

The role of mycotoxins in pig reproduction: a review

A. KANORA¹, D. MAES²

¹Huvepharma NV, Antwerp, Belgium

²Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium

ABSTRACT: Mycotoxins are commonly present in feed for farm animals. Sows and gilts are highly susceptible to mycotoxins. This article presents a review describing the main mycotoxins encountered in pig feed which have a negative impact on sow fertility and reproduction. Consumption of feed that is contaminated with these mycotoxins may cause a variety of symptoms, depending on the type of mycotoxin, quantity and duration of exposure, as well as the health status and condition of the animal at the time of exposure. Two types of fungi are recognized, field fungi and storage fungi. Field fungi such as *Fusarium* spp., *Aspergillus* spp. and *Claviceps* spp. may produce toxins that lead to disturbed reproductive performance. Storage fungi occur if the humidity during storage is too high. In daily practice, the symptoms related to mycotoxicosis can occur at toxin concentrations below the detection limit. Knowledge of the effects of mycotoxins is expanding rapidly. Mycotoxins may still be present in feedstuffs despite negative analytical findings and because of the presence of hot spots in feed and or feedstuffs. Clinical symptoms can be very pronounced, making the diagnosis for the practitioner quite easy but in many cases the symptoms are vague and not at all present at herd level on a regular basis. The practitioner is in the first line of raising awareness in all parties whenever the first indication exists of a possible mycotoxicosis problem causing reproductive failure in breeding pigs. The problems can be resolved only if all parties involved in pig herd health take the necessary preventive measures and actions. The main toxins causing reproductive failure discussed in this article are aflatoxins, ergot alkaloids, trichothecenes and zearalenone.

Keywords: mycotoxins; zearalenone; T-2; ergot; aflatoxins; reproduction; storage fungi

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1. Introduction

Mycotoxins are toxic products produced by naturally occurring metabolic processes in fungi. The four main genera of mycotoxin-producing fungi are

Aspergillus spp., *Fusarium* spp., *Penicillium* spp. and *Claviceps* spp. Mold growth can occur at various stages during the production process of animals and plants. Mycotoxins can invade the seeds before the actual harvest, while the crop is still on the field, or

alternatively, mold growth can occur during storage at the feed mill or on the farm. As a result, high numbers of mycotoxins may already be present in the ingredients before these are received in feed mills or farms. Hence, preventing the occurrence of mycotoxins in feed ingredients can be a very difficult task. Mold can also grow during feed processing, especially when the mixer increases temperature and humidity in the feed. Finally, mold growth and mycotoxin production could also occur in insufficiently cleaned silos, transport systems and feeders at farm level. The fungi can contaminate various feed components like maize, wheat, barley, millet, peanuts, peas and oily feedstuffs. The production of mycotoxins is enhanced by factors like the humidity of the substrate (10 to 20%), the relative humidity ($\geq 70\%$), the temperature (0 to 50°C, depending on the fungus species) and the availability of oxygen.

Mycotoxins may cause various toxic effects or mycotoxicosis. Symptoms caused by mycotoxin contamination depend on the level and type of mycotoxins, but also on several factors such as animal species, sex, environment, nutritional status and other toxic entities. However, they are not transmissible between animals and contaminated feed is mostly the cause. Diagnosis of mycotoxicosis is often very difficult because the effects of mycotoxins in animals are diverse, varying from specific to unspecific symptoms like immune suppression, diarrhea, hemorrhages or reduced performance.

Generally, the occurrence of mycotoxins in food and animal feed often shows a geographical pattern,

Table 1. Results of the Biomin mycotoxin report for the first six months of 2009 (Source: Biomin Austria (2009): Mycotoxin report, 1st and 2nd quarter)

Geographical region	Positive feed samples containing zearalenone (%)
North America	26
Central America	0
South America	0
Northern Europe	25
Central Europe	25
Southern Europe	20
Middle East	18
Africa	35
North Asia	53
South East Asia	37
South Asia	35
Oceania	12

e.g., *Aspergillus* spp. find optimal conditions in tropical and subtropical regions, whereas *Fusarium* spp. and *Penicillium* spp. are more adapted to the climate of North America and Europe (Table 1). On the other hand, due to the international trade of food and feed, problems with mycotoxins occur worldwide (Table 2). According to Lawlor and Lynch (2001), 25% of the global crop is contaminated with mycotoxins.

