whey protein can reduce the activity of osteoclasts (Toba et al. 2000), preserving bone from the remodeling activity typical of osteoporosis (Yoneme et al. 2015). The role of CPP as a mineral carrier is well known. The inclusion of Ca in a peptidic backbone improves its intestinal digestibility (FitzGerald 1998) and several studies have demonstrated the positive effect of CPP administration on bone density (Gerber & Jost 1996; Donida et al. 2009; Tulipano et al. 2010).

### ***Milk peptides and blood pressure***

Among the different types of peptides derived from the digestion of milk protein, the most investigated are the ones with Angiotensin Converting Enzyme (ACE)-inhibiting properties. ACE is a key enzyme in the



regulation of blood pressure that catalyses the conversion of angiotensin-1 to angiotensin-2, inducing vasoconstriction and, consequently, increasing blood pressure. Although the most part of ACE-inhibiting peptides have the last three C-terminal residues composed of Arginine (Arg), Threonine (Thr), Tryptophan (Trp), Tyrosine (Tyr), Phenylalanine (Phe) or Proline (Pro) (Contreras et al. 2009), most studies have focussed on the blood pressure lowering effects of the Ile-Pro-Pro (IPP) and Val-Pro-Pro (VPP) tri-peptides. A meta-analysis carried out by Cicero et al. (2011) showed the lowering effect of IPP and VPP peptides on blood pressure in humans, with a stronger effect on Asiatic population compared to Caucasian subjects (−6.93 mm vs. −1.17 mm of systolic blood pressure).

### **Are meat, milk and dairy products dangerous for bone health?**

Bone health is strictly linked to the balance between calcium absorption and excretion. Several authors found that hyperproteic diets, normally rich in high-protein foods such as milk and dairy foods, and foods rich in sulphur amino acids (e.g. meat, soybean and eggs), were associated with an increased risk of metabolic acidosis (unbalance in the acid-base equilibrium, with increasing levels of H<sup>+</sup>) that in turn would be associated with greater bone demineralisation (Bushinsky 2001; Arnett 2008), increased urinary calcium excretion (Barzel & Massey 1998) and increased risk of bone fracture (Feskanich et al. 2014; Michaëlsson et al. 2014). However, the review by Bonjour (2005) illustrated that this hypothesis was not based on clear experimental and clinical evidences, but on a combination of different *in vitro* trials, short-term human studies or retrospective studies. In addition, it was shown that several ingredients of the study diet may mitigate plasma acidification due to the catabolism of sulphur amino acids (Bonjour 2005). In fact, fruit and vegetables are sources of minerals able to act as buffers, equilibrating plasma pH and decreasing the risk of urinary calcium excretion (Bonjour et al. 2008). Therefore, possible problems for human health do not seem to be linked to the consumption of dairy products per se, but to an unbalanced diet. In fact, a balanced diet, with an adequate intake of protein and calcium combined with fruit and vegetables, would be beneficial for skeletal and cardiovascular health (Sahni et al 2010; O'Keefe et al. 2016). MacDonald et al (2001) found a positive effect of fruit intake on hip and spine BMD but they hypothesised that this effect could be due to the buffer activity of K

and weak organic acids (e.g. malic acid), found in high concentrations in fruit, rather than the possible negative effect of milk proteins. In this regard, the meta-analysis of Ho-Pham et al. (2009), using many studies on the relationship between different diets and femoral neck bone and lumbar spine bone density in menopausal women, showed that the BMD was reduced in women following vegetarian or vegan eating patterns compared to subjects having an omnivorous diet.

### **Importance of the sustainable intensification of ruminant production**

The security of food supply and improvement of food quality for large sectors of humanity are conditioned by the continuous increase in world population and, consequently, by the steady rise in demand for food, on the one hand, and the decline in available land due to its scarcity, fertility depletion, erosion or alternative use (natural, urban, energy), on the other hand (Pretty 2008; Lambin 2012).

According to Bruinsma (2003), only 11% (1.5 billion ha) of the Earth's land surface of approximately 13.4 billion hectares is used for agriculture (arable land and land with permanent crops), and about a quarter (3.4 billion ha) is used for grazing. Much of the land occupied by grassland has edaphic characteristics unsuitable for transformation into arable land. Therefore, grasslands are widely used for pastoral activities (mainly ruminants) and thus help to ensure sufficient production of food of animal origin, without interfering with plant production (Godfray et al. 2010) or causing soil carbon depletion. On the other hand, residues coming from croplands, which represent ~20% of the total biomass produced, are used to feed livestock (FAO 2011). In this scenario, sustainability of agriculture has become a global concern (Pretty 2008), and food security is no longer an exclusive problem of emerging or developing countries, being a challenge for all humanity (FAO 2015). According to the Global Footprint Network (2016), 'today humanity uses the equivalent of 1.6 planets to provide the resources we use and absorb our waste. This means it now takes the Earth one year and six months to regenerate what we use in a year. Moderate United Nations scenarios suggest that if current population and consumption trends continue, by the 2030s we will need the equivalent of two Earths to support us. And of course, we only have one'.

Considering that ruminants produce almost all the milk and much of the meat consumed by humans, there is a need for strategies to reduce their

environmental and economic costs, while increasing the quality and amount of the food of ruminant origin (Eisler et al. 2014), and protecting animal welfare and human health (Goldberg 2016). At the present time, because the public opinion in developed countries holds that conventional agriculture is less safe than organic agriculture, there is a strong tendency towards the conversion of land from the first to the second farming type. Despite being more sustainable (per unit of land) and having positive implications in terms of animal welfare, organic farming (at least as currently managed) is generally less productive per unit land than the conventional farming system, for both crop (Ryan et al. 2004; Savage 2015) and animal production systems (Sundrum 2001; de Boer 2003). Organic animal farming still faces several challenges. The suggestions for its improvement include bringing current organic livestock production closer to organic principles, developing selection tools that take into account adequate animal characteristics for organic systems, and identifying novel feed sources (Atkinson 2014). If the tendency to favour organic farming and the productivity of organic systems remain unchanged, a reduction in food production is foreseen. Moreover, if the increase in population continues as expected, the amount of arable land required in 2050 will surpass the amount available, leading to overexploitation and a potential reduction in biodiversity. Therefore, the only realistic scenario to meet human needs remains an increase in the efficiency and an improvement in the environmental sustainability of agricultural and livestock production systems (Bruinsma 2003; Pretty 2008; Godfray et al. 2010) – in other words sustainable intensification. Nonetheless, it is important to consider the relevance of local food movements (Goldberg 2016) and organic animal farming in marketing niches, where consumers are willing to pay a higher price for locally and organically produced food, including meat and dairy products. Obviously, this activity has to be counterbalanced by a widespread adoption of sustainable intensive ruminant systems throughout the world, so that we can ensure food safety and security in the planet (Figure 1). This requires an integrated approach that also takes into account the cultural and social values, environmental conditions, technical and scientific knowledge, and economic resources of the stakeholders involved in ruminant production and consumption.

### **Environmental impact of ruminant production**

Livestock production is often considered to be unsustainable, with the livestock sector contributing to 14.5% of anthropogenic GHG emissions (Eisler et al.

2014). These values are expressed in terms of carbon dioxide (CO<sub>2</sub>) equivalents (i.e. net exchange of GHG, as total or per unit of product or service), obtained considering that different gases – especially CO<sub>2</sub>, methane (CH<sub>4</sub>), and nitrous oxide (N<sub>2</sub>O) – contribute in distinct proportions to total GHG emissions. Ruminants are associated with the release of CH<sub>4</sub> from enteric fermentation in their gastrointestinal tract (Cassandro et al. 2013; Knapp et al. 2014) and manure decomposition (Dalla Riva et al. 2014), the production of N<sub>2</sub>O from the N present in manure (Dalla Riva et al. 2014), land use and degradation due to overgrazing, and water consumption and pollution. Obviously, intensive and sustainable ruminant systems should adopt appropriate management, nutrition and breeding techniques and ensure adequate animal welfare in order to favour animal performance and minimise animal impact on environment.

Given the high consumption of meat, milk and dairy products now and in the future, ruminant production will continue to contribute to a large part of the Ecological footprint of agriculture. Therefore, evaluating the impact of ruminant production on the environment is fundamental for the development and adoption of proper mitigation strategies. Animal carbon footprint represents the environmental impact of animal production and is usually estimated by the method of Life Cycle Assessment (LCA) (FAO 2010; Rotz et al. 2010; Thoma et al. 2013), a technique which assesses the environmental impact associated with a product or a service by compiling an inventory of major inputs and outputs of a production system. Animal carbon and water footprint are discussed herein, considering that the LCA approach has focussed for a long time on the animal impact in terms of GHG emissions (Carbon footprint), water consumption (Water Footprint), eroded soil (Soil footprint), or reduced biodiversity (Biodiversity footprint) per unit of product of animal origin. However, it is important to highlight that recently the LCA approach used by Dalla Riva et al. (2015) took into account a larger set of variables, i.e. climate change, terrestrial acidification, fresh water eutrophication, land occupation, water depletion and cumulative fossil energy demand. Moreover, Wiedemann et al. (2015) applied the LCA to compare the effects of four contrasting case-study farm systems of dual-purpose sheep (meat and wool) on GHG emissions, fossil energy demand and land occupation by evaluating seven methods, as follows: three biophysical allocation methods of GHG emissions based on protein requirements and partitioning of digested protein, protein mass allocation (PMA), economic allocation (EA), and two system expansion

methods. GHG emissions per kilogram of total product (i.e. wool and live weight, LW) were similar across farms, but varied highly with the method of co-product handling. The authors concluded that biophysical allocation methods based on partitioning between sheep wool and LW would be adequate for attributional studies, whereas sensitivity analysis using system expansion would be appropriate to understand the implications of system change, when alternative products or systems are chosen, and to evaluate system change strategies.

Flachowsky and Hachenberg (2009) showed that the values of Animal carbon footprint (in kg CO<sub>2</sub>eq/kg product) estimated with the LCA method were highly variable depending on the type of product and the specific methodology used, without a clear difference between the conventional and organic production systems. In an attempt to obtain a more reliable estimate of the Ecological footprint of livestock, Pulina et al. (2011b) developed a mathematical model with the Stella® software to calculate a partial Animal carbon footprint (i.e. limited to animal rearing, excluding crops, fattening and meat commercialisation) of a 'cow-calf line' of a farming system, considering 100 heifers from the beginning to the end of their reproductive career. The following values of CO<sub>2</sub>eq produced were obtained: on average 1636 kg CO<sub>2</sub>eq/head in one year and 12.4 kg CO<sub>2</sub>eq/kg carcass sold. The latter estimate is within the variability range of 10-21 kg CO<sub>2</sub>eq/kg product reported by Flachowsky and Hachenberg (2009). A study conducted in dairy cattle herds in Italy calculated average emissions of 1.3 kg CO<sub>2</sub>eq/L milk produced, with a strong tendency towards a reduction in impact, moving from less productive to more productive farms (Serra et al. 2013). In a comparative study of carbon footprint for dairy herds in the North-East of Italy and Slovenia (Gaspardo et al. 2015), the estimated kg CO<sub>2</sub>eq/L fat and protein corrected milk (FPCM) was significantly higher for Brown cows (1.61 kg CO<sub>2</sub>eq) than for Simmental and Holstein Friesian cows (1.15 and 1.04 kg CO<sub>2</sub>eq, respectively). In this study, data were collected with personal interviews with farmers and an LCA approach was used to estimate emissions (global warming potential, acidification, and eutrophication potentials) and consumption of non-renewable sources (energy and land use). The differences between breeds were related to the amount of milk produced, because the farms with Brown cows, sampled mostly in Slovenia, had a lower milk yield and a diet richer in forages compared to the farms that raised the other two breeds. However, whether or not the level of intensification per se is able to reduce carbon footprint is still

a matter of debate. According to Serra et al. (2013, 2014) and Bava et al. (2014), farming intensification and increased milk production per cow, dairy efficiency, and stocking density were negatively related to emissions per kilogram of product, suggesting a positive effect of these factors for the mitigation of GHG. However, the variability among farms was very high, indicating that other aspects such as management and structural characteristics played a relevant role. Another study indicated that farms with low producing cows had higher environmental impact per kg of milk; also, farms with lower stocking rates showed reduced acidification and eutrophication per kg of FPCM (Penati et al. 2013). Enhancing feed self-sufficiency by higher forage production and quality, and utilising highland pastures, together with increasing milk yield per cow, was suggested as the best strategy to improve the environmental sustainability of dairy farms in the Alps. In a simulation study designed to model the influence of breeds on GHG emissions, using the productive traits of Holstein and Jersey breeds in a typical intensive condition in Italy, the effect of different allocation factors for meat and milk in the LCA assessment was presented (Dalla Riva et al. 2014). The authors estimated higher emissions for a Holstein herd (0.96 kg CO<sub>2</sub>eq/kg energy corrected milk, ECM) than for a Jersey herd (0.80 kg CO<sub>2</sub>eq/kg ECM), the latter being characterised by lower milk yield but higher values of fat and protein in milk. In this case, the lower dry matter intake and the higher fertility of the Jersey breed in comparison to the Holstein breed caused a decrease in feed conversion ratio to milk and replacement of animals in the herd. These studies suggest that increasing milk yield and intensifying farming systems can be a strategy to mitigate GHG emissions when management – including manure, health and fertility of the herd – is not compromised (Lovett et al. 2006; Penati et al. 2013).

Many other studies have shown that the most efficient way to reduce GHG emissions in animal production is the sustainable intensification of animal production. For instance, Capper et al. (2009) found that the amount of CO<sub>2</sub>eq emitted from dairy cattle farms in the United States increased from 13.5 to 27.8 kg CO<sub>2</sub>eq/cow daily from 1944 to 2007 and paralleled the increase in feed intake, whereas CO<sub>2</sub>eq produced/kg milk decreased drastically from 3.66 to 1.35 kg CO<sub>2</sub>eq. This was due to a reduction in the number of animals per farm and an increase in milk production per animal, which varied linearly in the studied period. As a consequence, the amount of GHG emitted from dairy cattle farms in the US decreased from 194 million tons in 1944 to 114 million tons in

2007, despite the increase in total milk production in the country. In Italy, Esposito and Coderoni (2011) estimated that the CH<sub>4</sub> emissions from dairy cattle were reduced by almost 50% from 1951 to 2008 (from 370 to 200 thousand tons CO<sub>2</sub>eq). Considering that total milk yield doubled in the same period (from 5.5 to 11.1 million thousand tons), we estimated that the CH<sub>4</sub> emissions decreased from 1.9 to 0.5 kg CO<sub>2</sub>eq/L milk in Italy. Similarly, Capper (2011) found that intensification of the meat production process is the best strategy to reduce animal carbon footprint and meet the growing demand for food, especially in emerging countries. However, not all studies have considered that the increased requirements of highly productive animals lead to an increased demand for highly digestible feedstuffs and, especially, for certain crops. This is associated with an increase in cultivated arable land at the expense of pasture land or forest, with a consequent reduction in the capacity of carbon sequestration by the system and an increase in net GHG emissions. The environmental risks of converting a significant amount of grassland into cultivated cereals would be high. For example, less than 9% of pastureland in the United States is sufficiently productive to be considered suitable for growing other crops (Council for Agricultural Science and Technology 2013).

Another important issue concerning the impact of animal production on GHG emissions is related to manure management for both intensive and grazing systems. Mitigation of emissions arising from the accumulation of manure can be guaranteed at least in part by developing and disseminating increasingly efficient technologies for the use of animal waste for energy purposes, especially for biogas production (Kebreab et al. 2006). Biogas production is important, considering that the spreading of manure or slurry might not be able to ensure a long-term effective capture of carbon by the soil (carbon sink) (Schlesinger 2000).

In animal farming, the water footprint is mainly related to water used for irrigation of cultivated land and for production and processing technologies, but some is also associated with pollution of water reserves. The water footprint is usually divided into blue, green and grey, according to the type of water taken into consideration (WWF Italy 2014). Based on the definitions and methodology of a previous work (Hoekstra et al. 2009), Mekonnen and Hoekstra (2010) briefly defined the three types of water footprint as follows: 'The blue water footprint refers to consumption of blue water resources (surface and groundwater) along the supply chain of a product. "Consumption" refers to loss of water from the available ground-

surface water body in a catchment area. Losses occur when water evaporates, returns to another catchment area or the sea, or is incorporated into a product. The green water footprint refers to consumption of green water resources (rainwater insofar as it does not become run-off). The grey water footprint refers to pollution and is defined as the volume of freshwater that is required to assimilate the load of pollutants given natural background concentrations and existing ambient water quality standards'.

