



## Review article

## The role of omega-3 polyunsaturated fatty acids in reproduction of sheep and cattle

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## ABSTRACT

The positive effects of fat and energy supplementation on improvements in reproduction are well documented. However, the specific effects of omega-3 polyunsaturated fatty acids (n-3) on reproductive success in ruminants have not been examined in detail. While the link between n-3 and markers associated with reproduction, in particular, prostaglandin  $F_{2\alpha}$  ( $PGF_{2\alpha}$ ) and the link between  $PGF_{2\alpha}$  and reproductive outcomes are well established, evidence of a direct effect of high n-3 diets on measurable reproductive outcomes in ruminants is lacking. Therefore, the aim of the current review was to examine the effect of n-3 on a number of reproductive markers and measurable outcomes in sheep and cattle. There is strong evidence linking consumption of diets high in n-3 with reduced circulating peripheral inflammatory markers such as  $PGF_{2\alpha}$ . Inflammatory eicosanoids including  $PGF_{2\alpha}$ , in particular, can significantly affect reproduction outcomes such as the onset of oestrus, embryo survival and parturition. While there is also evidence linking n-3 supplementation with longer time to oestrus and parturition associated with reduced  $PGF_{2\alpha}$ , the effects of n-3 on other measurable outcomes of reproductive success, such as pregnancy rate, embryo survival and intergenerational effects on the health and production of offspring are largely unknown. Similarly, the effects of diets high in n-3 or n-6 polyunsaturated fatty acids on male fertility are also unknown.

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## 1. Introduction

Omega-3 polyunsaturated fatty acids (n-3) have a number of positive effects on human and animal health. In particular, the ratio of omega-6 polyunsaturated fatty acids (n-6) to n-3 may play an important role in several aspects of animal health, production and reproduction (Abayasekara and Wathes, 1999).

A number of reviews have examined the effect of dietary fatty acids on reproduction in sheep and cattle, however, these have primarily focussed on the effects of total dietary fat and energy balance (for example, see Funston, 2004; Hess et al., 2008; Santos et al., 2008; Staples et al., 1998; Sturme et al., 2009), rather than specific effects of n-3 or n-6. Similarly, reviews examining the effects of n-3 and n-6 have generally examined biomarkers of reproductive success, such as effects *in vitro* or effects on circulating concentrations of prostaglandin (PG, Abayasekara and Wathes, 1999; Cheng et al., 2001; Mattos et al., 2000), rather than measurable outcomes such as follicle development and ovulation, embryo survival and pregnancy rate or survival and behaviour of the neonate. While results from *in vitro* studies can provide important evidence of mechanisms linking the effect of n-3 on reproduction outcomes, especially where there is a lack of *in vivo* data, *in vivo* experiments determining the effects of n-3 on reproduction success are required in order to confirm their mechanisms of action. In addition, other reviews examining the effects of n-3 on animal and human reproduction have not focussed on ruminants (for example, see Wathes et al., 2007).

The aim of the current review is to examine the effects of n-3 and n-6 on measurable outcomes of reproductive success in sheep and cattle. A summary of dietary fatty acids and metabolism is followed by a review of the specific effects of n-3 and n-6 on *in vivo* measures of reproduction with supplemental information from *in vitro* studies where there is a lack of *in vivo* data.

## 2. Sources and metabolism of omega-3 and omega-6 fatty acids

The primary fatty acids of interest in studies examining reproduction in animals are the long-chain n-3 including eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3) and the long-chain n-6 arachidonic acid (AA, 20:4n-3). These long-chain polyunsaturated fatty acids (PUFA) are synthesised in the body from the short-chain n-3  $\alpha$ -linolenic acid (ALA, 18:3n-3) and n-6 linoleic acid (LA, C18:2n-6) through a number of steps involving

desaturation and elongation (Fig. 1). The short-chain ALA and LA cannot be synthesised by animals (Lands, 1992) and, therefore, must be consumed in the diet. While the conversion of ALA and LA to long-chain PUFA is rate limited (Emken et al., 1994; Pawlosky et al., 2001), there is considerable evidence that significant metabolism occurs in ruminants and concentrations of n-3 in plasma (Kemp et al., 1998), red blood cells (Gulliver et al., 2010), meat (Scollan et al., 2006), milk (Dewhurst et al., 2003) and reproductive tissue (Kim et al., 2001) are influenced by concentrations of ALA and LA in the diet.

There are several sources of the short-chain n-3 ALA in ruminant diets, including forages and linseed (Fig. 1). Long-chain n-3 (20 carbons or more) purified from sources such as fish oil and fishmeal can also be fed to ruminants and these are usually protected against rumen biohydrogenation (Ashes et al., 1992). These supplements are usually expensive, however, and are not often fed on a commercial basis and the feeding of fishmeal directly to sheep and cattle is banned in Europe and in many countries including Australia. Long-chain n-3 is also available from some species of algae (Pickard et al., 2008), which are often used for ethanol or bio-diesel production. The short-chain n-6 LA is available from a number of sources, including grains, soybean, safflower and sunflower (Fig. 1). Megalac, a rumen protected lipid supplement, also contains approximately 10% of total lipid as LA (see Table 1), however, there are few sources of the long chain n-6 AA in ruminant diets.

The long-chain PUFAs EPA and AA are the precursors for eicosanoids including prostaglandins (PG), prostacyclins (PGI), thromboxanes (TX) and leukotrienes (LT, Abayasekara and Wathes, 1999; Smith et al., 1991). The removal of two double bonds from AA (20:4n-6) by prostaglandin H synthase (PGHS, also called cyclooxygenase, COX) leaves two double bonds and leads to the formation of series-2 eicosanoids, while the removal of two double bonds from EPA (20:5n-3) leads to the formation of series-3 eicosanoids (Fig. 2).

The eicosanoids are signalling molecules associated with a number of functions in the body including inflammation (Peet and Stokes, 2005). The series-1 and series-3 PG are less inflammatory, while the series-2 PG are more inflammatory (Horrobin and Bennett, 1999; Lands, 1992). The PGs, in particular, series-2 PGs including PGF<sub>2 $\alpha$</sub> , play an important role in several aspects of reproduction, including ovulation, oestrus, embryo survival and parturition (for review, see Abayasekara and Wathes, 1999), roles which will be reviewed later.

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