From the point of view of animal production, there are five important classes of mycotoxins, i.e., trichothecenes, zearalenone, ochratoxins, aflatoxins and fumonisins. This paper reviews the effects of mycotoxins on pig reproduction.

2. Fungi important for pig reproduction

Reproductive failure and a drop in reproductive performances brought on by mycotoxins can be defined as reproductive mycotoxicoses. There are two types of fungi: pathogenic fungi (also called field fungi) which cause plant disease (pre-harvest) and saprophytic fungi (or storage fungi) which live only on dead organic material (post-harvest). In both cases, specific environmental conditions are required for the fungi to thrive. These conditions depend on the type of fungus and include a relatively high humidity, high temperatures and the presence of oxygen (Desjardins, 2006).

The three main genera of mycotoxin-producing pathogenic fungi that are important for sow reproduction are *Aspergillus* spp., *Fusarium* spp. and *Claviceps* spp. Of these three genera, not the fungi themselves, but the mycotoxins they produce are pathogenic for the pig.

The presence of toxin-producing fungi in animal feed or raw material does not automatically imply toxicity. Each feedstuff can be infected by more than one fungus and each of them can produce several mycotoxins. Consequently, it is common that many mycotoxins occur simultaneously in feeds (Koshinsky and Khachatourians, 1992). This combination can cause more adverse effects than a single mycotoxin due to additive or synergistic interaction.

3. Mycotoxins important for pig reproduction

The main mycotoxins encountered in pig reproduction are zearalenone as a major toxin, ergot

Table 2. Conditions for fungal growth and synthesis of mycotoxins affecting reproduction in pigs (Source: Osweiler, 2006)

Fungus Source	Grains affected	Optimal temperature (°C)	Moisture requirement	Mycotoxin	Agronomic influences
<i>Fusarium roseum</i>	corn, wheat and barley	7–21	EMC 24%	deoxynivalenol	alternating warm and cool growing season
<i>Claviceps purpurea</i>	rye, wheat, triticale oats and barley	likely moderate to cool during seed formation	moist, humid conditions favor production	ergot	warm humid conditions, wind and insects favor spread of ergot infection
<i>Fusarium sporotrichiodes</i>	corn, barley, milo and wheat	8–15		T-2 toxin	alternating warm and cool conditions; overwintered crops
<i>Fusarium roseum</i>	corn, wheat and barley	7–15		zearalenone	alternating high and low temperatures during maturations

EMC = equilibrium moisture content

alkaloids and trichothecenes represented by T-2. These toxins can be present in feed and feed components and are implicated in a high number of pathologies and instances of reproductive failure (Table 3).

3.1. Zearalenone

Zearalenone is a mycotoxin produced by *Fusarium* spp., mainly *F. graminearum* and *F. culmorum*. Maize and wheat are the most frequently af-

Table 3. Major features of mycotoxins that effect reproduction in pigs (Source: Osweiler, 2006)

Mycotoxin	Most effected	Clinical effects	Lesions	Diagnostic and tests	Therapy/prevention	Residues
Aflatoxin	piglets	reduced growth, immune dysfunction	hepatic necrosis, bile duct hyperplasia	aflatoxin in feed and metabolites in milk and tissues B1 and M1	vitamin E and selenium and aluminosilicate	residues occur in liver and milk for < 3 weeks
Diacetoxyscripenol or T-2 toxin	sows, feeder pigs	feed refusal diarrhea leucopenia oral ulcerations immune suppression	oral ulcers, gastric ulcers, lymphoid and thymic depletion	histological lesions of ulceration, lymphopenia, leucopenia and feed analysis	change batch of feed and treat for diarrhea and ulcers	not likely to cause residues
DON	sows	feed refusal, reduced growth	weight loss	DON > 1 ppm	change feed	no residues
Ergot	sows, nursing pigs	agalactia with piglet starvation peripheral gangrene	piglet starvation and peripheral gangrene	ergot bodies or alkaloids in urine or diet; perivascular lesions	avoid ergot in grain	residues brief, not likely to be significant
Zearalenone	prepuberal gilts, cycling sows, young boars	hyperestrogenism in young gilts pseudopregnancy, delayed cycling, early embryonic death reduced libido	vulvovaginitis vaginal keratinization elevated serum progesterone zearalenone in feed	histological lesions of vaginal keratinization elevated serum progesterone zearalenone found in feed	change batch of feed treat gilts for prolapsed administer 10 mg PGF _{2α} to pseudopregnant sows	rapidly excreted in urine, low residue probability