Drastig et al. (2010) calculated the blue water demand for dairy farms in Brandenburg (Germany), by assessing the water used for feeding, milk processing, and servicing of cows from 1999 to 2008. The blue water footprint of the dairy production decreased over the ten-year period due to intensification (i.e. decrease in animal number and increase in milk yield per cow), with an average animal water footprint of 3.94 L blue water/kg milk produced.

Intensification can also reduce the animal water footprint of meat production. For instance, Capper (2010) estimated a value of 3600 L/kg meat in intensive livestock farming (feedlot systems), which differed noticeably from the value of 15,400 L/kg meat, based on the average data at the global level, previously calculated by Mekonnen and Hoekstra (2010). The estimate of the animal water footprint in Italy performed by Pulina et al. (2011a), using the method of Drastig et al. (2010), showed that dairy cattle and beef cattle accounted for 82% and 10% of water consumption, respectively, because of their high intake of forage and the resultant high green water component. An alternative method of estimation, the Net Water Footprint (NWFP), was proposed by Atzori et al. (2015). In this model, the water footprint calculation subtracted the evapotranspiration from natural vegetation that would have grown if the surface had not been cultivated, from the total water consumed by a crop. The NWFP thus calculated for Mediterranean livestock systems was approximately about 4000 L water/kg beef meat and 200 L water/L milk (Atzori et al. 2015).

Matlock et al. (2013) found that the eutrophication impact for dairy production in the United States is more likely to occur from feed production than from on-farm dairy activities at regional (for nitrogen) and local (for phosphorus) scale. Nevertheless, given the increasing importance of water resources for the improvement of food production at a global scale, research should find effective solutions to save water resources and obtain a rational management of ruminant waste.

Effective mitigation of carbon footprint or water footprint, or both, from ruminant farms can be

achieved by improving animal welfare, adopting appropriate feeding techniques and following specific breeding programmes, as discussed in the subsequent sections of this review.

### **Welfare and biological efficiency of farmed ruminants**

The concept of animal welfare has ethical roots; therefore, it finds in itself its own reason for existence. Goldberg (2016) described in detail how the concept of animal welfare has evolved over time. Because animal welfare is a central aspect of intensive sustainable ruminant production, this section deals with (a) some aspects of current regulation on animal welfare and on-going activities to improve their implementation; (b) the importance of animal welfare and the use of a multidisciplinary approach to assess ruminant responses to stress; and (c) the effects of stress on the yield and quality of milk, dairy products and meat.

### **Legislation**

The European Union (EU) legislation on animal protection is very extensive. There are general rules for the protection of animals of all species kept for the production of food, wool or other farming purposes, and specific rules for swine, poultry, and calves. However, no specific legislation concerning cattle or dairy cows is available to date. For these categories, EFSA Scientific Opinions are available. In particular, specific rules for cattle kept for beef production and on welfare in intensive calf farming systems are based on the EFSA Panel on Animal Health and Welfare (AHAW) (EFSA 2012) and specific rules for dairy cows were reported by the EFSA Panel on Animal Health and Welfare (AHAW) (EFSA 2009b). Since the approval of the Common Agricultural Policy (CAP) reform (EC regulation no. 1782/2003) in 2003, the EU has made important changes to the existing rules and procedures for providing support to the agricultural system, and animal welfare has become a strategic element for the development of livestock systems. In the EC Reg. 73/2009 'Common rules concerning the support for farmers under the CAP', animal welfare is one of the Management Criteria Required. Minimum thresholds for animal welfare are defined, but at the same time animal welfare is part of a voluntary improvement policy.

In 2006 the Community Action Plan on the protection and welfare of animals for 2006–2010 was adopted. This programme highlights the importance of consumer information as part of a comprehensive communication strategy on animal welfare, as well as

the creation of a Community reference centre for harmonising standards and promoting the sharing and use of best animal welfare practices in livestock systems.

The European Union Strategy for the Protection and Welfare of Animals for 2012–2015 is a continuation of the 2006–2010 Community Action Plan that identifies the following main common factors that have an impact on animal welfare: (a) the lack of full application of EU legislation on animal welfare due in part to the diversity of farming systems and local contexts. For this reason, there is a need for simplification through the introduction, among the general rules, of more detailed provisions in relation to these four common factors for animal welfare; (b) the lack of appropriate information on animal welfare to consumers; (c) the lack of sufficient knowledge of animal welfare by operators and stakeholders; and (d) the need for a simplification and development of the principles related to animal welfare.

From these strongholds, the Italian National Plan for Animal Welfare has proposed ideas for its development. The 6th Framework Programme (FP) 'Welfare Quality®: Science and society improving animal welfare in the food quality chain' project (<http://www.welfarequality.net/everyone/26572/7/0/22>) involves researchers from several EU countries. It has among its work packages (a) the analysis of consumers' concerns about food animal welfare, the type of information demanded, and the most effective communication and information strategy; (b) the assessment of current and potential markets for welfare-friendly animal-based food products, welfare label characteristics, and inspection systems; and (c) the identification of potential barriers to the development of animal-friendly products faced by producers.

### **Importance and assessment of animal welfare**

Scientific research has evidenced that protection of animal welfare can turn into profit, in terms of reducing veterinary costs, increasing animal performance, improving the quality of products and maintaining hygienic standards of food production. Welfare is strictly related to health and efficiency of production of farmed animals, and sustaining animal welfare can also increase the commercial value of animal products. The demand for high quality food has been rising and an increasing number of consumers expect animal products to be obtained and processed with greater respect for the welfare of animals.

Farmed ruminants might face many stressors of different origin, as follows: (a) environmental stressors,



such as climatic extremes, air pollution and poor drinking water quality; (b) physical stressors, such as crowding and reduced air space; (c) physiological and nutritional stressors, such as transition period, unbalanced diets, under-nutrition and fasting; (d) management stressors, such as inappropriate milking, slaughter routine, transport, animal moving and handling, castration, and dehorning; (e) pathological and traumatic stressors, such as lameness, diarrhoea, and accidental trauma; and (f) psychogenic stressors, such as isolation and inappropriate human interaction. The animal response to stressors, in turn, depends on a number of factors, which can be grouped as follows: (a) breed differences, genetic selection, early influences and epigenetic factors, and individual life history, acting as endogenous factors; and (b) the source and nature of stressors, the frequency of exposure to stressor, and the length and intensity of stress, acting as exogenous factors.

In general, the defence mechanisms activated in response to stress are necessary to cope with emergency situations, but they can also lead to pathology or to an increase in animal susceptibility to diseases, often by initiating immuno-suppression (Broom & Kirkden 2004). Because of the variety of mechanisms activated by animals to face stress, welfare assessment requires a multidisciplinary approach, including the use of production, reproduction, behavioural, physiological and pathological indicators. Such a wide range of indicators is necessary because not all response mechanisms to stress are always, or simultaneously, activated.

The activation of the hypothalamic–pituitary–adrenal (HPA) axis is one of the best known and consistent neuroendocrine adaptive responses to stress. Psychological, environmental and physiological stressors can determine the release of the corticotrophin-releasing factor by the anterior hypothalamus, which stimulates the secretion of the adrenocorticotrophic hormone (ACTH) by the anterior pituitary gland. The target organ of ACTH is the adrenal cortex, and the main action of ACTH is to increase the secretion of glucocorticoids, especially cortisol, which in turn controls cytokine production and action (Black 2002). From a welfare perspective, we are not interested in short-lived changes occurring in acute stress situations; on the contrary, we are interested in long-term changes in response to chronic stress.

An increasing body of literature suggests the existence of crosstalk between the immune and nervous systems involved in the animals' response to stress. The mediators of the interaction between these two biological systems are the cytokines. Both

physiological and psychological stressors can determine the secretion of pro-inflammatory cytokines, i.e. IL-1 $\beta$ , IL-6 and TNF- $\alpha$  (Caroprese et al. 2006). Cytokines can increase the production of neutrophils, affect leukocyte adhesion and capillary permeability, and induce fever and the synthesis of acute phase proteins (APP) (Gregory 2004). In addition, pro-inflammatory cytokines act on the brain, causing a 'sickness behaviour', characterised by an increase in sleep and a decrease in social, aggressive and explorative behaviours, together with reduced feeding (Kemeny 2009).

The likely effects of cytokines at sub-clinical levels can be assessed objectively through changes in positive and negative APP in blood (Trevisi et al. 2011). Therefore, these proteins can provide a tool to objectively evaluate animal welfare (Bionaz et al. 2007; Bertoni et al. 2008; Calamari et al. 2014). For instance, inflammatory-like conditions have been often observed in the transition period, in dairy cows without clinical symptoms, and only the changes in positive and negative APP in blood reveal subclinical problems and low welfare (Bertoni et al. 2008).

Behavioural responses of animals are often correlated with both physiological and immune responses; as a consequence, behavioural indicators of stress can be used to estimate the effects of stress on the biological functions of the animal (Rushen 2000). A way to determine how an animal is coping with a challenge is to conduct a preference or an aversion test. In the first case the animal is asked to choose between two or more situations; in the second case the time taken by an animal to approach to an aversive situation or a place where an aversive treatment has taken place is recorded (Cook et al. 2000).

Apart from behavioural observations, measures of welfare assessment are mainly represented by physiological and immunological evaluations in blood. However, the assessment of perturbations in the levels of endocrine and immune indicators requires animal capture, handling and manipulation by stockmen, and animal venipuncture. Because these procedures can be stressful for animals, their effects may confound the stressors to be tested. In addition, welfare evaluation requires a cautious interpretation of the changes of these indicators in blood because their levels are affected by many factors such as circadian rhythms (Möstl & Palme 2002), sampling (Negrão et al. 2004), restraint (Bertoni et al. 2005a), lactation phase (Bertoni et al. 2006), and habituation (von Borell 2001). To reduce variability, it has been proposed to evaluate cortisol in biological samples other than blood. For example, some studies demonstrated that it is possible to estimate cortisol concentrations in the plasma of



cattle and sheep directly from salivary cortisol concentration (Fell et al. 1985; Negrão et al. 2004). In lactating animals, milk collection is a routine procedure that creates minimal disturbance to the animal. Milk cortisol in dairy cows can be considered a good indicator of stressors acting up to 2 h before the collection of milk samples (Verkerk et al. 1998), and some factors involved in its variation were shown by Fukasawa et al. (2008) and Sgorlon et al. (2015a, 2015b). Analytical methods using faeces (Morrow et al. 2002) and urine (Pompa et al. 2011) have been shown to be advantageous for measuring glucocorticoid metabolites as indicators of stress in dairy cattle. A direct and positive relationship between faecal glucocorticoid metabolites, blood cortisol, and adrenal activity was demonstrated by Morrow et al. (2002). A minimally invasive method to assess stress levels over time through cortisol determination in bristles of growing pigs and sows has been recently proposed by Martelli et al. (2014) and by Bacci et al. (2014). It would be interesting to test the feasibility and reliability of this technique in ruminant species as well.

The most widely recognised method to evaluate the adrenal cortex function is the challenge with ACTH, by using its analogue (ACTH1-24 or tetracosactide) (Verkerk et al. 1994), but there are several confounding factors that have to be considered, such as milk yield, age, ambient temperature and lactation stage (Bertoni et al. 2005b; Hasegawa et al. 1997) as well as genetic factors (Weiss et al. 2004). Therefore, a better standardisation, in terms of dose, time of bleeding and response measurements, is needed (Bertoni et al. 2005a). Welfare status can also be assessed by measuring immunological parameters in milk, such as antigen-specific IgG and serum amyloid A (Caroprese et al. 2006; Winter et al. 2006).

### **Effects of stress on ruminant production**

The effects of stress on yield and quality of milk and cheese are variable. Animal responses to stress are characterised by changes in different hormones and/or cytokines which are responsible for metabolism, nutrient partitioning among different tissues (Elsasser et al. 2000), and mammary gland activity (Bertoni et al. 2003). Therefore, the final consequences of stress on milk can be very different depending on the different sources of stress, i.e. acute or chronic, and cognitive or non-cognitive (e.g. metabolic, heat, disease and digestive troubles). In general, there are stressors that can significantly modify bulk milk production and others that have no effect. Generalised acute stress in the herd (e.g. abrupt climate change, vaccination, feed or

water deprivation or shortage for few hours, and routine disruption) is a possible cause of altered yield and quality of milk. The effects of chronic stress, which affects the animals for longer periods, on bulk milk characteristics depend on the proportion of the animals that are affected simultaneously.

The increased secretion of catecholamines in stressed animals, particularly in acute stress, may impair the release and access of oxytocin to the mammary gland and the action of oxytocin on the secretory epithelium, so that milking-related oxytocin release is strongly impaired. In addition, stress leads to energy deficit, which in turn results in reduced protein and fat content in milk, and might even alter amino acid and fatty acid profile in milk. Such modifications are responsible for a reduction in milk nutritional properties, renneting ability and cheese yield. A reduction in milk yield and an increase in milk fat concentration occurred when cows were moved from one farm to another (Varner et al. 1983). Similarly, milk yield, and milk protein and potassium concentration decreased, whereas milk fat and sodium concentration increased when dairy cows were injected with ACTH (Varner & Johnson 1983). Bertoni et al. (1985) showed that the effects of ACTH on milk yield and composition varied with the dose used and were often more prolonged than the observed rise in cortisol and glucose in blood. This suggests a mechanism involving the regulation of the  $\alpha$ -lactalbumin (Varner & Johnson 1983) and possibly other aspects of protein synthesis. In fact, after the ACTH treatment, Bertoni et al. (1985) observed an increase in titratable acidity and Ca and P contents together with some changes in the coagulation features in milk. The latter results suggest that a change at post-translational level (i.e. phosphorylation) could occur, as observed by Fox (1989).

Chronic stress is more related to the welfare status of the animals because it is determined by a prolonged unpleasant situation (e.g. heat or cold stress, psychological stress and physical stress). Furthermore, it can affect the general health status of the animals (e.g. digestive tract, mammary gland and locomotion apparatus), which in turn affects the welfare and efficiency of the animals, and then milk yield and composition.

Heat stress strongly affects the yield and quality of milk in ruminants (Sevi 2007; Bernabucci et al. 2010). The metabolic–endocrine changes that occur under heat stress conditions (Abeni et al. 2007; Calamari et al. 2007; Bernabucci et al. 2010) can directly affect the mammary gland activity and digestive activity (e.g.

fermentation, motility, secretion and absorption), which are a major source of nutrients and body heat.

Heat stress can decrease blood flow rate in the digestive tract, gut motility, with decreased flow rate, and chewing activity (Christopherson 1985), partially due to reduced thyroid hormone levels (Collier & Beede 1985). All these changes and the reduced feed intake following heat stress can explain the observed higher retention time and, therefore, higher digestibility (Collier & Beede 1985). Fermentation is also influenced by heat stress, thus increasing the risk of producing an excessive amount of acids in the rumen for at least three reasons: (a) the heat stressed animals tend to eat less fibrous feeds in order to reduce heat production (West 1994); (b) the rumen retention time increases; and (c) the salivary secretion decreases due to the reduced chewing activity. The consequent changes at endocrine and digestive levels modify the nutrient availability (amount and type) and partitioning and are, therefore, involved in the changes in milk yield and composition observed under heat stress.

Heat stress causes a reduction in milk yield, but the reduced nutrient intake (an indirect effect of heat) accounts for only ~35% of the heat stress-induced decrease in milk synthesis (Bernabucci et al. 2015). In dairy cows, the main milk components (fat, protein, total solids and solid not fat) are lower in summer than in winter (Bernabucci et al. 2015), and heat stress impacts negatively on milk characteristics (Bernabucci & Calamari 1998), with an impairment of the cheese-making properties (Calamari & Mariani 1998). In particular, titratable acidity decreases and milk coagulation properties (MCP) get worse, making milk less suitable for the production of hard cheese with a long ripening time (Calamari & Mariani 1998; Malacarne et al. 2005). Among the milk characteristics affecting the MCP, casein content and the casein composition are two important factors (Bertoni et al. 2001a, 2005c). Bernabucci et al. (2015) found that heat stress influenced milk protein fractions, with a reduction in the proportion of  $\alpha_s$ -CN and  $\beta$ -CN, which are the most sensitive to hot conditions, and an increase in the proportion of  $\kappa$ -CN and  $\gamma$ -CN during summer. The authors concluded that the worsening of the MCP observed during summer seems mainly attributable to the reduction in protein concentration and changes in milk protein fractions. In dairy ewes, besides heat stress (Sevi 2007), cold stress can cause reductions in the yield of milk and its components and a decrease in milk quality (Peana et al. 2007; Ramón et al. 2016).

