

# **Nutrition, Inflammation, Health: Improving Animal Production Robustness in the South**

by

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## **Résumé**

L'article tente de démontrer qu'une alimentation et une nutrition adéquates sont d'une importance capitale pour permettre à un animal de réagir face à une agression, qu'elle soit biologique ou non. Cette réaction consiste en une réponse inflammatoire suivie d'une phase d'acmé, elle-même suivie d'une phase de résolution. L'apport d'énergie, et secondairement de protéine, sont les deux principaux piliers de cette réponse. Les projets visant à développer les productions animales sont souvent basés sur l'amélioration génétique ou le croisement mais l'importance de l'alimentation est fréquemment négligée, alors qu'elle constitue la porte d'entrée vers la productivité et la survie de l'animal.

## **Samenvatting**

Het artikel probeert aan te tonen dat een goede voeding van het grootste belang is om een dier in staat te stellen te reageren op agressie, of die nu biologisch is of niet. Deze reactie bestaat uit een ontstekingsreactie gevolgd door een acme-fase, die wordt gevolgd door een resolutiefase. De toevoer van energie, en in de tweede plaats van eiwitten, zijn de twee belangrijkste pijlers van dit antwoord. Projecten gericht op de ontwikkeling van de dierlijke productie zijn vaak gebaseerd op genetische verbetering of kruising, maar het belang van voer wordt vaak verwaarloosd, ook al is het de toegangspoort tot dierlijke productiviteit en overleving.

## **Abstract**

The article attempts to demonstrate that proper feeding and nutrition are of paramount importance in enabling an animal to respond to aggression, whether biologic or not. This reaction consists of an inflammatory response followed by an acme phase, which ends in a resolution phase. The supply of energy, and secondarily of protein, are the two main pillars of this response. Projects aimed at developing animal production are often based on genetic improvement or cross-breeding, but the importance of feed is often neglected, even though it is a gateway to animal productivity and survival.

## 1. Introduction.

Feed quality is crucial for optimal animal production and thus contributes to food safety, as animal products are a source of desirable nutrients such as high quality protein, essential amino acids, very long chain fatty acids (fish), iron, folate, vitamin B12, zinc (McRae, 2005). All of these are important for improving human health.

Animal production requires illness absence and optimal response against threatening agents. Inflammation is a general response facing any biotic or abiotic threat. As observed in humans, nutrition is important to help animal coping inflammatory response (Milward, 2017). It was therefore interesting to raise the issue of the interrelation between animal nutrition, inflammation and animal production, particularly in a context of food security for the South.

## 2. Element overview on inflammatory response.

A biological cell contains a collection of membranes typically composed of glyceride bi-layers. A glyceride is a molecule having at one end, an hydrophylic portion in contact with aqueous medium, either inside or outside the cell, while the rest of the molecule – apolar – arranges with other ones to form lipid coat (Figure 1).

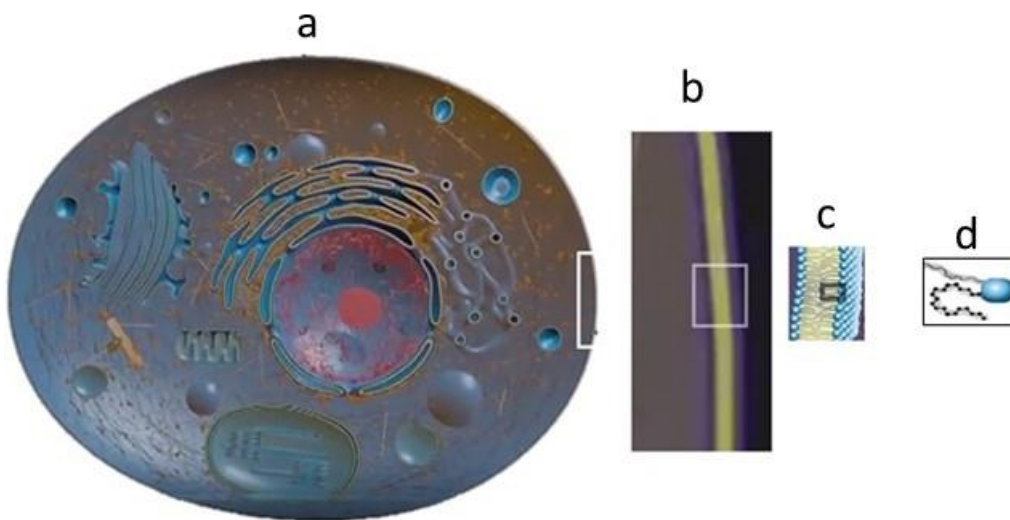


Figure 1. General cell (a) and membranes structure (b,c) with, at the extreme right, a glyceride (d) containing glycerol (in blue) linked to the curved chain of the arachidonic fatty acid (black punctuated line).