fectured cultures and a high relative humidity during storage favors the production of this mycotoxin (Desjardins, 2006).

Zearalenone has a resorcylic acid lactone structure and can cross cell membranes binding to the cytosolic 17 β -estradiol (E_2) receptors and forming a ZEA- E_2 R complex. This complex (ZEA- E_2 R) is transferred into the cell nucleus and binds to specific nuclear E_2 receptors activating the gene responsible for mRNA synthesis (normally generated by E_2). These estrogen-like effects cause anabolic and reproduction activity. ZEA interacts not only with both types of estrogen receptors but is also a substrate for hydroxysteroid dehydrogenases, which convert it into two stereo-isomeric metabolites, alpha-zearalenol and beta-zearalenol. Alpha-hydroxylation results in an increase of estrogenic potency and explains the species specific sensitivity towards ZEA intoxications, whereas glucuronidation capacity inactivates ZEA. In comparison with other species, pigs have a low glucuronidation capacity making them more sensitive to ZEA (Malekinejad et al., 2005; Fink-Gremmels and Malekinejad, 2007).

Pigs are very susceptible to zearalenone (Gareis et al., 1990; Gajecki, 2002; Andretta et al., 2008), which has a hyperestrogenic effect. The most common pathological effects are anoestrus, abortion, increased embryonic and fetal death, failure of induction programs with PGF_{2 α} (Alexopoulos, 2001), and an increased incidence of stillborn and splay-legged piglets. Gilts are more sensitive than sows (Etienne and Jemmali, 1982; Young and King, 1986; Edwards et al., 1987a).

3.1.1. Estrus cycle

3.1.1.1. Gilts

In gilts, experimental administration of zearalenone or contaminated feed at relatively low doses (1.5 to 2 ppm) leads to a swelling and thickening of the vaginal and vulvar wall, an increased uterus mass and atrophic ovaries, but without a standing reflex (Young et al., 1981; Edwards et al., 1987b; Obremski et al., 2003; Kauffold et al., 2005b; Andretta et al., 2008). Signs appear three to seven days after the initial administration and disappear 14 days after withdrawal of the contaminated feed (Farnworth and Trenholm, 1983; Kordic et al., 1992). Similar effects occur after injection of estradiol-17 β cyclopentyl propionate (Young et

al., 1990) or 2 mg estradiol benzoate (Flowers et al., 1987). These concentrations elicit similar effects in gilts, but not in mature cyclic and lactating sows (Etienne and Jemmali, 1982; Young and King, 1986; Edwards et al., 1987b). In sows, much higher doses are required (64 ppm) to obtain similar symptoms (Long et al., 1982).

Anestrus in gilts can appear with concentrations of 3 ppm zearalenone (Etienne and Jemmali, 1982; Young and King, 1986).

Zearalenone can also induce early puberty in gilts (at 70 days of age) if fed at a level of 2 ppm for 45 to 90 days (Rainy et al., 1990). However, the first heats of these gilts are mostly infertile without ovulation. Recent research indicated that feeding feed to gilts contaminated with low concentrations of zearalenone (0.235 to 0.358 ppm) significantly reduced the intrinsic quality of the oocyte collected from these animals (Alm et al., 2006). The level of contamination has dose dependent effects on granulosa cells, steroidogenesis and gene expression (Malekinejad et al., 2007; Ranzenigo et al., 2008).