Poor housing hygiene can endanger udder health in dairy ewes due to a reduction in the natural defence mechanisms of the teat and mammary gland

or an increase in the number and pathogenicity of the microorganisms in contact with the entrance of the teat canal or both (Sevi 2007). Bacterial colonisation of the udder is detrimental to milk quality *per se* and also provokes leukocyte recruitment in the mammary gland, which can cause extensive damage to secretory epithelial cells. These events are responsible for decreased synthesis and altered composition of milk, lower recovery of fat and protein during cheese making, and altered proteolysis during cheese ripening (Sevi 2007).

Sevi and Casamassima (2009) summarised the variations in the yield and quality of milk in response to changes in some physical and management parameters in housed sheep, showing that reduction in space allowance (from 2 to 1 m<sup>2</sup>/head), air space (from 7 to 4 m<sup>3</sup>/head) and air change (from 47 to 23 m<sup>3</sup>/head) as well as 'no litter management', in comparison to 'litter removal' or 'litter treatment with improvers', were detrimental. Variations ranged from -7 to -17% for milk yield, from 0 to -6% for casein content, from 0 to -8% for fat content, from 0 to +20% for clot formation time, from +9% to +24% for clot formation rate, from -5% to -19% for clot firmness, from +7% to +341% for somatic cell count, from +6% to +117% for total microbial count and from +5% to +51% for coliform count, depending on the stressor considered.

In growing and fattening animals, stressors can adversely affect feed intake, feed efficiency and weight gain. The meat production chain has very critical points, i.e. transport to abattoir, lairage prior to slaughtering and slaughter routine itself. Stressors acting on animals during each of these phases can lead to weight loss and have deleterious effects on meat quality, especially its rheological properties. One of the most frequent outcomes of exposure to pre-slaughter stressors is the Dark-Firm-Dry (DFD) syndrome in beef, which leads to a marked lowering of the commercial value of meat.

Poor welfare also limits the efficiency of reproduction. There is endocrine evidence showing that stressors interfere with the precise timing of the release of reproductive hormones within the follicular phase. Battaglia et al. (1997) provided a direct proof of the suppressive effects of an acute stressor, i.e. endotoxin administration, on the secretion of the gonadotropin releasing hormone (GnRH). In addition, there is evidence that exogenously increased ACTH concentrations or transport reduce the amount of luteinizing hormone released (Phogat et al. 1997). Dobson and Smith (2000) reported an increase in the interval from calving to conception by 13–14 days and the need for an additional 0.5 insemination per conception in cows

subjected to milk fever or lameness. Other effects of poor welfare on reproduction performance are related to the alteration in hormone secretion during the follicular phase, reduction in oestradiol release from ovarian follicles and delayed onset of the luteinizing hormone surge prior to ovulation.

Inflammatory stress is characterised by an increase in positive APP (e.g. haptoglobin and ceruloplasmin) and reductions in zinc and calcium in blood (Bertoni et al. 1989; Elsasser et al. 2000). Except for ceruloplasmin, which remains high for a long time (weeks), the other changes last for a short time (days) and can be observed only during a clinical or sub-clinical pathological event. Conversely, the effects of the inflammatory stress can be monitored for a longer time, particularly because cytokines cause a diversion of liver synthesis (Bionaz et al. 2007), with a rapid reduction in some negative APP (e.g. albumins, lipoproteins measured as cholesterol, and retinol binding proteins measured as vitamin A and paraoxonase), which tend to return to normal values quite slowly. These responses negatively affect reproduction for a long time after calving (Bertoni et al. 2001b) and can be recognised by changes in the negative APP in blood. In ewes, Enhert and Moberg (1991) studied the relationship between an emotional stressor (isolation) or a physical stressor (transport) and oestrous occurrence, finding that delayed, or interrupted, oestrous occurred in 44% and 75% of the animals subjected to isolation and transport, respectively.

### Adaptation of ruminants to climate change

Climate change will affect the livestock sector both directly and indirectly (Gaughan et al. 2009). Direct effects will be related primarily to heat stress conditions, whose frequency and severity are expected to increase because of the predicted increase in air temperature (global warming) (IPCC 2014), but also to the predicted higher frequency and magnitude of extreme weather events, such as heat waves and floods (IPCC 2013). A number of regional studies have been published on climate scenarios which could be of interest for farmed ruminants (de la Casa & Ravelo 2003; Somparn et al. 2004; Segnalini et al. 2013), based on predicted changes on the temperature humidity index (THI), an index which combines temperature and humidity into a single value and is widely considered as a useful tool to predict the effects of environmental warming on farm animals (Bohmanova et al. 2007). For example, Segnalini et al. (2013) provided scenario maps relative to the summer season in the Mediterranean basin. Such maps indicated an

enlargement of the areas in the basin where the THI during summer months (June, July and August) will likely cause thermal discomfort in farm animals. The authors concluded that the predicted increases in THI may aggravate the consequences of hot weather on animal welfare, performance, health and survival.

The reduction in animal welfare and the responses of ruminants to stressors, particularly heat stress discussed in the previous section, apply also to climate change scenarios. In fact, global warming is likely to aggravate the increase in maintenance energy requirements, and elicit adjustments in physiology and metabolism and modifications in feed intake (Bernabucci et al. 2010). As a consequence, relevant economic losses for the livestock industry are likely to occur (Johnson 1987) due to increased mortality rate, reproductive failure, reduced growth and decline of milk yield and quality (Lacetera et al. 2013). Recently, a significant higher risk of death was reported in dairy cows during heat wave events in both France and Italy (Morignat et al. 2014; Vitali et al. 2015).

The indirect impact of high temperatures follows more intricate pathways, including those deriving from the influence of climate on food and water shortages, feed quality reduction, microbial density and distribution, vector-borne disease distribution, and host resistance to infections (Gaughan et al. 2009). An example of such impact is the spread of the bluetongue virus (Purse et al. 2005), which causes an extremely serious disease in ruminants, across European countries several hundred kilometres further North than previously reported. Purse et al. (2005) suggested that this spread was driven by changes in European climate, which led to the increase in virus persistence during winter months, the northward expansion of *Culicoides imicola*, the most important bluetongue virus vector, and, beyond this vector's range, the transmission of the disease by indigenous *Culicoides* species, thereby expanding the risk of transmission over wider geographical areas.

Definitions of adaptation include those provided by the Intergovernmental Panel on Climate Change (IPCC) and by the European Commission (EC). IPCC defines adaptation as an adjustment in natural or human systems, in response to actual or expected climatic stimuli or their effects, which moderates harm or exploits beneficial opportunities (Adger et al. 2007). Similarly, the EC (2016) reports that adaptation means anticipating the adverse effects of climate change, and taking appropriate and economically sustainable actions to prevent or minimise the damage they can cause, or taking advantage of opportunities that may arise. Furthermore, the IPCC also distinguished adaptation

into the following types: anticipatory (taking place before climate change occurs, anticipating changes in climate and preparing accordingly), reactive (taking place following the observation and analysis of climate changes), autonomous (spontaneous adaptation that is triggered by both ecological changes in natural systems and market or welfare changes in human system), planned (resulting from a deliberate policy decision, based on an awareness that conditions have changed or are about to change), private (initiated by individuals, household or private companies for self-interest), and public (initiated by public body for collective public needs) (Adger et al. 2007).

Therefore, when referred to the ruminant sector, adaptation includes actions that may help to alleviate the direct or indirect negative effects of climate on animal health, welfare and productivity. The adaptation measures that can minimise the direct effects of climate change on animals are classified as structural interventions and management practices. Under intensive and semi-extensive production systems, the main structural interventions of adaptive significance include building orientation, insulation and reflectance, shading and ventilation, with or without the use of water (Kuczynski et al. 2011). Provision of shade may represent an effective adaptation measure under grazing or pastoral production systems as well. Management practices that may alleviate negative impacts of climate change on ruminants include hormonal treatments to improve fertility (Chandra et al. 2015), and nutritional and genetic approaches, discussed later in this review. Adoption of systems that increase water availability may be useful to limit the negative indirect effects of climate on ruminant production that may arise from reduced grassland or crop production. Furthermore, alleviation of the indirect effects of climate change on animal production may be also obtained by selecting plants with low water needs or high resistance to water shortages, and high resistance to emerging pathogens. Increasing surveillance and developing preventive tools (i.e. vaccines) for the control of emerging animal diseases would also be crucial to cope with climate change and its impact on farmed ruminants. Finally, adaptation options include developing and implementing meteorological warning systems and insurance systems, which are needed to reduce the impact of severe weather events and prevent loss of livestock (Lacetera et al. 2013).

The impact of hot climate on animal production and the predicted climate scenarios underline the importance and urgency of developing and transferring appropriate adaptation strategies to attenuate the negative effects of global warming on farm animals.

Therefore, adaptation options that are appropriate for specific livestock production systems (Nardone et al. 2010) and that can contribute to environmental sustainability, economic development and poverty alleviation should be identified and adopted.

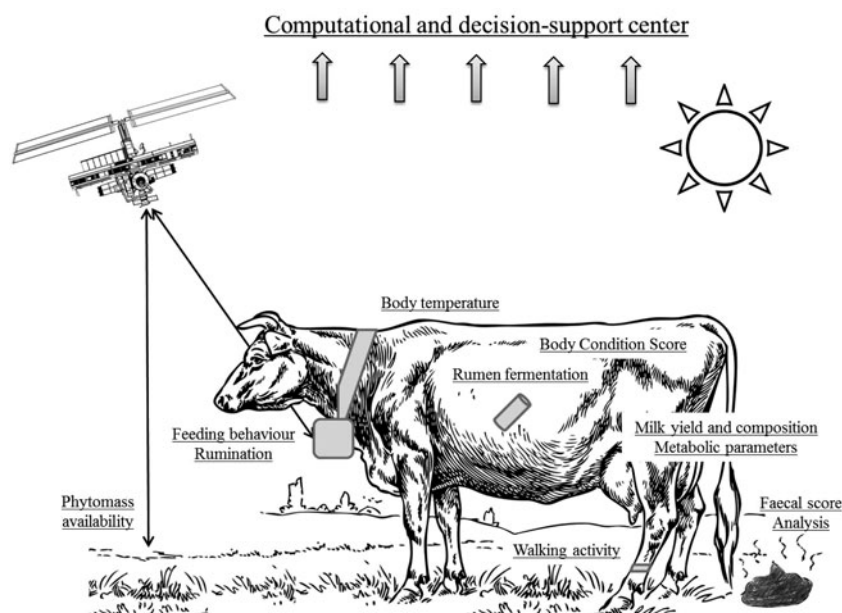
### Sustainable ruminant feeding

Through the use of innovative feed and feeding solutions, farmed ruminants can be raised in a sustainable way. In the last decade there have been many scientific and technological advances, such as precision livestock feeding, identification and characterisation of new feed resources, reutilisation of agricultural industry residues and biotechnologies for animal feed and animal feeding. There has also been a rediscovery and re-evaluation of agroforestry and silvopastoral systems, regarding food quality aspects and the maintenance of ecosystem services (e.g. carbon sequestration, landscape maintenance, and biodiversity enhancement).

The goals of precision feeding are to increase production efficiency and profitability, reduce environmental impact, improve product quality and safety, and improve animal health and well-being (Bewley 2010). During the last decades, many practices have been adopted in an attempt to achieve these objectives in livestock farms, especially in intensive systems. Although precision animal nutrition and diet formulation cannot be considered as a new concept in livestock management, in recent years new information technologies have been developed to help in monitoring accurately many components of livestock systems, such as animals (e.g. feed intake, diet selection, digestive activity, metabolic parameters and productive level), animal products, feeds and the environment.

An example of a precision feeding system for grazing dairy cows is illustrated in Figure 3. The first component is the real-time estimation of phytomass (grass) availability, by calculating vegetation indices (Normalized Difference Vegetation Index) from Landsat 8 image using ArcGis. A second component is the estimation of animal behaviour (grazing activity, walking activity, and rumination activity) by means of a master collar with global positioning system (GPS). Some animals are equipped with internal and external physiological sensors for detection and short-distance transmission of information like rumen status and body temperature. Animals can also be automatically controlled for body weight, body condition score, milk yield and composition, milk metabolic parameters, and faecal score. All this information is transmitted in real time to a computational and decision-support centre,





**Figure 3.** Schematic overview of a potential application of new information technologies, together with the state of knowledge on dairy cow nutrition and metabolism, for the management of precision feeding in semi-intensive grazing-based dairy cow farming systems.

to be processed and integrated for management decisions.

Recent advances on virtual fencing could further improve precise grazing, enabling exclusion or permitting grazing in certain areas, and could also be useful for conservation management of specific habitats (Umstatter et al. 2015).

GHG emissions could be reduced by adopting precision feeding techniques that decrease nitrogen and phosphorus excretion, by finding the correct match between the ingested and required elements (Arriaga et al. 2009). Technologies currently available allow continuous monitoring of rumen activity and biomarkers of milk quality, thus maximising organic matter and protein digestibility in the ration, increasing the use of lipids in the diet of ruminants, and optimising the use of natural substances of plant origin that prevent methane production in the rumen. In addition, a more sustainable manure management can be achieved by improving the precision of feeding techniques, especially by increasing organic matter and protein digestibility.

Diet adjustments to counteract the effects of climatic factors are also of great importance. For example, in hot environments, changes in feeding strategies, macronutrient and micronutrient composition of diets, and water management could increase intake or compensate for reduced feed consumption and nutrient utilisation (Renaudeau et al. 2012).

Due to the global intensification of food production, larger quantities of food by-/co-products (e.g.

cereal distillers, bran, sprouts, gluten meal, legume hulls, fruit molasses and peels) and wastes are available, causing economic and environmental impacts due to the loss of nutrients and pollution, respectively. The utilisation of food residues along the food chain is an interesting alternative to reduce environmental impact and to increase profitability, by transforming low-value, low-quality materials into high-quality food (Kasapidou et al. 2015).

The possibility of increasing ruminant productivity and sustainability is largely dependent on the possibility of increasing feed resources adapted to local environmental constraints, and finding resources not in competition with human nutrition. In many cases, it is necessary to assess not only the availability of alternative or complementary feeds but also their nutritional value, with the aim of defining their correct use in animal feeding. The value of crop residues, discarded fruits and vegetables, and other indigenous feed resources could be enhanced by silaging or by producing densified total mixed ration blocks or pellets (Makkar 2014).

In many parts of the world, insects are currently consumed by humans; consequently, global attention on insects as a protein source for animal feed and human food has recently increased (Bukkens 1997). Insects can guarantee a very high feed conversion ratio, can be reared on waste biomass, require a low amount of water, and cause low GHG emissions. At the same time, insect products have a high protein content, containing most of the essential amino acids,

together with fatty acids, minerals, and vitamins. For a future large-scale use of insects as feed, there is a need to develop trials that assess the potential risks for human health, related to the use of bio-wastes for insect growth. It would also be necessary to develop some common legislative acts and regulatory frameworks regarding this issue.

The use of algae both for aquaculture and animal feeding as a renewable source to substitute conventional feeds in livestock production systems has been widely investigated in recent decades, but interest in their use in ruminant nutrition is still increasing. In addition to their high nutritional value, micro- and macroalgae are gaining importance for the possibilities of extracting micro-feed ingredients (e.g. provitamins and minerals of high biological value) for the feed industry (Shields & Lupatsch 2012) and feeding animals with beneficial bioactive and nutraceutical compounds, which could be transferred into milk, meat and derived products for human nutrition.

Some biotechnological tools are available to improve animal nutrition, acting on feeds or directly on animals, or both. In the first case, the objective is to improve feed quality and nutritive value by enhancing the availability of nutrients (e.g. proteins, oils, starch, amino acids and vitamins), by means such as reducing rumen degradability for ruminants, reducing the losses into the environment due to partial digestion, and decreasing the content of undesirable components (Flachowsky et al. 2005). In the second case, the main goal is to improve animal health by means including the use of prebiotics or probiotics to control the functions of the gastro-intestinal system, the manipulation of rumen microbes, the addition of vaccines to feeds, and the use of metabolic modifiers such as recombinant bovine somatotropin.

Since 1996, when the first genetically modified (GM) crop was launched on the market, the cultivation and commercialisation of GM feeds have increased steadily. At a global level, it has been estimated that food-producing animals use from 70% to 90% of the GM crop biomass (Van Eenennaam & Young 2014), derived mainly from soybean, maize, cottonseed and rapeseed. In order to assess the nutritional quality of GM feeds, there has been the introduction of the concept of 'substantial equivalence', which evaluates the differences between a GM feed and the homologous/isogenic conventional one, in terms of chemical composition and undesirable contents. Many experiments have demonstrated that GM feeds are substantially equivalent to the conventional ones (Tufarelli et al. 2015), with no appreciable differences in ingestion, digestion, animal health and performance, and product quality.