Inflammation occurs when membranes are injured, whatever the cause: physical (heat, mechanical injury...), chemical (acids...), biological (viruses, bacteria, parasites). Under these conditions, the bilayers open. Rapidly, lipases naturally present in cell separate fatty acids out of hydrophilic glyceride

head, favoring oxidizing activity of oxygenases on them. The arachidonic fatty acid, once oxidized, is very attractive against certain types of surrounding white blood cells, such as mast cells (Imagawa, 1983). These cells contain protein-based molecules named inflammatory mediators or "cytokines" that are capable of recruiting - through a chemotactic mechanism - cells that are primarily responsible for inflammation. Afterwards, other mediators recruit white blood cells that are responsible for reducing inflammation. For example, "interleukin 1" has inflammatory properties, while "interleukin 10" has anti-inflammatory properties (Feghali and Wright, 1997). Some white blood cells have a specific response to pathogens. In particular, lymphocytes produce key proteins capable of locking on to the pathogen - usually of biological origin - and allowing to destroy it more easily.

In summary, inflammation could be considered as a battlefield where some cells respond aspecifically - like a flamethrower - to threatening agents while other cells help - like firefighter - to reduce fire, remove debris, and clean up. These actions are sequentially mediated by specific cytokines.

### 3. Nutrition and inflammation control.

A healthy diet helps to reduce inflammation and to optimize animal response to stress. A first animal need is just eating, and to enjoy what is eaten. This refers to food palatability and, when feed intake are sufficient, animal reaches satiety feeling. This phenomenon is associated with a nervous gratification circuit named "endocannabinoid system" (Marco et al., 2012), and is similar to hedonism in humans. It allows animal to consume enough nutrients.

The most important of these nutrients is energy. Energy is not a nutrient strictly speaking, but is delivered as a result of certain true nutrients catabolism - carbohydrates, proteins, fats. Carbohydrates are the main source of energy for most farm animals. They are crucial for animal health. Glucose is the final step in carbohydrate hydrolysis. When this molecule enters the cell, it is first broken down under anaerobic conditions, releasing little energy. But the residues of this fermentation process (and also of lipids and proteins degradation) enter mitochondria, where degradation is achieved. In mitochondria, the residues are fully degraded and CO<sub>2</sub> and H<sub>2</sub>O are produced. This phenomenon of controlled combustion releases large amounts of energy. This stage requires oxygen, but also iron and vitamins, especially from the B group.

Energy is then used to carry out a lot of reactions, for example proteins synthesis (Calder and al, 2007) thanks to amino acids themselves obtained from feed protein digestion and absorption. Protein is therefore the second most important nutrient. Newly synthesized proteins are also molecules involved in inflammation and defense. Certain essential amino acids - named branched-chain amino acids (BCAAs) - appear to be involved in the processes of inflammation clearance. Thus, energy and protein are key nutrients that enable inflammation setting up, regulation, and resilience.

Lipids are a source of energy, but some of them are directly involved in inflammatory reactions. This is notably the case of polyunsaturated fatty acids from two families: omega3 and omega6. The aforementioned ARA belongs to the omega6 family and initiates inflammation, while omega3 fatty acids reduce inflammation by competing with ARA (Dunbar et al., 2014). For example, fresh grass is rich in omega3, which could contribute to good ruminant health on pasture.

Because of their catalytic or co-factorial functions in many physiological reactions, dietary minerals and vitamins, whether directly or indirectly, help to harmonize and regulate inflammatory processes. Some of them alleviate inflammation by reducing the oxidation step of ARA. This is the case, for example, of selenium, vitamin A, vitamin E or vitamin C (Bermond, 1989).

Fibre are not a nutrient per se, but are food for gut microbes, that ferment them, resulting in production of short fatty acids - named acetic acid, propionic acid, butyric acid - or lactic acid, which are not only nutrients for the host, but also help to fight against pathogenic bacteria in gut and to reduce intestinal inflammation (Tilg et al., 2019). Fibre are particularly important for herbivores.

Finally, other dietary "nutrient-like" molecules are beneficial for animal. They are called secondary plant metabolites, e.g. tannins, flavonoids... and for a while are widely studied ethnopharmacologically (de Souza Araujo, 2008). They possess antioxidant properties and stimulate certain white blood cells that are competent to fight against various intestinal parasites. Some pastures has botanical populations more favorable to animal health than others.