3.1.1.2. Sows

In cyclic sows, zearalenone contamination at levels of 5 to 10 ppm in feed causes, after weaning, a prolonged cycle or even anestrus (Chang et al., 1979; Edwards et al., 1987a; Meyer et al., 2000). Young et al. (1990) showed a linear relation between the level of zearalenone in ppm and the length of anestrus in days. This effect can also be present in gilts if fed at the same quantities from Day 5 to Day 20 of the cycle. The luteal bodies remain active due to a high progesterone level. The persistent corpora lutea disappear spontaneously 30 days after withdrawal of the contaminated feed (Edwards et al., 1987b). Since zearalenone has no effect on gonadotropic hormones, the mycotoxin is thought to have a direct impact on the ovaries (Flowers et al., 1987). However, Diekmann et al. (1986) found that, in an ovariectomized gilt, very high doses (1 mg/kg body weight) also inhibit FSH and LH secretion.

3.1.2. Embryos

Many studies have examined the possible impact of zearalenone during gestation (e.g. Christensen et al., 1972). Pregnant gilts and sows receiving contaminated feed (> 2.8–3.0 ppm ZEA), espe-

cially during early pregnancy, show smaller litters. Premature estrogenic stimulation by ZEA interferes with the proper secretory response of the endometrium to progesterone (P_4) during implantation of the embryos at Day 11–12 after breeding. If the ZEA exposure is severe (> 25 ppm ZEA in feed), symptoms like stillbirth and neonatal mortality will occur. In feed containing 2.8–3.0 ppm ZEA, “mummification” is often seen. At the end of the gestation period, difficulties can be found when attempting programmed farrowing induction using $PGF_{2\alpha}$ which causes splay-leg of newborn piglets and neonatal estrogen syndrome. This results in heavily swollen vulva in one day old female piglets. Experimental administration of feed containing 10 ppm zearalenone has been shown to have no impact on ovulation or on the nidated fetuses (Etienne and Jemmali, 1982; Edwards et al., 1987a; Green et al., 1990; Rainy et al., 1990). Similarly, experimental administration of 9 ppm zearalenone in the feed during the entire duration of gestation had no impact on the number of piglets born or on the survival rate of the piglets (Etienne and Jemmali, 1982; Young and King, 1986). Zearalenone administration between Days 7 and 10 of pregnancy seems to be the most critical period, with a higher rate of embryonic death compared to administration before or after that period (Long and Diekman, 1986).

Experimental administration of 1 ppm to gilts between Days 7 and 10 of pregnancy, showed an increasing degeneration of embryos starting from Day 9. The researchers observed that the remaining blastocysts were degenerated by Day 13 (Long et al., 1992). Although the various studies found no clear cause for the early embryonic death, it is presumed that zearalenone has an impact on the secretory mechanism of the endometrium, thereby changing the intra-uterine environment during early pregnancy (Etienne and Jemmali, 1982).

Higher contamination levels of zearalenone (64 ppm) meanwhile, lead to the death of the entire litter (Chang et al., 1979; Long et al., 1982), while moderate levels (up to 60 ppm) lead to smaller litters and less vigorous piglets. A dose-related effect was demonstrated by Long et al. (1982), who showed that the number of small litters (1–3 piglets) increased with incremental zearalenone contamination rate (0, 7, 38 and 64 ppm). An inverted linear relationship between the level of contamination and litter size was also demonstrated (Young et al., 1981; see Table 4).

The influence of zearalenone on litter size can be explained by a negative impact on fertilization, but also by embryonic and fetal death of the piglets. This is probably due to the negative impact on the luteinizing effect (Obremski et al., 2003).