In addition, in most trials no quantifiable traces of GM components were detected in animal products derived from the consumption of GM feeds (Alexander et al. 2007; Furgał-Dierzuk et al. 2014).

Further studies are needed for a better assessment of the effects of GM feeds on animals, animal products and humans, especially for what concerns the so-called 'second generation' GM crops, designed for the modification of specific output traits and resulting not 'substantially equivalent' to the isogenic non-GM varieties. There is also a need for an international standardisation of the regulatory framework for GM feed production, analysis and trade.

Finally, it is also important to take into account silvopastoralism and agroforestry, which are strictly inter-related, with the silvopastoral system being a type of agroforestry system. In silvopastoralism the main components are trees and pastures for livestock production, whereas in agroforestry trees are integrated with annual crops or livestock or both (Devendra & Ibrahim 2004). In some parts of the world, such as in Southeast Asia, there are large areas under permanent tree crops and forests. These areas offer many opportunities for an optimal integration with livestock systems, so that animal products can be obtained without interfering with other feed sources for animals, and different ecosystem services can be offered.

Deep rooting shrubs and trees are very important in many climatic areas of the world, because they are able to provide a more stable source of nutrients throughout the year, which can cover the nutrient requirements of livestock and possibly of wild animals. Some plant species, such as salt bush (*Atriplex* spp.), have received increasing interest due to their capacity to grow under high soil salinity and low rainfall conditions (Rowe & Corbett 1999).

### **Present and future challenges in animal breeding**

In addition to meeting the growing demand for animal products, animal breeding will have to address a number of future challenges to ensure the economic sustainability and social acceptance of ruminant farming. In particular, selection will have to redirect breeding objectives to improve animal health and welfare, increase tolerance to stressors, reduce livestock environmental impact and produce milk and meat having improved nutritional and functional properties.

Two strategies are possible to meet these objectives: (a) selection in cosmopolitan breeds, by integrating traditional and new breeding goals; and (b) exploitation of local breeds and their genes. Local



breeds are the most adapted to low-input production systems and to a range of environments, are able to produce food with unique properties, and can preserve cultural and social values. Local breeds also hold a reservoir of valuable genes that, once discovered, may be introgressed in cosmopolitan breeds by traditional or innovative methods.

The first approach has been partially implemented, as in many countries functional traits are steadily increasing in importance and being considered in selection schemes of commercial populations (Merks et al. 2012; Anafi 2016). However, selection for animal welfare and animal products for better human health is still in its infancy. Reaching these selection objectives is very challenging because genetic parameters for these traits and functional properties of animal products are not routinely measured. Consequently, their heritability and genetic determination remain poorly understood. Notwithstanding, genetics can be used indirectly to reduce GHG emissions, one of the major concerns for the sustainability of livestock, especially ruminants (Garnsworthy 2004; Gill et al. 2010; Martin et al. 2010; Cassandro et al. 2013). Two European projects, i.e. the cost Action (Methagene, [http://www.cost.eu/COST\\_Actions/fa/FA13022](http://www.cost.eu/COST_Actions/fa/FA13022)) and the FP7 Ruminomics (<http://www.ruminomics.eu/>) have generated knowledge in this direction. In fact, improved productivity can reduce GHG per kilogram of product by acting on traits such as feed efficiency and longevity, and by decreasing wastage at herd or flock level (e.g. premature losses, poor fertility and poor health). Moreover, differences among individual animals for traits such as plant selection during grazing, rumen digestion, retention rate, and host-microbe interactions may be heritable and therefore amenable to genetic selection for animals with less enteric CH<sub>4</sub> emission, on a daily or dry matter intake basis (Knapp et al. 2014). The mitigation of GHG emissions can be achieved by intensifying and specialising the production system (e.g. rearing more productive animals that use more refined feed). However, the intensification of animal production will lead to a loss of the advantages of extensive systems in terms of biodiversity preservation, management of renewable natural sources, conservation of cultural landscapes and enhancement of the socio-economic viability of many rural areas (Marino et al. 2016).

The second approach implies the exploitation of local breed biodiversity. Current livestock biodiversity is the result of a process that started approximately 10,000 years ago. Following domestication, herds were taken from the domestication site to colonise the world during agriculture expansion and thereafter,

human migrations, conquests and trade (Ajmone Marsan et al. 2010; Larson & Burger 2013). Livestock genomes and phenotypes were hence shaped by a combination of natural and anthropogenic selection, random drift, frequent crosses between populations and, depending on the species, intercrossing with wild relative species (Groenen et al. 2012). Conversely, the standard-breed concept of selection for a common morphology and production aptitude, and of reproductive isolation is very recent, as it was proposed only a few hundred years ago. In addition, breed is a Western world model that does not hold in many Southern world countries, where animal populations are not isolated or standardised. For example, Italy has a population of approximately 1,088,000 goats, of which 250,000 are subdivided into more than 40 different registered goat local breeds (Nicoloso et al. 2015), whereas Bangladesh has more than 20 million goats and a single native population, the Black Bengal goat, subdivided into Central, Western and Eastern populations (Afroz et al. 2010).

Overall, livestock species are subdivided into thousands of distinct local populations and breeds adapted to a range of agro-environmental conditions that can be very different from those of the domestication sites (e.g. Yacutian cattle originally domesticated in the Fertile Crescent), and to a variety of husbandry systems. In some cases, humans have increased the diversity taken from wild ancestors during domestication, by capturing useful mutations that would most probably have been lost by genetic drift or reduced fitness (e.g. myostatin mutations causing double muscling in beef cattle). This genetic pool of diversity is a treasure for humankind that can now be explored, valued and exploited with novel genomics and other -omic tools to understand the genetic basis of traits that are becoming fundamental for modern livestock sustainable breeding, such as adaptation to difficult environmental and feeding conditions, resilience to stress and pathogen challenges, high production efficiency and low environmental impact. Once genes relevant to these traits are discovered, they may be exploited through traditional breeding or using novel technologies that allow the quick dissemination of favourable genetic variants across breeds and populations.

The Senepol breed is a clear example of the importance and value of local breeds and of the ability of modern technologies to investigate and then exploit traits of worldwide relevance. This local cattle breed was developed on the Caribbean Island of St. Croix in the last century. Early investigations indicated the high heat tolerance of this breed, classified at the time as pure taurine, like Angus and Hereford (Hammond

et al. 1996). This trait is particularly interesting for future breeding to reduce the negative impacts of global warming on animal welfare and performance (Bernabucci et al. 2014). Later on, it was found that the Senepol heat tolerance was associated with the slick and short hair of this breed, when compared to the hair of other taurine breeds, and that a single gene mutation was responsible for this trait (Olson et al. 2003). The SLICK mutation was mapped on BTA20 using microsatellite markers (Mariasegaram et al. 2007) and its origin was investigated in detail using the Illumina BovineHD Beadchip containing 777,001 SNP markers (Huson et al. 2014). The slick hair haplotype also conferred heat tolerance to high producing Holstein cows introgressed with Senepol in a programme started at the University of Florida in 1990 (Dikmen et al. 2014). This trial confirmed that Holstein cows with slick hair had a superior thermoregulatory ability compared with non-slick animals, thus showing a lower milk yield depression during summer. The SLICK causal variant has been recently identified in a frameshift mutation of the Prolactin Receptor gene inducing a premature stop in the protein (Littlejohn et al. 2014). This mutation carried by the Senepol breed is therefore turning out to be extremely valuable for industrial animal breeding in many countries, including Italy. Its diffusion and introgression in different breeds with recurrent backcross designs would be possible but slow. Genomic tools may speed up this process and minimise the donor genome introgression, but a few backcross generations would still be needed to recover most of the recipient genome even in the most optimistic scenarios. New technologies have been recently developed to induce targeted and tailored mutations in resident genes. These gene-editing techniques are based on restriction enzymes to introduce a DNA double stranded break at a targeted location with the guide of homologous binding proteins, such as zinc finger nucleases (ZFNs; Kim et al. 1996) and transcription activator-like effector nucleases (TALENs; Miller et al. 2011), or RNA, e.g. clustered regularly interspaced short palindromic repeats and their associated protein 9 (CRISPR/Cas9) (Jinek et al. 2012). In all these cases, mutation occurs because of incidental deletion by endogenous nucleases which can be repaired by spontaneous non-homologous end-joining or homology-directed repair. This results in a small deletion or insertion at the target locus or a knock-in at the target locus if a donor sequence is provided. Frequently, homozygous mutants can be obtained. The CRISPR/Cas9 approach is particularly interesting because it does not require the engineering of complex proteins. In this case, cells or fertilised eggs are

injected with a guide RNA (gRNA) and the Cas9 protein, techniques that can be used in basic molecular biology and cell culture laboratories to produce targeted double strand breaks. Very recently, CRISPR/Cas9-based protocols which completely avoid *ex-vivo* manipulations have been proposed in the Genome-editing via Oviductal Nucleic Acids Delivery (GONAD) technology (Takahashi et al. 2015). Although all these methods have so far been applied to the production of animal models of human diseases, they have a great potential for application in agriculture for quickly transferring valuable alleles, discovered by genomic approaches, across populations. It is important to highlight that these are targeted mutation techniques that do not produce GM organisms, because neither exogenous genes nor antibiotic resistance markers are inserted in the host genome. We underline this in the hope that research using these technologies will not be blocked in Europe as happened with GM organisms, on the basis of a precaution that does not properly consider scientific evidence and could cost an enormous amount of resources.

In developing countries, cross-breeding of local and selected breeds could be a quick way to improve the production performance of ruminants while maintaining the characteristics of resistance to local environmental and sanitary hazards. However, due to the disjunction of characters after the first generation (F1), this method should be accompanied by a plan of selective cross-breeding, to stabilise the desired characters and obtain a new breed, thus requiring a long time. Moreover, as discussed in the review by Phocas et al. (2016), when cross-breeding is used to obtain an F1, a programme to improve the parental breeds is required. In organic dairy cattle production, cross-breeding has been used to increase robustness and longevity and to decrease the incidence of diseases such as mastitis (Atkinson 2014).

In summary, we are facing a challenging and stimulating time. Breeding goals in selection schemes of cosmopolitan breeds have progressively changed, and some functional traits now have a relevant weight in selection indexes. However, selection indexes have to be redefined to include new traits related to emerging and future needs, such as environmental sustainability, healthier foods and better animal welfare. To include these new traits in selection schemes, research is needed to identify the best selection criteria, implement efficient and low-cost collection of phenotypes, and investigate their genetic determination and genomic make up. We believe that cosmopolitan breeds will continue to be intensively reared but in a more sustainable way, and local breeds will have a relevant

role in producing food in different, less-intensive and still sustainable husbandry systems, acting as a reservoir of unique genes that are now being discovered, without the need to modify the environment in which they are adapted to live. Moreover, local breeds will preserve the cultural heritage and contribute to the maintenance of social sustainability in rural areas, being well suited to family farming. Finally, the revolutionary development of low-cost genomic analysis methods, integrated with the multi-omic data analysis (Suravajhala et al. 2016), has created tremendous opportunities for the genetic analysis of livestock populations when searching for valuable alleles able to improve animal production, health and welfare. Full exploitation of the knowledge resulting from this research through its application in breeding and conservation programmes is difficult, but it appears possible through newly developed breakthrough technologies. Under these circumstances, any loss of biodiversity before characterisation risks the loss of valuable opportunities for both science and agriculture.

### **Ruminant production in developing countries**

When looking for solutions that increase ruminant production or productivity in developing countries (DC), it is necessary to differentiate between emerging markets and poor countries. Emerging countries such as China, India, Brazil, Mexico, Russia, Indonesia and Turkey, and many other countries located in Europe (from the former Soviet Union), Africa (e.g. Egypt, Morocco, Nigeria, Kenya and South Africa), and America (e.g. Argentina), have embarked on the process of development. For most of these countries, the primary sector itself (crops and livestock) is still 'emergent', thus requiring the time needed for a full development, as it happened in the already developed countries. In this section, we will focus on poor countries, i.e. countries where the rural population is more than 70% of the total population and small family farms prevail.

Worldwide, farms smaller than 2 ha account for 84% of the total number of farms (570 million) but only 12% of the Earth's land surface used for agricultural purposes (FAO 2014). Particularly, small-scale farms likely account for only 25–30% of the cultivated surface. Prairies, grasslands and other uncultivable areas (approximately 3 billion ha) are of interest for animal systems only when large areas are available. Small-scale family farms, where subsistence farming is often practiced, devote most of their activities and arable land to produce human food. However, it must be

underlined that these small-scale farms supply a low amount of food worldwide, and may hardly meet the requirements of the farming family.

In small-scale family farms, the presence of livestock is scarce and the expertise and knowledge of animal husbandry is very limited and linked to traditions with little, if any, scientific basis. In these farms, livestock (mainly chickens and laying hens, waterfowls, sheep and goats, and, if not forbidden by religious norms, pigs) are normally reared around the huts and kept in shelters only for the night (Costa et al. 2013). In some areas of Asia and Africa, labour animals are also reared, mainly for field labour and transport (e.g. water buffaloes, cattle, horses and donkeys), but with limited possibilities to yield meat and milk.

Extensive or semi-extensive livestock farming systems do exist and are mainly focussed on sheep and goats in Asia, cattle in Africa and camelids in South America. These farming systems are practised by populations that traditionally are pastoralists, with the main goal of supplying food (meat and milk) and textile fibres, but also for other reasons, such as social role, 'currency', and religious value and significance. This is the reason why increasing the number of animals is often preferred to having a high production per animal, thus frequently causing overgrazing, with consequent soil degradation and desertification, favoured by the common property of land and little interest in preserving that land over time. Paradoxically, the improved hygienic-sanitary tools available today, which are able to reduce animal mortality, have worsened this situation.

Satisfying the need to integrate foods of plant origin with foods of animal origin in a balanced human diet can be difficult in small-scale family farms which cultivate crops, mainly cereals and tubers, rich in starch, but poor in protein, lipids and micro-nutrients. In these subsistence farming systems, where the level of production seldom exceeds family requirements, the following is observed: (a) small surpluses, which are mostly temporary, are immediately sold to get cash; (b) there is no actual way or awareness to transform such surpluses into animal products; and (c) there is a lack of awareness that staple foods (e.g. rice, maize, cassava, and potatoes) could be integrated with other foods that the farmer could produce at limited amounts, such as peanuts, legumes and vegetables in general, and also chicken and goats. As a consequence, the population groups at higher risk of malnutrition, particularly children, are those living in rural areas. In fact, people with other working activities and, therefore, cash can buy almost any food and acquire

complementary foods, which are sold by farmers to make some money.

In small-scale farming systems, animal production accounts for only 10–13% of the income (FAO 2009). This is mainly attributable to the following: (a) health problems (i.e. infectious and parasitic diseases) able to decrease the already low animal production and population; (b) the low genetic merit of the animals; (c) the insufficient availability of feeds, particularly during drought and cold periods, partially due to a lack of knowledge of techniques for drying forages; (d) lack of structures such as shelters and stalls, hatcheries, animal feed producers and slaughterhouses; and (e) an almost complete lack of expertise and knowledge of animal management, because local people are traditionally hunters, gatherers, fishermen or crop farmers and not animal farmers. If these are the actual difficulties, which are the tools necessary to achieve substantial improvement in this situation?

Animal farming has many goals, but the most important is to supply food in order to combat malnutrition. Over the last 20–30 years, meat, eggs and, recently, milk have been consumed in greater amounts in the DC (FAO 2009). This holds true only for some countries among those considered still developing, particularly China and Brazil, which together account for almost 2 billion people. The low consumption of food of animal origin is typical of the countries still affected by high levels of malnutrition, such as India, Kenya, Democratic Republic of Congo, Ghana and Nigeria, and, in general, the low and the lower-middle income countries (FAO 2009), accounting for about half of the population of the planet, where 30% of the children suffer from malnutrition (Crovetto 2015).

According to FAO (2009), livestock production follows economic development. Therefore, lack of development is correlated with few animals being farmed and this contributes to widespread malnutrition, especially among children. In fact, the nutritional status of children from 3 to 10 years old registered in economically poor countries reveals a serious situation, with a percentage of underweight children which reaches 60% and 42% in the Congo Democratic Republic and the tribal area of Northeastern India, respectively (Bertoni et al. 2015). Unfortunately, after being breastfed, poor-country children consume the same food as adults, and their diet is almost free of animal products (except for some fish, mainly in India). Therefore, in addition to food availability, a specific nutritional education is required to improve this situation.