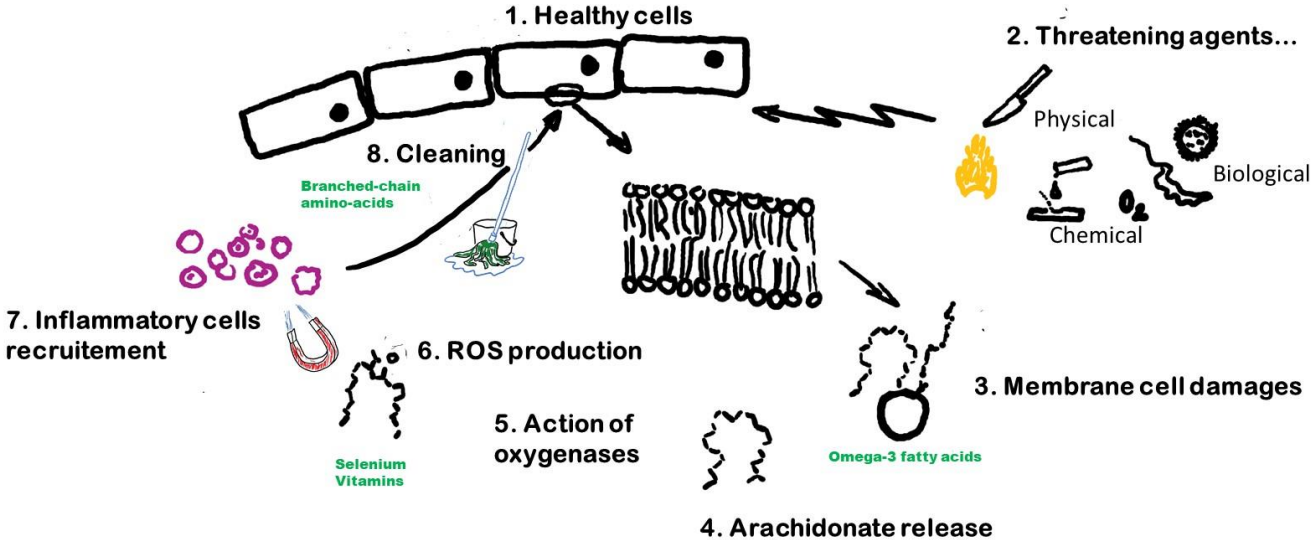


Figure 2. Inflammatory process and, in green, some modulators of inflammation (ROS : reactive oxydative species).

#### 4. Inflammatory responses in animals.

Certain production states or circumstances are particularly sensitive where inflammatory reactions may be observed, e.g., reproduction and parturition (Lenyasunya et al., 2005). They are associated with a strong increase in milk production and thus in energy and protein needs. The animal is therefore more easily in negative energy and protein balance state, which promotes fat mobilization (lipolysis), fatty acid oxidation, and consequently "pseudo-inflammatory state". Significant negative energy balance decreases appetite, alters intestinal microbiota quality, decreases mucus production by intestine wall, which increases contact between mucosa and bacterial lipopolysaccharides (LPS); LPS act as ARA. In response, reactive oxygen species appear (first stage of inflammation).

Similarly, obesity or overgrowth may favor inflammatory states (Klasing and Korver, 1997; de Heredia et al., 2012). In the first case, large amounts of fat increase insulin resistance and thus blood glucose levels. Glucose being an oxidant molecule, the probability of inflammatory arachidonic acid delivering increases. Rapid growth, as for it, is often associated with higher robustness against pathogens (personal observation) but also requires greater amounts of oxygen, favoring ROS production. Body also has few time to stabilize body structure, which can, for example, weaken animal skeleton. Frequently, the most beautiful animals are also the most fragile.

Finally, low antioxidant status, due for example to low selenium or omega-3 intake, strengthen oxidation phenomenon, leading in some cases to sudden death.

#### 5. Nutrition and inflammation viewed as a socio-economic interaction

Food and animal can be considered like interacting socio-economic actors. Figure 3 is a metaphor of the relationships between feed and animal physiology. The store (shop) symbolizes the economic activity that the animal has to carry out in order to eat: feeding requires energy expenditure that theoretically allows for recovery of a proportionally higher amount of energy and nutrients than that spent for this activity. In the medium term, this activity has to be economically beneficial for the animal. The profit can be saved in stock-banking form (fat tissue), or it can also be partially used to allow the organism (the industry - the cells) to function. When required, the factory withdraws funds from the bank (use of fat tissue). The factory produces labour to preserve healthy the body (building structure), or to produce goods for export, such as milk. From the factory also arise the different actors of inflammation, defense, mitigation, recovery, resilience (tank, police, fire brigade, ambulance).