Table 4. Clinical guide to mycotoxins affecting reproduction in pigs (Source: Osweiler, 2006)

Mycotoxin	Category of pig	Dietary level	Clinical effect
Aflatoxins	sows and gilts	$> 2\,000$ ppb	acute hepatosis, death in 3–10 days
		500–750 ppb	no effects on conception, normal piglets, slower growth due to aflatoxins in sow's milk
	nursery pigs	1 ppm	no effect
Trichothecenes T-2 and DAS	growers	3 ppm	decreased feed consumption
	sows	10 ppm	decreased feed consumption; oral/dermal irritation; immune-suppression
		20 ppm	complete feed refusal and vomiting
Zearalenone	prepuberal gilts	1–3 ppm	estrogenic; vulvovaginitis, prolapsed in puberal gilts
	cycling sows and gilts	3–10 ppm	retained corpora lutea; anestrus: pseudopregnancy
	pregnant sows	> 30 ppm	early embryonic death when fed 1–3 weeks post mating
Ergot	all pigs	0.1%	reduced weight gain
		0.3%	gangrene of ears, tail and foot
		3.0%	decreased feed consumption
	sows last trimester	0.3%	agalactia, reduced piglet birth weight, piglet starvation

3.1.3. Fetuses

Experimental administration of 4 ppm zearalenone in the feed of sows during the entire gestation, leads to a reduced weight of the fetuses (Etienne and Jemmali, 1982). It also leads to a larger weight variation between piglets of the same litter. Young and King (1986) found a negative association between the plasma level of zearalenone and average birth weight of the piglets. This might explain, due to the variation in birth weight, the increase in the number of piglets born with splay-leg from sows that were fed more than 4 ppm zearalenone. Fetal death was demonstrated by the presence of fetal tissue residues in the uterus on Day 40 after fertilization (Long et al., 1982; Long and Diekman, 1984).

3.1.4. Newborn piglets

Little is known about the effect of providing zearalenone-contaminated feed to lactating sows. Piglet mortality during the first two weeks after birth has been shown to be higher among sows that received feed with zearalenone levels of 4.8 ppm during gestation and lactation.

It is thought that zearalenone or its metabolites (α - and β -zearalenone) affect the piglets via the sow's milk, with potential toxic effects (Palyusik et al., 1980).

3.1.5 Boars

Feeding young immature boars with contaminated feed containing zearalenone (up to 600 ppm) over a period of 6–15 weeks resulted in animals with a testicular weight significantly lower (up to 30%) than control boars (Christensen et al., 1972; Young and King, 1983). Also, the epididymis and the vesicular glands are smaller, even following administration of feed with 100 ppm of zearalenone. A temporary inhibition of spermatogenesis has been observed, but can be reversed after withdrawal of the contaminated feed.

A reduced libido was observed after administration of 40 ppm zearalenone, associated with a decreased testosterone concentration in plasma (Berger et al., 1981). However, this effect could only be observed in young boars (under 38 weeks of age). Another report, using a variation in dosage

between 20–200 ppm fed to older boars during a period of eight weeks (Ruhr et al., 1983), reported the same parameters, a drop of libido and a decrease of testosterone. In recent research using extended boar semen with various doses of ZEA and alpha-zearalenol ranging between 40, 60 and 80 $\mu\text{g/ml}$, it was concluded that the concentrations used reduced the ability of the boar spermatozoa to bind to the zona pellucida (Tsakmakidis et al., 2007).

3.2. Ergot alkaloids

Ergot alkaloids are produced by *Claviceps purpurea*, *Claviceps paspalli* and *Claviceps fusiformis*. These pathogenic fungi are mainly found on rye, wheat and barley. The fungi form a sclerotium in the ear of grain. Modern cleaning and storage are the reasons that ergot feed contamination has become very rare as the sclerotia are removed by these processes (Diekman and Green, 1992).

Ergot alkaloids affect reproductive performance and clinical signs include oxytocin-resistant agalactia, small litters, premature farrowing, mummification, repeat estrus, metritis and mastitis (Barnikol et al., 1982). The effect on milk production is caused by prolactin inhibition (Whitacre and Threlfall, 1981; Kopinski et al., 2007). A concentration of 0.3% sclerotia in the lactation feed is sufficient to cause agalactia in 50% of sows. Newborn piglets of affected sows develop diarrhea within the first eight days. Some sows or gilts can show lameness, in particular lameness of the hind-quarters and often necrosis can develop on the tail, ears and hooves. The development of clinical signs takes place in a matter of weeks and these are exacerbated by poor weather conditions (Osweiler et al., 1990). Simple withdrawal of contaminated feed leads to a rapid reduction in clinical signs. Milk production returns to normal levels three to seven days after cessation of feeding the contaminated feed.