Besides contributing to child mortality (Crovetto 2015), the fact that malnutrition due to a lack of food of animal origin in the diet also causes serious damage

to cognitive development (Black et al. 2013) is a major obstacle for economic development and this, in turn, is correlated with a low level of animal production. Hence, a new vicious circle having the animals at the centre occurs. Animal production is considered an ideal complement to agricultural production, increasing the human working capacity and integrating the nutritional properties of crops, which are mostly rich in carbohydrates.

Considering the very high number of people living in malnutrition conditions, it is frustrating to realise that this situation cannot be solved without economic development and in turn livestock production (again a vicious circle). As a matter of fact, FAO (2014) considers that the development of small-scale family farms requires the dissemination of innovation which, in turn, implies research, experimentation, technical assistance, roads, markets, schools, hospitals and so on. Unfortunately, the governments and local authorities of these countries are by no means able to comply with this request, simply because they are not able to start development. Moreover, even if it were possible to start development, the so-called 'last mile problem', i.e. the transfer of technologies to local populations, would remain. As the old proverb says: 'Give a man a fish, and you feed him for a day. Teach a man to fish, and you feed him for a lifetime'.

We are therefore convinced that the vicious cycles cited above must be broken, in order to overcome or alleviate the problems discussed here. This must happen, above all in the DC, starting from the small-scale farms and promoting an increase in animal husbandry activities and knowledge.

Sheep and goats are very common among small-holder farmers in DC. Normally they are raised in small numbers and are free to range and graze nearby the huts of the village, sometimes tethered to a pole or a tree. This situation is common in the rural areas of Africa and in India, particularly during the season of rice cultivation.

For cattle there is a great difference between the pastoralist and the agricultural areas. In pastoralist farming systems, cattle are raised mainly in the savannah, far from the tilled fields and, therefore, with low risk of causing damage and having quarrels. In this case, some improvements have been obtained through the control and reduction of external parasites, but a much better management should be applied in order to reduce the number of animals while improving animal performance (by means of genetics, health care, and feeding). In this way, livestock production could be maintained and over-grazing would be reduced. In agricultural areas where crop

production prevails, different situations occur in terms of livestock farming, varying from a total lack of knowledge (as in the Democratic Republic of Congo) to good knowledge but with a lack of improved and efficient techniques (as in many areas of India).

Several improvement efforts have been made in DC, but the results are not always positive and it is evident that introducing advanced technologies to be just copied and applied often results in failure. Our proposal is totally different and based on the involvement of local people, who must engage directly, despite having some external technical and financial support.

As an example, we summarise the agri-food chain Burundi Smallholders Livestock Network (BUSLIN) launched in Burundi by André Ndereyimana, a PhD student at University of Piacenza (Italy) involved in the project 'Production of appropriate food: sufficient, safe and sustainable'. The first phase of the project consisted of the following: (a) setting up a capillary network of rural and peri-urban family farms specialised in animal and horticulture productions; (b) offering microcredit proportional to production potentialities (e.g. land and other resources) and respecting the local cultural and religious habits; (c) ensuring no risk for all the partner families ready to give constant and responsible support to the project; (d) offering health check and sanitary support to producers, as well as monitoring the production and reproduction performance of the animals farmed; and (e) writing an agreement between BUSLIN and every family involved in the project to protect and make responsible all parties involved. The second phase of the project is based on the following: (a) in order to grow and become more effective, BUSLIN must involve as many families as possible as quickly as possible; (b) the economic gain for the BUSLIN families should be 50% of the income obtained from the sale of every animal reared; and (c) the family income (i.e. added economic value) derives from the sale of live animals to be slaughtered or used for reproduction, and from the sale of manure. The extension service is associated with the BUSLIN project and can give advice on genetics, feeding, health, commercial aspects and so on. However, based on our limited experience, we think that the dogmatic imposition of the most advanced and modern techniques is absolutely not effective, mainly due to social and ethical reasons, although theoretically capable of giving high yields in comparison with those obtained traditionally. The reason for this ineffectiveness is that these techniques are very hard to be adopted by local farmers, if left alone. Our opinion is that, pragmatically, it is advisable to start from what local people are able to do in terms of suggesting actions to be carried out

by themselves. Local people must be in charge of and responsible for their own development.

As far as ruminants are concerned, at present BUSLIN is effective only for goats, because the extremely limited land availability (about 0.5 ha/farm) is not compatible with cattle husbandry. With the exception of very few large farms, cattle are not farmed even in the Democratic Republic of Congo, despite the presence of huge underutilised areas (savannah). In this case, the gap is mainly due to a lack of tradition and of technical, managerial and financial resources. This is confirmed by the positive experience inspired by the bishop of Kabinda (east Kasai, Democratic Republic of Congo) that focussed on beef cattle of local breeds (Ankole) or of South African origin. This experience, characterised by high economic sustainability and wide margins of technical improvement, was possible due to three factors: (a) funding from western Caritas organisations, (b) availability of a wide area of savannah not far from Kabinda, thanks to a rental agreement with the local headman, and (c) presence of a Congolese priest who graduated in Agricultural Sciences at the University of Piacenza. Clearly, this solution would not be feasible for small farms, in which it would be advisable to operate following the criteria described for BUSLIN, i.e. forming associations which receive specific support, particularly at the beginning of the project/activity. Notwithstanding, it would be advisable to exploit the huge unexplored areas of the savannah in a country like Congo, which has a high demand for meat.

A completely different case-study is that of the North-Eastern area of India (Meghalaya state), where farms are small (1–2 ha) and cultivate mainly crops (rice, fruits and vegetables), but also have a tradition of livestock farming. Farms normally rear goats, small-size zebu, pigs and poultry, and often have a pair of oxen, one dairy cow, which produces milk in some periods of the year, and 1–2 calves or heifers. In this case, an increase in crop productivity could allow a reduction in the land used for crops at the benefit of forage for livestock. Only after achieving this basic resource (land availability), will it be possible to make an improvement in animal performance (e.g. milk yield) using cross-breeds (Jersey) and adequate feeding practices such as using blocks of molasses or urea to supply energy and protein. This would be particularly important in an area where most of the fodder is represented by rice straw and low-quality grass. Some on-going attempts aiming at the use of local raw materials (e.g. jaggery from sugarcane instead of molasses, and rice bran instead of wheat bran) seem promising from this point of view.



To summarise, the basic idea is that development actions must be compatible with the possibilities of local people and beneficiaries. However, a certain level of local organisation is required to implement the new practices needed for improvement. This can be done only by local people and entities (e.g. non-governmental organisations (NGO), religious communities and organisations), and the developed countries can contribute economically, technically and scientifically, by supplying local technicians and extension agents with teaching material and giving them advice on possible solutions compatible with local constraints and situations (Bertoni et al. 2015). All this cannot be done all of a sudden and implies collaborative relationships that can allow people of developed countries (e.g. university personnel and other experts) to really understand the nature of problems in the DC and the suitability of any proposal that the parties involved make for the benefit of DC.

## Conclusions










A long-term global strategy for the adoption of intensive and sustainable ruminant production systems is needed in order to supply a proper amount of high-quality food to the planet's growing population. Milk and meat are a complex food matrix that provides not only macronutrients such as protein, lipids or Ca, but also molecules, such as ACE-inhibiting peptides, fatty acids and vitamins, which have an extra-nutritional role. Meat and dairy products have some nutrients (e.g. saturated fatty acids and Fe-heme) that can pose a risk to human health if introduced in excessive amount. However, if we consider all the beneficial effects of meat, milk and dairy foods on human health (e.g. osteoporosis prevention, and neuro-psychic and cognitive development), it is clear that these products have a positive role in a balanced human diet. The sustainable intensification of ruminant production can be achieved by improving animal health, welfare and production, without harming the environment. This could be obtained by combining different approaches in ruminant farms, such as the use of precision feeding, optimisation of grazing systems, use of food residues and unconventional products as feed, adoption of productive, adapted and low-impact animal genotypes, use of animal waste for energy purposes, and proper management (e.g. presence of shelter, availability of drinking water, proper animal handling, adequate space and ventilation, disease prevention and treatment, appropriate feeding time and frequency and adjustment of diet amount and composition). In some cases, agroforestry and silvopastoral

systems are a good alternative to obtain animal products in a sustainable way and ecosystem services such as carbon sequestration, landscape maintenance, and biodiversity enhancement. We believe that cosmopolitan breeds will continue to be intensively reared but in a more sustainable way, and local breeds will have a relevant role in producing food in different, less-intensive but still sustainable husbandry systems, acting as a reservoir of unique genes that are now being discovered, without the need to modify the environment in which they are adapted to live. In developing countries animal farming can positively contribute to combat malnutrition, in spite of the small size of family farms. However, many improvements need to be made to these small-scale farms, and development projects carried out by NGOs and supported by universities can play an important role in this respect. In terms of prospects for producers and consumers, the sustainable intensification of ruminant production appears to be the only way to ensure farm profitability in developing countries, and ensure food security for an increasing part of the world population. From a food industry perspective, sustainable intensification must be programmed to ensure a constant supply of high-quality food, respecting the environment and improving animal health and welfare. This would be fundamental in order to answer ethical questions, which are becoming more and more pressing in the society of developed countries and which pose serious limits on exports of these products from the developing to the developed countries. Finally, the scientific research covered in this review provides the knowledge basis for the development and adoption of appropriate technologies to meet the future needs of humanity, in terms of amount and quality of food and ethical issues.

## Disclosure statement

The authors report no conflicts of interest. All authors are responsible for the content and writing of this article.

## ORCID

Giuseppe Pulina  <http://orcid.org/0000-0001-5579-0677>  
Ana Helena Dias Francesconi  <http://orcid.org/0000-0003-0378-4018>  
Bruno Stefanon  <http://orcid.org/0000-0002-7414-5830>  
Agostino Sevi  <http://orcid.org/0000-0001-6107-1724>  
Luigi Calamari  <http://orcid.org/0000-0002-1632-9762>  
Nicola Lacetera  <http://orcid.org/0000-0003-2088-2744>  
Vittorio Dell'Orto  <http://orcid.org/0000-0001-8401-3615>  
Fabio Pilla  <http://orcid.org/0000-0002-1781-994X>  
Paolo Ajmone Marsan  <http://orcid.org/0000-0003-3165-4579>



Marcello Mele  <http://orcid.org/0000-0002-7896-012X>  
 Filippo Rossi  <http://orcid.org/0000-0002-0313-4210>  
 Giuseppe Bertoni  <http://orcid.org/0000-0003-1247-0344>  
 Gianni Matteo Crovetto  <http://orcid.org/0000-0003-1156-2087>  
 Bruno Ronchi  <http://orcid.org/0000-0002-9405-2949>

## References

- Abeni F, Calamari L, Stefanini L. 2007. Metabolic conditions of lactating Friesian cows during the hot season in the Po valley. 1. Blood indicators of heat stress. *Int J Biometeorol.* 52:87–96.
- Adger WN, Agrawala S, Mirza MMQ, Conde C, O'Brien K, Pulhin J, Pulwarty R, Smit B, Takahashi K. 2007. Assessment of adaptation practices, options, constraints and capacity. In: Parry ML, Canziani OF, Palutikof JP, van der Linden PJ, Hanson CE, editors. *Climate change 2007: impacts, adaptation and vulnerability. Contribution of Working Group II to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change.* Cambridge (UK): Cambridge University Press; p. 717–743.
- Afroz MF, Faruque MO, Husain SS, Han JL, Paul B. 2010. Genetic variation and relations in different goat populations of Bangladesh Bang. *J Anim. Sci.* 39:1–8.
- Ajmone Marsan P, Garcia JF, Lenstra JA; Globaldiv Consortium. 2010. On the origin of cattle: how Aurochs became cattle and colonized the world. *Evol Anthropol.* 19:148–157.
- Alexander TW, Reuter T, Aulrich K, Sharma R, Okine EK, Dixon WT, McAllister TA. 2007. A review of the detection and fate of novel plant molecules derived from biotechnology in livestock production. *Anim Feed Sci Technol.* 133:31–62.
- Anafi. 2016. Schede Calcolo Indici [Internet]. Associazione Nazionale Allevatori Frisone Italiana; [cited 2016 Jan 17]. Available from: <http://www.anafi.it/>.
- Andrews FJ, Griffiths RD. 2002. Glutamine: essential for immune nutrition in the critically ill. *Br J Nutr.* 87(Suppl 1):S3–S8.
- Arnett TR. 2008. Extracellular pH regulates bone cell function. *J Nutr.* 138:415S–418S.
- Arriaga H, Pinto M, Calsamiglia S, Merino P. 2009. Nutritional and management strategies on nitrogen and phosphorus use efficiency of lactating dairy cattle on commercial farms: an environmental perspective. *J Dairy Sci.* 92:204–215.
- Ashmore JH, Lesko SM, Miller PE, Cross AJ, Muscat JE, Zhu J, Liao J, Harper G, Lazarus P, Hartman TJ. 2013. Association of dietary and supplemental iron and colorectal cancer in a population-based study. *Eur J Cancer Prev.* 22:506–511.
- Atkinson C. 2014. Organic animal husbandry in Europe – current and future challenges. In: Schmid O, Chander M, Escosteguy A, Frueh B, editors. *Organic animal husbandry across the world: towards an action plan for development of organic animal husbandry.* Schweiz, Switserland: IAHA-IFOAM Animal Husbandry Alliance; p. 25–27.
- Atzori AS, Canalis C, Francesconi AHD, Pulina G. 2015. A preliminary study on a new approach to estimate water resource allocation: the net water footprint applied to animal products. *Agric Agric Sci Procedia.* 8:50–57.
- Bacci ML, Nannoni E, Govoni N, Scorrano F, Zannoni A, Forni M, Martelli G, Sardi L. 2014. Hair cortisol determination in sows in two consecutive reproductive cycles. *Reprod Biol.* 14:218–223.
- Bansal V, Kim KH. 2015. Review of PAH contamination in food products and their health hazards. *Environ Int.* 84:26–38.
- Barzel US, Massey LK. 1998. Excess dietary protein can adversely affect bone. *J Nutr.* 128:1051–1053.
- Bastide NM, Pierre FHF, Corpet DE. 2011. Heme iron from meat and risk of colorectal cancer: a meta-analysis and a review of the mechanisms involved. *Cancer Prev Res (Phila).* 4:177–184.
- Battaglia DF, Bowen JM, Krasa HB, Thrun LA, Viguié C, Karsch FJ. 1997. Endotoxin inhibits the reproductive neuroendocrine axis while stimulating adrenal steroids: a simultaneous view from hypophyseal portal and peripheral blood. *Endocrinology.* 138:4273–4281.
- Bava L, Sandrucci A, Zucali M, Guerci M, Tamburini A. 2014. How can farming intensification affect the environmental impact of milk production? *J Dairy Sci.* 97:4579–4593.
- Beard JL, Unger EL, Bianco LE, Paul T, Rundle SE, Jones BC. 2007. Early postnatal iron repletion overcomes lasting effects of gestational iron deficiency in rats. *J Nutr.* 137:1176–1182.
- Bernabucci U, Biffani S, Buggiotti L, Vitali A, Lacetera N, Nardone A. 2014. The effects of heat stress in Italian Holstein dairy cattle. *J Dairy Sci.* 97:471–486.
- Bernabucci U, Basiricò L, Morera P, Dipasquale D, Vitali A, Piccioli Cappelli F, Calamari L. 2015. Effect of summer season on milk protein fractions in Holstein cows. *J Dairy Sci.* 98:1815–1827.
- Bernabucci U, Calamari L. 1998. Effects of heat stress on bovine milk yield and composition. *Zoot Nutr Anim.* 24:247–258.
- Bernabucci U, Lacetera N, Baumgard LH, Rhoads RP, Ronchi B, Nardone A. 2010. Metabolic and hormonal acclimation to heat stress in domesticated ruminants. *Animal.* 4:1167–1183.
- Bertoni G, Calamari L, Maianti MG, Battistotti B. 2005c. Milk for protected denomination of origin (PDO) cheeses: I. The main required features. In: Hocquette JF Gigli S, editors. *Indicators of milk and beef quality 2005.* Wageningen, the Netherlands: EAAP Publication No. 112, Wageningen Academic Publishers; p. 217–228.
- Bertoni G, Calamari L, Maianti MG. 2001a. Producing specific milks for speciality cheeses. *Proc Nutr Soc.* 60:231–246.
- Bertoni G, Calamari L, Maianti MG. 2003. Factors of welfare status in dairy cows and the relationship with milk features. In: Greppi GF, Enne G, editors. *38° Simp. Int. di Zootecnica 'Milk & Research'.* Milan, Italy: MG Editori; p. 63–94.
- Bertoni G, Maianti G, Cappa V. 1985. L'acidità del latte: nuove prospettive di ricerca [Milk acidity: new research perspectives]. *Atti del VI Congr. Naz. A.S.P.A.; 1985 May 28–June 30; Perugia, Italy.* p. 327–334.
- Bertoni G, Piccioli Cappelli F, Calamari L, Trevisi E. 1989. Digestive upsets of ruminants: possible role of endotoxins and/or histamine. *Proc. 7th Int. Conf. Production Disease in Farm Animals; 1989 July 27–29; Ithaca, NY, USA.* p. 370–373.