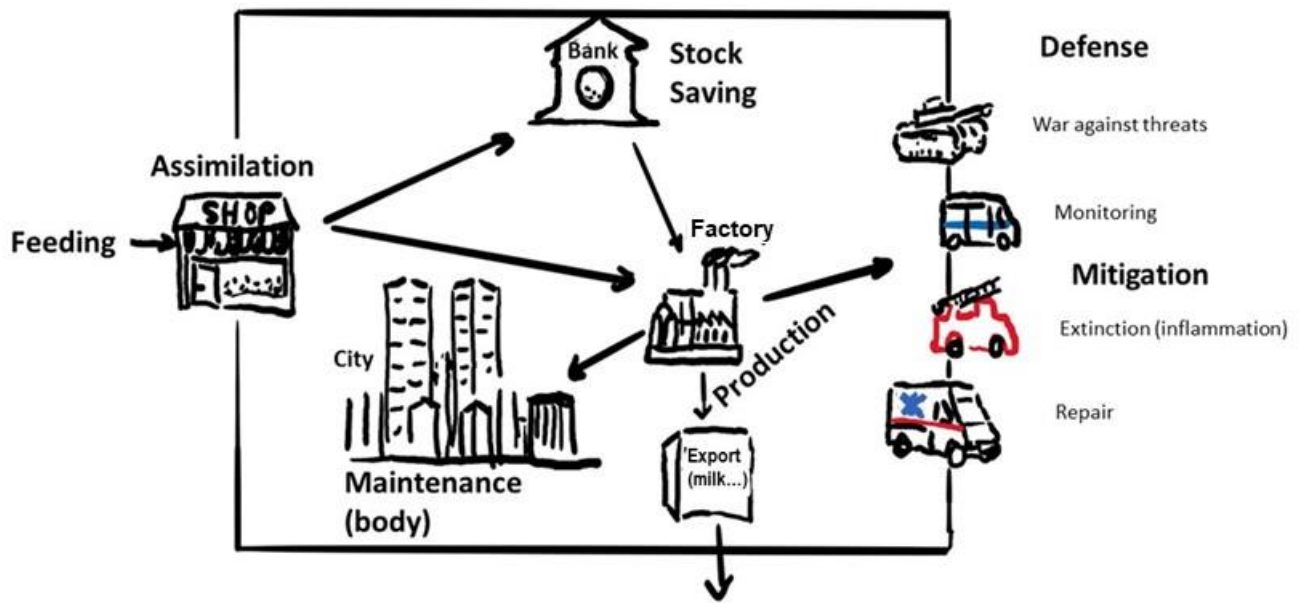


Figure 3. A socio-economic metaphor of the relationships between feeding activity and animal physiology.

When applied to low-productive animal, such as local breed in Africa, it could be considered that the store, bank, factory, production level, are adapted to body scale, and defense cells manufacture is not very expensive, so the body is sufficiently well protected. Whether nutrition is poor, store activity is low, the bank does not own a lot of savings, and in order to preserve a stable body condition or guarantee production and safety, the factory has to withdraw or borrow money (from lipolysis), but not to a great extent, because the city is modest. Thus, the body keep on to demonstrate, to some extent, quite a lot resistance.

By contrast, high producing animal (such as Holstein cow) needs high feed levels (trade is flourishing), but preventing to perform any economy: the organism is in just-in-time state: profits are used to preserve a real estate, to produce high levels of exports, and to some extent, to enable safety and health. But the process is not easy. Most of the energy and protein is expended on goods production, promoting sub-inflammatory state. Any food scarcity is thus a disaster: no flow of profits, high withdrawal or borrowing in a situation of bankruptcy, high effort to produce goods and to preserve large building stock, very little provision for defense (lack of protein and energy) but nevertheless a situation of inflammation (because inflammation requires few communication molecules between white blood cells). The organism is not in well-being state and is not encouraged to trade for food (inappetence).

Thus, under tropical conditions, breeds are generally unproductive, but justifiably, namely to maximize the chances of resisting to threats. Climate is one such threat (Barendse, 2017). In this context, it is crucial to allow youngsters to receive colostrum, because this “first milk” provides energy, essential amino acids, growth factors and ready-to-use antibodies. Similarly, trypanotolerant cattle are less productive than breeds selected for meat production, and when feed is scarce trypanotolerance traits diminish or disappear. In any circumstances, wild fish, pigs, poultry... are more resistant than selected breeds. Introduction of selected western breeds (such as Holstein or Jersey cattle) or selected local breeds (such as Azawak breed) ineluctably requires increase in feed quality offered to animals. As a rule, removal of animals from their natural environment, for example for stabling, should be a first step to consider, at first with the aim of reducing animal efforts to find energy sources. Feed improvement (bio)technologies – qualitative and quantitative – should then be implemented.

## 6. Conclusions.

Adequate and uninterrupted feeding, particularly in terms of energy and secondarily of protein, is the first step to help animal setting up and preserving strong lines of defense against threatening agents. These considerations are hardly taken into account when attempts are made to acclimatize improved breeds in tropical areas.

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