Apart from the reproductive symptoms, ergot intoxication can cause vasoconstriction and endothelial damage leading to ischemia and dry gangrene especially in the tail, ears and hooves of unweaned piglets. Affected pigs show a drop in feed intake, increased cardiac and respiratory frequency and wasting. In fattening pigs, the drop in ADG is the main symptom and can already be noted at a level of 0.1% ergot in the feed. Higher concentrations lead

to increased wastage of the feed and an increased drop in ADG.

3.3. Trichothecenes

Trichothecenes, produced by *Fusarium* spp. include Desoxynivalenol (DON) and T-2. T-2 is the most important Trichothecene impacting on the reproductive system.

3.3.1. T-2

T-2 is produced by *Fusarium tricinctum* and is one of the most toxic mycotoxins present in wheat, rye, maize and soybeans. T-2 mycotoxicosis or ‘moldy corn disease’ in pigs is characterized by multiple hemorrhages on the serosa of the liver, stomach and esophagus (at necropsy). Blood can be found in the intestines and in the abdominal cavity, and a cream-colored paste on the lining of the esophagus and the ileum (Weaver et al., 1978c).

T-2 has a radiomimetic effect, which makes it a strong immunosuppressant. Experimental contamination of the feed (2 and 3 mg/kg feed) of growing pigs leads to a decreased red blood cell count, and a fall in the MCV and hemoglobin levels of red blood cells. Furthermore, a significant reduction in the number of T lymphocytes can also occur. The effect is dose-related (Rafai et al., 1995).

T-2 also has an important impact on reproductive performance in pigs. One study, feeding contaminated feed of 1–2 ppm to sows during the last third of gestation (Glavits et al., 1983), found an inhibitory effect on the ovaries, with histological degeneration and accompanying atrophy.

Experimental intoxication of sows with T-2 contaminated feed at a level of 12 ppm for 220 days, leads to repeat breeders and small litters with underweight piglets (Weaver et al., 1978a, b). In this study, T-2 had no impact on the general condition of the sows and no lesions were found in the piglets. Another study (Vanyi et al., 1991) looked at the impact of T-2 on piglets following an experimental intoxication of pregnant sows with a daily dose of 24 mg of T-2 during the final third of gestation. The piglets from these sows showed diarrhea, wasting and coma, and died soon after birth. T-2 metabolites were found in the sow’s milk and in the piglets’ stomach content. The coma can be due to hypoglycemia due to a drop in liver glycogen.

3.3.2. Desoxynivalenol (DON)

Desoxynivalenol (DON) or vomitoxin is mainly produced by *Fusarium roseum* or *Fusarium graminearum* under poor storage conditions of grains, leading to a high humidity of the grains (20–22%). Feed contaminated by DON leads to a decreased feed uptake, while high DON levels may lead to vomiting (Diekman and Green, 1992). Research showed that the presence of fusaric acid (FA) enhanced the effect of DON (Smith et al., 1997), already causing feed refusal and vomiting at levels of 0.14 ppm of DON. Increasing levels of FA at constant DON levels, lead to a more severe DON intoxication. FA is usually introduced into the feed by cereals, but can also originate from other feed components such as soy beans.

The feeding of contaminated feed containing DON (Table 4), as well as decreasing food intake, can influence the immune system (cellular and humoral), effect metabolic disturbances in liver and spleen mainly due to inhibition of RNA, DNA and protein synthesis (Smith and Az-Llano, 2009), and cause reproductive alterations resulting in decreased oocyte and embryo development (Tiemann and Danicke, 2007; Ranzenigo et al., 2008). Prepuberal gilts react more sensitively to DON > ZEA feeding compared to pregnant sows. The effects of DON and its relationship to reproduction in pigs is a more indirect effect, mainly linked to the reduced feed intake and with subsequent dysfunction of vital organs like the liver and spleen.