- Bertoni G, Tabaglio V, Ganimede C, Trevisan M, Pellizzoni M, Anaclerio M, Cappa F, Grossi P, Fiorani M, Ndereyimana A, et al. 2015. Food production and use. Security, safety and sustainability. Milan, Italy: EGEA S.P.A.
- Bertoni G, Trevisi E, Han XT. 2001b. Relationship between the liver activity in the puerperium and fertility in dairy cows. Proc. 52nd Annual Meeting of E.A.A.P.; 2001 August 26–29; Budapest, Hungary. p. 189.
- Bertoni G, Trevisi E, Gandolfi E, Lombardelli R. 2006. Factors of plasma cortisol changes in dairy cows. Proc. 79th Convegno Nazionale SIBS; 2006 September 28–30; Riccione, Italy. p. 19.
- Bertoni G, Trevisi E, Han X, Bionaz M. 2008. Effects of inflammatory conditions on liver activity in puerperium period and consequences for performance in dairy cows. *J Dairy Sci.* 91:3300–3310.
- Bertoni G, Trevisi E, Lombardelli R, Bionaz M. 2005a. Plasma cortisol variations in dairy cows after some usual or unusual manipulations. *Ital J Anim Sci.* 4; Suppl. 2:200–202.
- Bertoni G, Trevisi E, Lombardelli R, Calamari L. 2005b. The ACTH challenge test to evaluate the individual welfare condition. Proc. 56th Annual Meeting EAAP; 2005 June 5–8; Uppsala, Sweden. p. 176.
- Bewley J. 2010. Precision dairy farming: advanced analysis solutions for future profitability. Proc. 1st North Am. Conf. Precision Dairy Management; 2010 March 2–5; Toronto, Ontario, Canada. p. 1–8.
- Bionaz M, Trevisi E, Calamari L, Librandi F, Ferrari A, Bertoni G. 2007. Plasma paraoxonase, health, inflammatory conditions, and liver function in transition dairy cows. *J Dairy Sci.* 90:1740–1750.
- Black MM. 2008. Effects of vitamin B<sub>12</sub> and folate deficiency on brain development in children. *Food Nutr Bull.* 29(Suppl. 2):S126–S131.
- Black PH. 2002. Stress and the inflammatory response: a review of neurogenic inflammation. *Brain Behav Immun.* 16:622–653.
- Black RE. 2003. Zinc deficiency, infectious disease and mortality in the developing world. *J Nutr.* 133:1485S–1489S.
- Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis M, Ezzati M, Grantham-McGregor S, Katz J, Martorell R, et al. 2013. Maternal and child undernutrition and overweight in low-income and middle-income countries. *Lancet.* 382:427–451.
- Bohmanova J, Misztal I, Cole JB. 2007. Temperature-humidity indices as indicators of milk production losses due to heat stress. *J Dairy Sci.* 90:1947–1956.
- Bonjour J-P, Brandolini-Bunlon M, Boirie Y, Morel-Laporte F, Braesco V, Bertièrre M-C, Souberbielle J-C. 2008. Inhibition of bone turnover by milk intake in postmenopausal women. *Br J Nutr.* 100:866–874.
- Bonjour J-P. 2005. Dietary protein: an essential nutrient for bone health. *J Am Coll Nutr.* 24(Suppl. 6):S265–S365.
- Broom DM, Kirkden RD. 2004. Welfare, stress, behaviour and pathophysiology. In: Dunlop RH, Malbert CH, editors. *Veterinary pathophysiology.* Ames (IA): Blackwell; p. 337–369.
- Bruinsma J, editor. 2003. *World agriculture: towards 2015/2030: an FAO perspective.* London, UK: Earthscan; Rome, Italy: FAO.
- Bukkens SGF. 1997. The nutritional value of edible insects. *Ecol Food Nutr.* 36:287–319.
- Bushinsky DA. 2001. Acid-base imbalance and the skeleton. *Eur J Nutr.* 40:238–244.
- Calamari L, Abeni F, Calegari F, Stefanini L. 2007. Metabolic conditions of lactating Friesian cows during the hot season in the Po valley. 2. Blood minerals and acid-base chemistry. *Int J Biometeorol.* 52:97–107.
- Calamari L, Mariani P. 1998. Effects of the hot environment conditions on the main milk cheesemaking properties. *Zootec Nutr Anim.* 24:259–271.
- Calamari L, Soriani N, Panella G, Petrera F, Minuti A, Trevisi E. 2014. Rumination time around calving: An early signal to detect cows at greater risk of disease. *J Dairy Sci.* 97:3635–3647.
- Capper JL, Cady RA, Bauman DE. 2009. The environmental impact of dairy production: 1944 compared with 2007. *J Anim Sci.* 87:2160–2167.
- Capper JL. 2010. The carbon and water footprint of beef and dairy production. Proc. Symp. Bovine Sustainability, 26th World Buiatrics Congress, Santiago, Chile. (cd rom).
- Capper JL. 2011. Replacing rose-tinted spectacles with a high-powered microscope: the historical versus modern carbon footprint of animal agriculture. *Anim Front.* 1:26–32.
- Caroprese M, Albenzio M, Annicchiarico G, Sevi A. 2006. Changes occurring in immune responsiveness of single- and twin-bearing Comisana ewes during the transition period. *J Dairy Sci.* 89:562–568.
- Cassandro M, Mele M, Stefanon B. 2013. Genetic aspects of enteric methane emission in livestock ruminants. *Ital J Anim Sci.* 12:450–458.
- Castaneda C, Chamely JM, Evans WJ, Crim MC. 1995. Elderly women accommodate to a low-protein diet with losses of body cell mass, muscle function, and immune response. *Am J Clin Nutr.* 62:30–39.
- Chan DSM, Lau R, Aune D, Vieira R, Greenwood DC, Kampman E, Norat T. 2011. Red and processed meat and colorectal cancer incidence: meta-analysis of prospective studies. *PLoS One.* 6:e20456. doi: 10.1371/journal.pone.0020456.
- Chandra V, Sejian V, Sharma GT. 2015. Strategies to improve livestock reproduction under the changing climate scenario. In: Sejian V, Gaughan J, Baumgard L, Prasad C, editors. *Climate change impact on livestock: adaptation and mitigation.* New Delhi (India): Springer; p. 425–439.
- Christopherson RJ. 1985. The thermal environment and the ruminant digestive system. In: Yousef MK, editor. *Stress physiology in livestock. Basic principles, Vol I.* Boca Raton, Florida (USA): Crc Press; p. 163–177.
- Cicero AFG, Gerocarni B, Laghi L, Borghi C. 2011. Blood pressure lowering effect of lactotripeptides assumed as functional foods: a meta-analysis of current available clinical trials. *J Hum Hypertens.* 25:425–436.
- Coëffier M, Déchelotte P. 2005. The role of glutamine in intensive care unit patients: mechanisms of action and clinical outcome. *Nutr Rev.* 63:65–69.
- Collier RJ, Beede DK. 1985. Thermal stress as a factor associated with nutrient requirements and interrelationships. In: McDowell LR, editor. *Nutrition of grazing ruminants in warm climates.* New York (USA): Academic Press; p. 59–71.

- Conference Report. 1993. Consensus development conference: diagnosis, prophylaxis and treatment of osteoporosis. *Am J Med.* 94:646–650.
- Contreras MM, Carrón R, Montero MJ, Ramos M, Recio I. 2009. Novel casein-derived peptides with antihypertensive activity. *Int Dairy J.* 19:566–573.
- Cook CJ, Mellor DJ, Harris PJ, Ingram JR, Matthews LR. 2000. Hands-on and hands-off measurement of stress. In: Moberg GP, Mench JA, editors. *The biology of animal stress.* Wallingford (UK): CABI Publishing; p. 23–42.
- Costa S, Crovetto GM, Bocchi S. 2013. Family farming in Africa. Overview of good agricultural practices in Sub Saharan Africa [Internet]. Milan (Italy): Ed. Istituto Oikos. Available from: [http://www.istituto-oikos.org/files/download/2014/HANDBOOK\\_WEB\\_final.pdf](http://www.istituto-oikos.org/files/download/2014/HANDBOOK_WEB_final.pdf).
- Council for Agricultural Science and Technology. 2013. Animal feed vs. human food: challenges and opportunities in sustaining animal agriculture toward 2050. Issue paper 53. Ames, Iowa (USA): CAST.
- Crovetto GM. 2015. Poultry and pig production systems in developing countries. In: Bertoni G., editor. *World food production. Facing growing needs and limited resources.* Milan (Italia): Vita e Pensiero; p. 437–456.
- Dalla Riva A, Burek J, Kim D, Thoma G, Cassandro M, de Marchi M. 2015. The environmental impact of cow milk in the northeast of Italy. *Poljoprivreda.* 21(Suppl. 1):105–108.
- Dalla Riva A, Kristensen T, De Marchi M, Kargo M, Jensen J, Cassandro M. 2014. Carbon footprint from dairy farming system: comparison between Holstein and Jersey cattle in Italian circumstances. *Acta Agr Kaposváriensis.* 18(Suppl. 1):75–80.
- Dalle Zotte A, Szendrő Z. 2011. The role of rabbit meat as functional food. *Meat Sci.* 88:319–331.
- Daly JM, Reynolds J, Sigal RK, Shou J, Liberman MD. 1990. Effect of dietary protein and amino acids on immune function. *Crit Care Med.* 18(Suppl. 2):S86–S93.
- de Boer IJM. 2003. Environmental impact assessment of conventional and organic milk production. *Livest Prod Sci.* 80:69–77.
- de la Casa AC, Ravelo AC. 2003. Assessing temperature and humidity conditions for dairy cattle in Córdoba, Argentina. *Int J Biometeorol.* 48:6–9.
- De Smet S, Michels N, Polfliet C, D’Haese S, Roggen I, De Henauw S, Sioen I. 2015. The influence of dairy consumption and physical activity on ultrasound bone measurements in Flemish children. *J Bone Miner Metab.* 33:192–200.
- Devendra C, Ibrahim M. 2004. Silvopastoral systems as a strategy for diversification and productivity enhancement from livestock in the tropics. In: Mannelje L, Ramirez L, Ibrahim M, Sandoval C, Ojeda N, Ku J, editors. *The importance of silvopastoral systems in rural livelihoods to provide ecosystem services.* Proc. 2nd Int. Symp. of Silvopastoral Systems; Autonomous University of Yucatan, 2004 February 9–11; Merida, Yucatan, Mexico. p. 10–24.
- Dikmen S, Khan FA, Huson HJ, Sonstegard TS, Moss JI, Dahl GE, Hansen PJ. 2014. The *SLICK* hair locus derived from Senepol cattle confers thermotolerance to intensively managed lactating Holstein cows. *J Dairy Sci.* 97:5508–5520.
- Dobson H, Smith RF. 2000. What is stress, and how does it affect reproduction? *Anim Reprod Sci.* 60–61:743–752.
- Donida BM, Mrak E, Gravaghi C, Villa I, Cosentino S, Zacchi E, Perego S, Rubinacci A, Fiorilli A, Tettamanti G, et al. 2009. Casein phosphopeptides promote calcium uptake and modulate the differentiation pathway in human primary osteoblast-like cells. *Peptides.* 30:2233–2241.
- Drastig K, Prochnow A, Kraatz S, Klaus H, Plöchl M. 2010. Water footprint analysis for the assessment of milk production in Brandenburg (Germany). *Adv Geosci.* 27:65–70.
- [EC] European Commission: Climate action. c1995–2016. Adaptation to climate change [Internet]. European Union; [cited 2016 March 21]. Available from: [http://ec.europa.eu/clima/policies/adaptation/index\\_en.htm](http://ec.europa.eu/clima/policies/adaptation/index_en.htm).
- EFSA. 2009a. Scientific Opinion on the substantiation of health claims related to calcium and maintenance of bones and teeth (ID 224, 230, 231, 354, 3099), muscle function and neurotransmission (ID 226, 227, 230, 235), blood coagulation (ID 230, 236), energy-yielding metabolism (ID 234), function of digestive enzymes (ID 355), and maintenance of normal blood pressure (ID 225, 385, 1419) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA J.* 7:1210. doi: 10.2903/j.efsa.2009.1210.
- EFSA. 2009b. Scientific opinion on the overall effects of farming systems on dairy cow welfare and disease. *EFSA J.* 1143:1–38. doi: 10.2903/j.efsa.2009.1143.
- EFSA. 2012. Scientific opinion on the welfare of cattle kept for beef production and the welfare in intensive calf farming systems. *EFSA J.* 10:2669. doi: 10.2903/j.efsa.2012.2669.
- Eisler MC, Lee MRF, Tarlton JF, Martin GB, Beddington J, Dungait JAJ, Greathead H, Liu J, Mathew S, Miller H, et al. 2014. Agriculture: Steps to sustainable livestock. *Nature.* 507:32–34.
- Elsasser TH, Klasing KC, Filipov N, Thompson F. 2000. The metabolic consequences of stress: targets for stress and priorities of nutrient use. In: Moberg GP, Mench JA, editors. *The biology of animal stress. Basic principles and implications for animal welfare.* New York (USA): CABI Publishing; p. 77–110.
- Enherst K, Moberg GP. 1991. Disruption of estrous behavior in ewes by dexamethasone or management-related stress. *J Anim Sci.* 69:2988–2994.
- Esposito R, Coderoni S. 2011. L’evoluzione delle emissioni agricole di gas serra nelle regioni italiane [Evolution of agricultural greenhouse gases emissions in Italian regions] [Internet]. *Agriregionieuropa* 7: 71. Available from: <http://agriregionieuropa.univpm.it/it/content/article/31/27/levoluzione-delle-emissioni-agricole-di-gas-serra-nelle-regioni-italiane>.
- Evans WJ. 2004. Protein nutrition, exercise and aging. *J Am Coll Nutr.* 23:601S–609S.
- FAO. 2009. *The state of food and agriculture: livestock in the balance.* Rome, Italy: Food and Agriculture Organization of the United Nations.
- FAO. 2010. *Greenhouse gas emissions from the Dairy sector: a life cycle assessment.* Rome, Italy: FAO.
- FAO. 2011. *Mapping supply and demand for animal-source foods to 2030.* In Robinson TS, Pozzi F, editors. *Animal Production and Health Working Paper. N. 2,* Rome, Italy: FAO.
- FAO. 2013. *World food and agriculture. FAO Statistical Yearbook 2013.* Rome, Italy: FAO.