3.4. Aflatoxicosis

Aflatoxins are mainly produced by *Aspergillus flavus* and *Aspergillus parasiticus* and are present in many frequently used feedstuffs (Thieu et al., 2008). Four aflatoxins are described, according to their fluorescence at chromatography: blue (B1, B2) or green (G1, G2). B1 is considered as being the most toxic. A fifth metabolite, M1, is mainly found in milk of animals that have ingested B1-contaminated feed. M1 is also found in tissues and urine of affected animals and is highly carcinogenic. The most susceptible feed components and those used in commercial available pig feedstuffs are peanuts, maize and cotton seeds.

Pigs are highly susceptible to aflatoxins. Aflatoxins bind to the nuclear DNA, thus preventing the pro-

duction of RNA, enzymes and other proteins. M1 binds to the endoplasmatic reticulum and macromolecules, which explains its carcinogenic effect (Booth and McDonald, 1982). These metabolites can be present in the sow's milk and different levels are possible depending on the initial contamination of the feed. Aflatoxins B1, G1 and M1 can all be found in sow's milk (Silvotti et al., 1997). Experimental intoxications have shown damaged lymphocytes and macrophages in piglets, indicating a loss of immune-competence due to the exposure of sows to aflatoxins.

In cases of acute aflatoxicosis, centrilobular necrotic hepatitis can be seen at histology. Clinical signs of acute aflatoxicosis include anorexia, nervous signs and sudden death (Hale and Wilson, 1979).

The half-life for aflatoxin residues is very short. In case of feed concentrations between 355 and 551 µg/kg, the average half-life time is 24 hours. After 48 hours, only minute quantities of residues were found (< 0.5 µg/kg) and after four days there were no residues left (Furtado et al., 1982) (Table 5).

Table 5. Chronic intoxication with aflatoxin B1 (Source: Furtado et al., 1982)

Adult pigs	300–500 ppb during 1 month 450 ppb during 8 to 11 months
Newborn piglets	230 ppb during 4 days
2 week-old piglets	170 ppb during 23 days
6 week-old piglets	400–700 ppb during 42 days
< 23 kg	150–200 ppb during months
Finishers	140 ppb during 3 months 280 ppb during 3 to 4 months 385 ppb during 7 weeks

Jacobson et al. (1978) revealed a logarithmic relationship between the ingested quantity of aflatoxin and the level of B1, B2 and M1 residues. The liver was confirmed as being the ideal organ to monitor aflatoxicosis and determine residue levels. To quantify these levels of contamination Stubblefield et al. (1991) adapted the AOAC method of thin-layer chromatography (TLC) to a LC with fluorescence detection. Using this adapted method, levels of intoxication of up to 0.04 ppb for B1 and up to 0.1 ppb for M1 metabolites in liver could be found.

4. DISCUSSION

4.1. Diagnosis and treatment

The mycotoxins described in this literature review can cause specific reproductive symptoms. The reported symptoms will not only depend on the concentration in the feed and the duration of exposure, but also on the age and life stage of the animal at the time of contamination. Establishing cause and effect is more easily accomplished under controlled experimental single toxin contamination, than under field conditions where multi-toxin contaminations are possible. However, even under experimental conditions, it may be necessary to inject or inoculate the mycotoxin, as pigs may refuse contaminated feed.

Intoxication due to mycotoxins generally cause reproductive failure in a limited number of animals and is rarely seen as a herd problem. The golden rule remains in each suspicious case to have a thorough anamnesis and history of the farm reproductive management, taking into account handlings, movements and imports of gilts, sows and/or boars, hygiene and existing feeding habits. This anamnesis will allow the veterinarian to establish an appropriate differential diagnosis. When the practitioner is clinically convinced that mycotoxin intoxication is causing the reproductive failure, he has to advise the farmer to take preventive and farm management control measures.

Apart from prevention or withdrawal of the contaminated feed, there is as yet no specific treatment.

4.2. Control and prevention

Mycotoxins can already be produced before the feed enters the feed mills and/or animal feeds (e.g. in the field). Prevention of the occurrence of mycotoxin contamination may not always be possible in these cases. Therefore, preventing animals from getting contaminated and the harmful effects of mycotoxin intoxication may often be the only option. It is necessary to understand which effect the mycotoxins have on the health and physiological condition of the animal and to know when mycotoxins can be present in the feed, e.g., uncleaned silos and/or feeders. Quality programs organized in feed mills and regular checking by nutritionists of the quality of feed ingredients, including

possible levels of mycotoxins present in the feed stuffs, can be hugely advantageous in controlling these intoxications and often give a better basis for the evaluation of these toxins than bile and blood examinations (Kauffold et al., 2005a; Danicke et al., 2008). Although analyzing the level of mycotoxins in ingredients may be an option, it is not always easy and requires extensive sampling programs, mainly due to the presence of “hot spots”, i.e. localized colonies of different mold families in a batch of feedstuffs, in the new delivered batches of feedstuffs. The Rapid Alert system for Food and Feed (RASFF) provides responsible end-users with an updated information system showing contamination levels of feed stuffs on a European level. These databases can be consulted at <https://webgate.ec.europa.eu/rasff-window/portal/>. Food or feed inspectors inspect products on the market or at international borders. When the product is non-compliant after sampling it needs to be reported inside the national system, if the concerned authority decides if the issue falls under the scope of the RASFF it will be reported to them. Templates are used to collect all information on the RASFF notification form; the mycotoxins which are mainly reported are aflatoxins, zearalenone and *Fusarium* spp. (6 270, 10 and three times, respectively, since reporting started in 1981). Aflatoxins dominate the database due to their relationship with food for human consumption.

On a global scale, several new analytical methods have been developed, allowing these monitoring programs to be implemented better and more efficiently.

Management and hygiene conditions in the feed mill recorded in the present Good Manufacturing Practices (GMP) manuals, together with farm monitoring by the responsible veterinarian, remain the major tools for prevention of mycotoxicosis. Creating better awareness of certain critical conditions (such as dust, hygiene, temperature and moisture) that facilitate the growth of fungi in feed mills, equipment and on farms (e.g. silos, automatic transport systems and feeders), will lead to more regular cleaning and disinfection of the identified critical points at the different levels in the feed mill and/or farm. Next to these preventive programs, analyzing and monitoring systems need to be in place, especially in modern feed mills using the most recent analytical techniques (Lawlor and Lynch, 2001; Berthiller et al., 2007). Mycotoxins may also be masked from analytical detection by

small molecules (glycosides, glucuronides, fatty acid esters and proteins) attached to the toxin, thus giving a false negative result. Consequently, these masked mycotoxins are not detectable with conventional analytical methods (Berthiller et al., 2005). As well as hygiene, prevention and analytical systems, also other tools may be helpful in the control of mycotoxicosis. They include (1) toxin binders (different natures; Ramos et al., 1996), (2) acidifiers (different combinations of acids for use in feedstuffs and or complete feed; Binder, 2007) and (3) dis-activators of the different mycotoxins present in feed and or feedstuffs (Danicke et al., 2004; Volke et al., 2004).

5. CONCLUSIONS

Symptoms related to mycotoxicosis can occur at toxin concentrations below the detection limit. Knowledge of the effects of mycotoxins is expanding rapidly, mainly because of the development of novel analytical techniques. Despite negative analytical findings, mycotoxins still may be present in feedstuffs. Also, mycotoxins are often not homogeneously dispersed in the feed. This makes sampling difficult and mycotoxins may stay analytically undetected, even with perfect sampling procedures (Binder, 2007). Clinical symptoms are in many cases not very pronounced. The practitioner is a key person on the farm in terms of raising the awareness of a possible mycotoxicosis problem causing reproductive failure in breeding pigs. Problems can only be solved if all parties involved in pig health monitoring take concerted preventive measures and actions.

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Corresponding Author:

Alain Kanora DVM, Huvepharma NV, Uitbreidingstraat 80, 2600 Antwerp, Belgium
E-mail: alain.kanora@huvepharma.com