- FAO. 2014. The state of food and agriculture: innovation in family farming. Rome, Italy: Food and Agriculture Organization of the United Nations.
- FAO. 2015. The state of food insecurity in the world - Meeting the 2015 international hunger targets: taking stock of uneven progress. Rome (Italy): FAO.
- Fell LR, Shutt DA, Bentley CJ. 1985. Development of a salivary cortisol method for detecting changes in plasma 'free' cortisol arising from acute stress in sheep. *Aust Vet J.* 62:403-406.
- Feskanich D, Bischoff-Ferrari HA, Frazier AL, Willett WC. 2014. Milk consumption during teenage years and risk of hip fractures in older adults. *JAMA Pediatr.* 168:54-60.
- FitzGerald RJ. 1998. Potential uses of caseinophosphopeptides. *Int Dairy J.* 8:451-457.
- Flachowsky G, Chesson A, Aulrich K. 2005. Animal nutrition with feeds from genetically modified plants. *Arch Anim Nutr.* 59:1-40.
- Flachowsky G, Hachenberg S. 2009. CO<sub>2</sub>-footprints for food of animal origin - present stage and open questions. *J Verbr Lebensm.* 4:190-198.
- Fox PF. 1989. The milk protein system. In: Fox PF, editor. Development in dairy chemistry-4, functional milk proteins. London, UK: Elsevier Applied Science; p. 1-53.
- Fukasawa M, Tsukada H, Kosako T, Yamada A. 2008. Effect of lactation stage, season and parity on milk cortisol concentration in Holstein cows. *Livest Sci.* 113:280-284.
- Fung TT, Schulze M, Manson JE, Willett WC, Hu FB. 2004. Dietary patterns, meat intake, and the risk of type 2 diabetes in women. *Arch Intern Med.* 164:2235-2240.
- Furgal-Dierzuk I, Strzetelski J, Kwiatek K, Twardowska M, Mazur M, Sieradzki Z, Kozaczyński W, Reichert M. 2014. The effect of genetically modified maize (MON 810) and soyabean meal (roundup ready) on rearing performance and transfer of transgenic DNA to calf tissues. *J Anim Feed Sci.* 23:13-22.
- Garewal G, Narang A, Das KC. 1988. Infantile tremor syndrome: a vitamin B<sub>12</sub> deficiency syndrome in infants. *J Trop Pediatr.* 34:174-178.
- Garnsworthy PC. 2004. The environmental impact of fertility in dairy cows: a modelling approach to predict methane and ammonia emissions. *Anim Feed Sci Tech.* 112:211-223.
- Gaspardo B, Sgorlon S, Fanzago M, Stefanon B. 2015. La sostenibilità ambientale: emissioni di CO<sub>2</sub> dagli allevamenti del Friuli Venezia Giulia e della Slovenia [Environmental sustainability: CO<sub>2</sub> emissions from dairy farms in Friuli Venezia Giulia and Slovenia]. In: Gaspardo B, Guiatti D, editors. Bellimpresa, soluzioni per la sostenibilità dell'allevamento [Bellimpresa, solutions for sustainability of livestock production system] [Internet]. eBook. Udine, Italy: Dipartimento di Scienze Agrarie e Ambientali; p. 78-103. Available from: [http://bellimpresa.uniud.it/fileadmin/user\\_upload/Manuale\\_Bellimpresa.pdf](http://bellimpresa.uniud.it/fileadmin/user_upload/Manuale_Bellimpresa.pdf).
- Gaughan JB, Lacetera N, Valtorta SE, Khalifa HH, Hahn GL, Mader TL. 2009. Response of domestic animals to climate challenges. In: Ebi KL, Burton I, McGregor GR, editors. Biometeorology for adaptation to climate variability and change. Heidelberg, Germany: Springer-Verlag; p. 131-170.
- Gerber HW, Jost R. 1996. Casein phosphopeptides: their effect on calcification of *in vitro* cultured embryonic rat bone. *Calcif Tissue Int.* 38:350-357.
- Gill M, Smith P, Wilkinson JM. 2010. Mitigating climate change: the role of domestic livestock. *Animal.* 4:323-333.
- Global Footprint Network. 2016. World footprint: do we fit on the planet? [Internet]. [updated 2016 Mar 8; cited 2016 Mar 25]. Available from: [http://www.footprintnetwork.org/en/index.php/GFN/page/world\\_footprint/](http://www.footprintnetwork.org/en/index.php/GFN/page/world_footprint/).
- Godfray HCJ, Beddington JR, Crute IR, Haddad L, Lawrence D, Muir JF, Pretty J, Robinson S, Thomas SM, Toulmin C. 2010. Food security: the challenge of feeding 9 billion people. *Science.* 327:812-818.
- Goldberg AM. 2016. Farm animal welfare and human health. *Curr Environ Health Rep.* 3:313-321.
- Gregory NG. 2004. Sickness and disease. In: Gregory NG, editor. Physiology and behaviour of animal suffering. Oxford (UK): Blackwell. p.183-192.
- Groenen MA, Archibald AL, Uenishi H, Tuggle CK, Takeuchi Y, Rothschild MF, Rogel-Gaillard C, Park C, Milan D, Megens HJ, et al. 2012. Analyses of pig genomes provide insight into porcine demography and evolution. *Nature.* 491:393-398.
- Guéguen L, Pointillart A. 2000. The bioavailability of dietary calcium. *J Am Coll Nutr.* 19(Suppl. 2):119S-136S.
- Hammond AC, Olson TA, Chase CC Jr, Bowers EJ, Randel RD, Murphy CN, Vogt DW, Tewolde A. 1996. Heat tolerance in two tropically adapted *Bos taurus* breeds, Senepol and Romosinuano, compared with Brahman, Angus, and Hereford cattle in Florida. *J Anim Sci.* 74:295-303.
- Hasegawa N, Nishiwaki A, Sugawara K, Ito I. 1997. The effects of social exchange between two groups of lactating primiparous heifers on milk production, dominance order, behavior and adrenocortical response. *Appl Anim Behav Sci.* 51:15-27.
- Hawker GA, Forsmo S, Cadarette SM, Schei B, Jaglal SB, Forsén L, Langhammer A. 2002. Correlates of forearm bone mineral density in young Norwegian women: the Nord-Trøndelag health study. *Am J Epidemiol.* 156:418-427.
- Heaney RP. 1996. Calcium. In: Bilezikian JP, Raisz LG, Rodan GA, editors. Principles of bone biology. New York (USA): Academic Press; p. 1007-1018.
- Heaney RP. 2000. Calcium, dairy products and osteoporosis. *J Am Coll Nutr.* 19(Suppl. 2):83S-99S.
- Heaney RP. 2009. Dairy and bone health. *J Am Coll Nutr.* 28:82S-90S.
- Herrero M, Wirsenius S, Henderson B, Rigolot C, Thornton P, Havlík P, de Boer I, Gerber PJ. 2015. Livestock and environment: what have we learned in the past decade? *Annu Rev Environ Resour.* 40:177-202.
- Higginbottom MC, Sweetman L, Nyhan WL. 1978. A syndrome of methylmalonic aciduria, homocystinuria, megaloblastic anemia and neurologic abnormalities in a vitamin B<sub>12</sub>-deficient breast-fed infant of a strict vegetarian. *N Engl J Med.* 299:317-323.
- Ho-Pham LT, Nguyen ND, Nguyen TV. 2009. Effect of vegetarian diets on bone mineral density: a Bayesian meta-analysis. *Am J Clin Nutr.* 90:943-950.
- Hoekstra AY, Chapagain AK, Aldaya MM, Mekonnen MM. 2009. Water footprint manual: state of the art 2009. Water Footprint Network, Enschede, The Netherlands.
- Hodgson JM, Ward NC, Burke V, Beilin LJ, Puddey IB. 2007. Increased lean red meat intake does not elevate markers



- of oxidative stress and inflammation in humans. *J Nutr.* 137:363–367.
- Huson HJ, Kim ES, Godfrey RW, Olson TA, McClure MC, Chase CC, Rizzi R, O'Brien AM, Van Tassell CP, Garcia JF, et al. 2014. Genome-wide association study and ancestral origins of the slick-hair coat in tropically adapted cattle. *Front Genet.* 5:101. doi: 10.3389/fgene.2014.00101.
- Huth PJ, DiRienzo DB, Miller GD. 2006. Major scientific advances with dairy foods in nutrition and health. *J Dairy Sci.* 89:1207–1221.
- IARC. 2015. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol.* 16:1599–1600.
- IPCC. 2013. Climate change 2013: The physical science basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Stocker TF, Qin D, Plattner G-K, Tignor M, Allen SK, Boschung J, Nauels A, Xia Y, Bex V, Midgley PM, editors. Cambridge, UK and New York, NY, USA: Cambridge University Press.
- IPCC. 2014. Climate change 2014: Impacts, adaptation, and vulnerability. Part A: Global and sectoral aspects. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Field CB, Barros VR, Dokken DJ, Mach KJ, Mastrandrea MD, Bilir TE, Chatterjee M, Ebi KL, Estrada YO, Genova RC, Girma B, Kissel ES, Levy AN, MacCracken S, Mastrandrea PR, White LL, editors. Cambridge, UK and New York, NY, USA: Cambridge University Press.
- Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna JA, Charpentier E. 2012. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science.* 337:816–821.
- Johnson HD. 1987. Bioclimate effects on growth, reproduction and milk production. In: Johnson HD, editor. *Bioclimatology and adaptation of livestock.* Amsterdam: Elsevier Science Publisher; p. 35–57.
- Kalkwarf HJ, Khoury JC, Lanphear BP. 2003. Milk intake during childhood and adolescence, adult bone density, and osteoporotic fractures in US women. *Am J Clin Nutr.* 77:257–265.
- Kaplan RJ, Greenwood CE, Winocur G, Wolever TMS. 2001. Dietary protein, carbohydrate, and fat enhance memory performance in the healthy elderly. *Am J Clin Nutr.* 74:687–693.
- Kasapidou E, Sossioui E, Mitlianga P. 2015. Fruit and vegetable co-products as functional feed ingredients in farm animal nutrition for improved product quality. *Agriculture.* 5:1020–1034.
- Kebreab E, Clark K, Wagner-Riddle C, France J. 2006. Methane and nitrous oxide emissions from Canadian animal agriculture: a review. *Can J Anim Sci.* 86:135–158.
- Kemeny ME. 2009. Psychobiological responses to social threat: Evolution of a psychological model in psychoneuroimmunology. *Brain Behav Immun.* 23:1–9.
- Kim YG, Cha J, Chandrasegaran S. 1996. Hybrid restriction enzymes: zinc finger fusions to *Fok I* cleavage domain. *Proc Natl Acad Sci USA.* 93:1156–1160.
- Knapp JR, Laur GL, Vadas PA, Weiss WP, Tricarico JM. 2014. Invited review: Enteric methane in dairy cattle production: quantifying the opportunities and impact of reducing emissions. *J Dairy Sci.* 97:3231–3261.
- Kuczynski T, Blanes-Vidal V, Li B, Gates RS, de Alencar Nääs I, Moura DJ, Berckmans D, Banhazi TM. 2011. Impact of global climate change on the health, welfare and productivity of intensively housed livestock. *Int J Agric Biol Eng.* 4:1–22.
- Lacetera N, Segnalini M, Bernabucci U, Ronchi B, Vitali A, Tran A, Guis H, Caminade C, Calvete C, Morse A, et al. 2013. Climate induced effects on livestock population and productivity in the Mediterranean area. In: Navarra A, Tubiana L, editors. *Regional assessment of climate change in the Mediterranean: Volume 2: Agriculture, forests and ecosystem services and people.* Advances in Global Change Research 51. Dordrecht, Netherlands: Springer Science + Business Media; p. 135–156.
- Lambin EF. 2012. Global land availability: Malthus versus Riccardo. *Global Food Secur.* 1:83–87.
- Larson G, Burger J. 2013. A population genetics view of animal domestication. *Trends Genet.* 29:197–205.
- Lindsay R, Nieves J. 1994. Milk and bones. *BMJ.* 308:930–931.
- Littlejohn MD, Henty KM, Tiplady K, Johnson T, Harland C, Lopdell T, Sherlock RG, Li W, Lukefahr SD, Shanks BC, et al. 2014. Functionally reciprocal mutations of the prolactin signalling pathway define hairy and slick cattle. *Nat Commun.* 5:5861. doi: 10.1038/ncomms6861.
- Lombardi-Boccia G, Martínez-Domínguez B, Aguzzi A, Rincón-León F. 2002. Optimization of heme iron analysis in raw and cooked red meat. *Food Chem.* 78:505–510.
- Lopez-Garcia E, Schulze MB, Fung TT, Meigs JB, Rifai N, Manson JE, Hu FB. 2004. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr.* 80:1029–1035.
- Lötters FJB, Lenoir-Wijnkoop I, Fardellone P, Rizzoli R, Rocher E, Poley MJ. 2013. Dairy foods and osteoporosis: an example of assessing the health-economic impact of food products. *Osteoporos Int.* 24:139–150.
- Lovett DK, Shalloo L, Dillon P, O'Mara FP. 2006. A systems approach to quantify greenhouse gas fluxes from pastoral dairy production as affected by management regime. *Agr Syst.* 88:156–179.
- Lozoff B, Georgieff MK. 2006. Iron deficiency and brain development. *Semin Pediatr Neurol.* 13:158–165.
- MacDonald HM, Downie FH, Moore F, New SA, Grubb DA, Reid DM. 2001. Higher intakes of fruit and vegetables are associated with higher bone mass in perimenopausal Scottish women. *Proc Nutr Soc.* 60:202A.
- Makkar HPS. 2014. Sustainable increase in livestock productivity in developing countries through efficient utilisation of feed resources. *Cuban J Agr Sci.* 48:55–58.
- Malacarne M, Fieni S, Tosi F, Franceschi P, Formaggioni P, Summer A. 2005. Seasonal variations of the rennet-coagulation properties of herd milks in Parmigiano-Reggiano cheese manufacture: comparison between Italian Friesian and Italian Brown cattle breeds. *Ital J Anim Sci.* 4(Suppl. 2):242–244.
- Mancini R. 2013. Meat color. In: Kert CR, editor. *The science of meat quality.* Oxford (UK): Wiley-Blackwell; p. 177–199.
- Mariasegaram M, Chase CC Jr, Chaparro JX, Olson TA, Brenneman RA, Niedz RP. 2007. The slick hair coat locus maps to chromosome 20 in Senepol-derived cattle. *Anim Genet.* 38:54–59.
- Marino R, Atzori AS, D'Andrea M, Iovane G, Trabalza-Marinucci M, Rinaldi L. 2016. Climate change: production

- performance, health issues, greenhouse gas emissions and mitigation strategies in sheep and goat farming. *Small Rumin Res.* 135:50–59.
- Martelli G, Sardi L, Stancampiano L, Govoni N, Zannoni A, Nannoni E, Forni M, Bacci ML. 2014. A study on some welfare-related parameters of hDAF transgenic pigs when compared with their conventional close relatives. *Animal.* 8:810–816.
- Martin C, Morgavi DP, Doreau M. 2010. Methane mitigation in ruminants: from microbe to the farm scale. *Animal.* 4:351–365.
- Matlock M, Thoma G, Cummings E, Cothren J, Leh M, Wilson J. 2013. Geospatial analysis of potential water use, water stress, and eutrophication impacts from US dairy production. *Int Dairy J.* 31:S78–S90.
- Mekonnen MM, Hoekstra AY. 2010. The green, blue and grey water footprint of farm animals and animal products. Value of Water Research Report Series No. 48. Delft, The Netherlands: UNESCO-IHE.
- Mele M, Nudda A, Pauselli M, Roscini V, Casarosa L, Secchiari P, Pulina G. 2016. Consumo di carne e salute umana [Meat consumption and human health]. In: Mele M, Pulina G, editors. *Alimenti di origine animale e salute [Foods of animal origin and health]*. Milan, Italy: Franco Angeli; p. 81–182.
- Melton LJ, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, Riggs BL. 2000. Epidemiology of sarcopenia. *J Am Geriatr Soc.* 48:625–630.
- Merks JWM, Mathur PK, Knol EF. 2012. New phenotypes for new breeding goals in pigs. *Animal.* 6:535–543.
- Michaëlsson K, Wolk A, Langenskiöld S, Basu S, Warensjö Lemming E, Melhus H, Byberg L. 2014. Milk intake and risk of mortality and fractures in women and men: cohort studies. *BMJ.* 349:g6015. doi: 10.1136/bmj.g6015.
- Miller JC, Tan S, Qiao G, Barlow KA, Wang J, Xia DF, Meng X, Paschon DE, Leung E, Hinkley SJ, et al. 2011. A TALE nuclease architecture for efficient genome editing. *Nat Biotechnol.* 29:143–148.
- Montville JB, Ahuja JKC, Martin CL, Heendeniya KY, Omolewa-Tomobi G, Steinfeldt LC, Anand J, Adler ME, LaComb RP, Moshfegh AJ. 2013. USDA Food and Nutrient Database for Dietary Studies (FNDDS), 5.0. *Procedia Food Sci.* 2:99–112.
- Morignat E, Perrin J-B, Gay E, Vinard J-L, Calavas D, Hénaux V. 2014. Assessment of the impact of the 2003 and 2006 heat waves on cattle mortality in France. *PLoS One.* 9:e93176. doi: 10.1371/journal.pone.0093176.
- Morrow CJ, Kolver ES, Verkerk GA, Matthews LR. 2002. Fecal glucocorticoid metabolites as a measure of adrenal activity in dairy cattle. *Gen Comp Endocrinol.* 126:229–241.
- Möstl E, Palme R. 2002. Hormones as indicators of stress. *Domest Anim Endocrinol.* 23:67–74.
- Murray TM. 1996. Prevention and management of osteoporosis: consensus statements from the Scientific Advisory Board of the Osteoporosis Society of Canada. 4. Calcium nutrition and osteoporosis. *Can Med Assoc J.* 155:935–939.
- Nardone A, Ronchi B, Lacetera N, Ranieri MS, Bernabucci U. 2010. Effects of climate changes on animal production and sustainability of livestock systems. *Livest Sci.* 130:57–69.
- Negrão JA, Porcionato MA, de Passillé AM, Rushen J. 2004. Cortisol in saliva and plasma of cattle after ACTH administration and milking. *J Dairy Sci.* 87:1713–1718.
- Neumann CG, Bwibo NO, Murphy SP, Sigman M, Whaley S, Allen LH, Guthrie D, Weiss RE, Allen LH, Demment MW. 2003. Animal source foods improve dietary quality, micronutrient status, growth and cognitive function in Kenyan school children: background, study design and baseline findings. *J Nutr.* 133:3941S–3949S.
- Neumann CG, Murphy SP, Gewa C, Grillenberger M, Bwibo NO. 2007. Meat supplementation improves growth, cognitive, and behavioral outcomes in Kenyan children. *J Nutr.* 137:1119–1123.
- Newsholme P. 2001. Why is L-glutamine metabolism important to cells of the immune system in health, postinjury, surgery or infection? *J Nutr.* 131:2515S–2522S.
- Nicoloso L, Bomba L, Colli L, Negrini R, Milanese M, Mazza R, Sechi T, Frattini S, Talenti A, Coizet B, et al. 2015. Genetic diversity of Italian goat breeds assessed with a medium-density SNP chip. *Genet Sel Evol.* 47:62. doi: 10.1186/s12711-015-0140-6.
- O'Keefe JH, Bergman N, Carrera-Bastos P, Fontes-Villalba M, DiNicolantonio JJ, Cordain L. 2016. Nutritional strategies for skeletal and cardiovascular health: hard bones, soft arteries, rather than vice versa. *Open Heart.* 3:e000325. doi: 10.1136/openhrt-2015-000325.
- Olson TA, Lucena C, Chase CC Jr, Hammond AC. 2003. Evidence of a major gene influencing hair length and heat tolerance in *Bos taurus* cattle. *J Anim Sci.* 81:80–90.
- Oostindier M, Alexander J, Amdam GV, Anderson G, Bryan NS, Chen D, Corpet DE, De Smet S, Dragsted LO, Haug A, et al. 2014. The role of red and processed meat in colorectal cancer development: a perspective. *Meat Sci.* 97:583–596.
- Peana I, Dimauro C, Carta M, Gaspa M, Fois G, Cannas A. 2007. Cold markedly influences milk yield of Sardinian dairy sheep farms. *Ital J Anim Sci.* 6 (Suppl.1):580.
- Penati CA, Tamburini A, Bava L, Zucali M, Sandrucci A. 2013. Environmental impact of cow milk production in the central Italian Alps using Life Cycle Assessment. *Ital J Anim Sci.* 12:584–592.
- Phocas F, Belloc C, Bidanel J, Dealby L, Dourmad JY, Dumont B, Ezanno P, Fortun-Lamothe L, Foucras G, Frappat B, et al. 2016. Review: towards the agroecological management of ruminants, pigs and poultry through the development of sustainable breeding programmes. II. Breeding strategies. *Animal.* 10:1749–1759.
- Phogat JB, Smith RF, Dobson H. 1997. Effect of adrenocorticotrophic hormone on gonadotrophin releasing hormone-induced luteinizing hormone secretion in vitro. *Anim Reprod Sci.* 48:53–65.
- Pompa G, Arioli F, Casati A, Fidani M, Bertocchi L, Dusi G. 2011. Investigation of the origin of prednisolone in cow urine. *Steroids.* 76:104–110.
- Pretty J. 2008. Agricultural sustainability: concepts, principles and evidence. *Philos Trans R Soc Lond, B, Biol Sci.* 363:447–465.
- Pulina G, Francesconi AHD, Battacone G, Atzori AS. 2011a. Water footprint of animal products. In: Greppi GF, Mura S, editors. *45° International Symposium of Animal Production 'WATER & FOOD sustainability and biosecurity'*. Sassari, Italy: EDES, p. 25–34.
- Pulina G, Francesconi AHD, Mele M, Ronchi B, Stefanon B, Sturaro E, Trevisi E. 2011b. Sfamare un mondo di nove miliardi di persone: la sfida per una zootecnia sostenibile



- [Feeding a world of 9 billion people: a challenge for sustainable animal production]. *Ital J Agron*. 6(Suppl. 2):e7.
- Purse BV, Mellor PS, Rogers DJ, Samuel AR, Mertens PP, Baylis M. 2005. Climate change and the recent emergence of bluetongue in Europe. *Nat Rev Microbiol*. 3:171–181.
- Ramón M, Díaz C, Pérez-Guzman MD, Carabaño MJ. 2016. Effect of exposure to adverse climatic conditions on production in Manchega dairy sheep. *J Dairy Sci*. 99:5764–5779.
- Renaudeau D, Collin A, Yahav S, De Basilio V, Gourdine JL, Collier RJ. 2012. Adaptation to hot climate and strategies to alleviate heat stress in livestock production. *Animal*. 6:707–728.
- Rizzoli R, Bianchi ML, Garabédian M, McKay HA, Moreno LA. 2010. Maximizing bone mineral mass gain during growth for the prevention of fractures in the adolescents and the elderly. *Bone*. 46:294–305.
- Rizzoli R. 2014. Dairy products, yogurts, and bone health. *Am J Clin Nutr*. 99(5 Suppl.):1256S–1262S.
- Rohrman S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, Nailler L, Boutron-Ruault M-C, Clavel-Chapelon F, Krogh V, et al. 2013. Meat consumption and mortality—results from the European Prospective Investigation into Cancer and Nutrition. *BMC Med*. 11:63. doi: 10.1186/1741-7015-11-63.
- Rotz CA, Montes F, Chianese DS. 2010. The carbon footprint of dairy production systems through partial life cycle assessment. *J Dairy Sci*. 93:1266–1282.
- Rowe JB, Corbett JL. 1999. Production and use of feed for sustainable animal production in Australia. *Asian Aust J Anim*. 12:435–444.
- Rushen J. 2000. Some issues in the interpretation of behavioural responses to stress. In: Moberg GP, Mench JA, editors. *The biology of animal stress*. Wallingford (UK): CABI Publishing; p. 23–42.
- Ryan MH, Derrick JW, Dann PR. 2004. Grain mineral concentrations and yield of wheat grown under organic and conventional management. *J Sci Food Agric*. 84:207–216.
- Sahni S, Cupples LA, Mclean RR, Tucker KL, Broe KE, Kiel DP, Hannan MT. 2010. Protective effect of high protein and calcium intake on the risk of hip fracture in the Framingham offspring cohort. *J Bone Miner Res*. 25:2770–2776.
- Santamaria P. 2006. Nitrate in vegetables: toxicity, content, intake, and EC regulation. *J Sci Food Agric*. 86:10–17.
- Santarelli RL, Pierre F, Corpet DE. 2008. Processed meat and colorectal cancer: a review of epidemiologic and experimental evidence. *Nutr Cancer*. 60:131–144.
- Santarelli RL, Vendevre J-L, Naud N, Taché S, Guéraud F, Viau M, Genot C, Corpet DE, Pierre FHF. 2010. Meat processing and colon carcinogenesis: cooked, nitrite-treated, and oxidized high-heme cured meat promotes mucin-depleted foci in rats. *Cancer Prev Res (Phila)*. 3:852–864.
- Savage SD. 2015. The yield gap for organic farming: An independent analysis comparing the 2014 USDA Organic Survey data with USDA-NASS statistics for total crop production. [Internet]. [cited 2016 Mar 25]. Available from: <http://www.scribd.com/doc/283996769/The-Yield-Gap-For-Organic-Farming#scribd>.
- Schlesinger WH. 2000. Carbon sequestration in soils: some cautions amidst optimism. *Agr Ecosyst Environ*. 82:121–127.
- Segnalini M, Bernabucci U, Vitali A, Nardone A, Lacetera N. 2013. Temperature humidity index scenarios in the Mediterranean basin. *Int J Biometeorol*. 57:451–458.
- Serra MG, Atzori AS, Cannas A. 2013. Carbon footprint of dairy cattle farms in Southern Italy. *Ital. J Anim Sci*. 12(Suppl. 1):62. Abstract.
- Serra MG, Atzori AS, Cellesi M, Zanirato G, Cannas A. 2014. A multivariate approach to identify variables affecting the carbon footprint of dairy cattle farms. In: *EAAP Book of Abstracts of the 65th Annual Meeting of the European Federation of Animal Science*. Wageningen, The Netherlands: Wageningen Academic Publishers; p. 130.
- Sevi A. 2007. Ewe welfare and ovine milk and cheese quality. *Ital J Anim Sci*. 6(Suppl. 1):521–526.
- Sevi A, Casamassima D. 2009. Ovi-caprini [Sheep and goats]. In: Carenzi C, Panzera M, editors. *Etologia applicata e benessere animale [Applied ethology and animal welfare]*, vol. 2. Milano, Italy: Le Point Veterinarie Italie; p. 71–87.
- Sgorlon S, Fanzago M, Sandri M, Gaspardo B, Stefanon B. 2015a. Association of index of welfare and metabolism with the genetic merit of Holstein and Simmental cows after the peak of lactation. *Ital J Anim Sci*. 14:368–373.
- Sgorlon S, Fanzago M, Guiatti D, Gabai G, Stradaoli G, Stefanon B. 2015b. Factors affecting milk cortisol in mid lactating dairy cows. *BMC Vet Res*. 11:259. doi: 10.1186/s12917-015-0572-9.
- Shields RJ, Lupatsch I. 2012. Algae for aquaculture and animal feeds. *Tecnnikfolgenabshcätzung – Theorie Und Praxis*. 2:23–37.
- Somporn P, Gibb MJ, Markvichitr K, Chaiyabutr N, Thummabood S, Vajrabukka C. 2004. Analysis of climatic risk for cattle and buffalo production in northeast Thailand. *Int J Biometeorol*. 49:59–64.
- Soroko S, Holbrook TL, Edelstein S, Barrett-Connor E. 1994. Lifetime milk consumption and bone mineral density in older women. *Am J Public Health*. 84:1319–1322.
- Straub DA. 2007. Calcium supplementation in clinical practice: a review of forms, doses, and indications. *Nutr Clin Pract*. 22:286–296.
- Sundrum A. 2001. Organic livestock farming. A critical review. *Livest Prod Sci*. 67:207–215.
- Suravajhala P, Kogelman LJA, Kadarmideen HN. 2016. Multi-omic data integration and analysis using systems genomics approaches: methods and applications in animal production, health and welfare. *Gent Sel Evol*. 48:38.
- Takahashi G, Gurumurthy CB, Wada K, Miura H, Sato M, Ohtsuka M. 2015. GONAD: Genome-editing via Oviductal Nucleic Acids Delivery system: a novel microinjection independent genome engineering method in mice. *Sci Rep*. 5:11406 doi: 10.1038/srep11406.
- Thoma G, Popp J, Nutter D, Shonnard D, Ulrich R, Matlock M, Kim DS, Neiderman Z, Kemper N, East C, et al. 2013. Greenhouse gas emissions from milk production and consumption in the United States: a cradle-to-grave life cycle assessment circa 2008. *Int Dairy J*. 31(Suppl. 1):S3–S14.
- Toba Y, Takada Y, Yamamura J, Tanaka M, Matsuoka Y, Kawakami H, Itabashi A, Aoe S, Kumegawa M. 2000. Milk basic protein: a novel protective function of milk against osteoporosis. *Bone*. 27:403–408.
- Trevisi E, Amadori M, Archetti I, Lacetera N, Bertoni G. 2011. Inflammatory response and acute phase proteins in the

- transition period of high-yielding dairy cows. In: Veas F, editor. Acute phase protein/Book 2. Rijeka, Croatia: InTech; p. 355–380.
- Tucker KL. 2009. Osteoporosis prevention and nutrition. *Curr Osteoporos Rep.* 7:111–117.
- Tufarelli V, Selvaggi M, Laudadio V. 2015. Genetically modified feeds in poultry diet: safety, performance, and product quality. *Crit Rev Food Sci.* 4:562–569.
- Tulipano G, Bulgari O, Chessa S, Nardone A, Cocchi D, Caroli A. 2010. Direct effects of casein phosphopeptides on growth and differentiation of in vitro cultured osteoblastic cells (MC3T3-E1). *Regul Pept.* 160:168–174.
- Umstatter C, Morgan-Davies J, Waterhouse T. 2015. Cattle responses to a type of virtual fence. *Rangeland Ecol Manage.* 68:100–107.
- [UN] United Nations. 2015. Department of Economic and Social Affairs. Population Division. World Population Prospects, the 2015 revision [Internet]. [cited 2016 March 25]. Available from: <http://esa.un.org/unpd/wpp/Graphs/Probabilistic/POP/TOT/>.
- Van Eenennaam AL, Young AE. 2014. Prevalence and impacts of genetically engineered feedstuffs on livestock population. *J Anim Sci.* 10:4255–4278.
- Varner MA, Johnson BH. 1983. Influence of adrenocorticotropin upon milk production, milk constituents, and endocrine measures of dairy cows. *J Dairy Sci.* 66:458–465.
- Varner MA, Johnson BH, Britt JH, McDaniel BT, Mochrie RD. 1983. Influence of herd relocation upon production and endocrine traits of dairy cows. *J Dairy Sci.* 66:466–474.
- Verkerk GA, Macmillan KL, McLeay LM. 1994. Adrenal cortex response to adrenocorticotrophic hormone in dairy cattle. *Domest Anim Endocrinol.* 11:115–123.
- Verkerk GA, Phipps AM, Carragher JF, Matthews LR, Stelwagen K. 1998. Characterization of milk cortisol concentrations as a measure of short-term stress responses in lactating dairy cows. *Anim Welfare.* 7:77–86.
- Vitali A, Felici A, Esposito S, Bernabucci U, Bertocchi L, Maresca C, Nardone A, Lacetera N. 2015. The effect of heat waves on dairy cow mortality. *J Dairy Sci.* 98:4572–4579.
- von Borell EH. 2001. The biology of stress and its application to livestock housing and transportation assessment. *J Anim Sci.* 79(E. Suppl):E260–E267.
- von Schenck U, Bender-Götze C, Koletzko B. 1997. Persistence of neurological damage induced by dietary vitamin B-12 deficiency in infancy. *Arch Dis Child.* 77:137–139.
- Weaver CM. 2009. Should dairy be recommended as part of a healthy vegetarian diet? Counter Point. *Am J Clin Nutr.* 89(Suppl.):1634S–1637S.
- Weiss D, Helmreich S, Möstl E, Dzidic A, Bruckmaier RM. 2004. Coping capacity of dairy cows during the change from conventional to automatic milking. *J Anim Sci.* 82:563–570.
- West JW. 1994. Interactions of energy and bovine somatotropin with heat stress. *J Dairy Sci.* 77:2091–2102.
- WHO. 2003. Diet, nutrition and the prevention of chronic diseases: report of a joint WHO/FAO expert consultation. Geneva (Switzerland): WHO (WHO Technical Report Series, No. 916).
- Wiedemann SG, Ledgard SF, Henry BK, Yan M-J, Mao N, Russell SJ. 2015. Application of life cycle assessment to sheep production systems: investigating co-production of wool and meat using case studies from major global producers. *Int J Life Cycle Assess.* 20:463–476.
- Williams PG. 2007. Nutritional composition of red meat. *Nutr Diet.* 64(Suppl. 4):S113–S119.
- Winter P, Miny M, Fuchs K, Baumgartner W. 2006. The potential of measuring serum amyloid A in individual ewe milk and in farm bulk milk for monitoring udder health on sheep dairy farms. *Res Vet Sci.* 81:321–326.
- Wolfe RR. 2006. Skeletal muscle protein metabolism and resistance exercise. *J Nutr.* 136:525S–528S.
- WWF Italy. 2014. Water footprint of Italy [Internet]. [cited 2016 March 25]. Available from: [http://waterfootprint.org/media/downloads/wf\\_english\\_version\\_final\\_1.pdf](http://waterfootprint.org/media/downloads/wf_english_version_final_1.pdf).
- Yoneme H, Hatakeyama J, Danjo A, Oida H, Yoshinari M, Aijima R, Murata N, Watanabe T, Oki Y, Kido MA. 2015. Milk basic protein supplementation enhances fracture healing in mice. *Nutrition.* 31:399–405.