Mycotoxins – Overview and effects in pigs

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Introduction

Mycotoxins are a relatively large, diverse group of naturally occurring, fungal toxins, many of which have been strongly implicated as chemical agents of toxic disease in humans and animals. They are unavoidable contaminants in foods and feeds and are a major problem all over the world (Wood, 1992). The word *mycotoxin* simply means a toxin produced by a fungus commonly known as moulds. Moulds can invade feed and produce toxic compounds that contaminate the feed. Moulds can infect grain in the field, during harvesting, handling, and storage. The number of mycotoxins known to induce signs of toxicity in mammalian and avian species is unknown and different numbers are suggested. The number exceeds 300 (Fink-Gremmels, 1999; Leeson *et al.,*, 1995) and is steadily increasing. The most significant mycotoxins in naturally-contaminated foods and feeds are aflatoxins, ochratoxins, zearalenone, T-2 toxin, vomitoxin and fumonisins (Devegowda *et al.*, 1998) and in many cases these mycotoxins can be found in combination in contaminated feed. Each plant can be affected by more than one fungus and each can produce more than one mycotoxin. Consequently, there is a great probability that many mycotoxins are present in one feed, thus increasing the odds of interactions between mycotoxins and the occurrence of synergistic effects, which are of great concern in livestock health and productivity. It is evident that due to different production, handling, transport and storage conditions, toxin profiles can differ substantially between area, locality, season and even countries. The consequences of these differences is that worldwide trade of food and feed commodities has also resulted in a worldwide distribution of contaminated materials with different toxin profiles.

From the large number of identified mycotoxins, only a few are believed to affect swine performance. Risk to the pig from mycotoxin-contaminated feed depends on the age and health of the pig and level of toxin in the feed. The most severe effect is death, but low levels of mycotoxin can reduce pig performance and general well being. When pigs eat feed containing a harmful mycotoxin, the toxin can affect the pig's central nervous system, liver, kidney, immune system, or reproductive process.

Aflatoxin, zearalenone, and tricothecene (vomitoxin and T-2 toxin) are the most often reported mycotoxins in swine feed. Each toxin is produced by a different mould. The conditions that promote growth of moulds vary, although high moisture and warm temperatures are responsible for most mould growth on feedstuffs (Cranshaw, 2008).

Current status of mycotoxin awareness in South Africa.

In the formal animal feed industry, The Animal Feed Manufacturers Association (AFMA) addressed mycotoxins in order to give guidance as far as mycotoxin management and responsible production of safe animal feeds for safe food in South Africa is concerned. AFMA published a “Code of practice for the control of mycotoxins in the production of animal feed for livestock June 2003”. The code provides an overview on mycotoxins; guidelines for establishing Good Practices for the control of

mycotoxins in the Feed Industry; and interim guidelines on maximum acceptable levels of mycotoxins in animal feeds until local and/or internationally accepted regulations are set.

More efforts are currently under way by a National Mycotoxin Group supported and funded by the Maize Trust with participation by interested industries. Five focus areas were identified in the field of Mycotoxins research:

1. Guidelines for Mycotoxins in food and feed;
2. A MycoMap to be established for Mycotoxins;
3. A Prediction Model to be established for Mycotoxins;
4. Identification of the Risk Areas where Mycotoxins occurs; and
5. Identifying new areas of research in Mycotoxins.

Due to the fact that the Maize Trust indicated its willingness to fund projects related to the above focus areas it was confirmed that as an initial phase, all the above research should focus on Maize and Maize related products / aspects. Other Trusts could be approached after a good start has been made on the mentioned areas.

The Southern African Grain Laboratory (SAGL) annually publishes analytical results of the South African grain crop (Maize and Wheat) (available on their Website). As grains (maize) are one of the biggest contributors to mycotoxins in animal feeds, the information is handy in order to guide the different feed and animal production industries on the status of the South African crop (and imports) on levels and tendencies.

Short description of the major Genera of Mycotoxigenic Fungi and most common mycotoxins

The majority of the known toxigenic fungal species fall into three recognized genera. These genera are *Aspergillus*, *Penicillium*, and *Fusarium*. Also, most of the known mycotoxins are elaborated by these genera (Table, 1). The major classes of mycotoxins are aflatoxins, trichothecenes, fumonisins, zearalenone, ochratoxin A, and ergot alkaloids.

Aspergillus flavus and ***A. parasiticus*** produce primarily aflatoxins and they are important agents of disease; their effects range from acute death to chronic disease such as tumours.

Fusarium species represent several fungal Genera and produce a large class of mycotoxins of which the trichothecenes are the most notable (*Stachybotrys* is a significant producer of selected trichothecenes as well). The most commonly occurring trichothecene is deoxynivalenol (DON or vomitoxin), which can be a significant contaminant of wheat, barley and maize. T-2 toxin is another trichothecene found frequently in grains.

The fumonisins occur primarily in maize and are produced by *F. verticillioides*, an almost-universal pathogen of maize. These toxins are capable of causing significant disease symptoms in horses and swine.

Zearalenone is produced primarily by *F. graminearum* and causes vulvovaginitis and estrogenic responses in swine. It may also co-occur with DON in grains such as wheat, barley, oats, and maize.

Penicillium verrucosum produces primarily ochratoxins and may cause disease, especially in swine, affecting the kidney.

Claviceps species primarily produce Ergot alkaloids, and elaborate their toxins in specialized masses of fungal tissue called sclerotia. Ergotism is one of the oldest recognized mycotoxicoses.

Table 1. ***Major fungi genera with associated mycotoxins (From Swamy, 2003)***

Fungi	***Mycotoxin***
Aspergillus	Aflatoxins, ochratoxins, cyclopiazonic acid, citrinin
Penicillium	Ochratoxins, citrinin, cyclopiazonic acid,
Fusarium	Trichothecenes [T-2 toxin, deoxynivalenol (DON), diacetoxyscirpenol (DAS)], Fumonisins, zearalenone, zearalenol, nivalenol, , HT-2 toxin, , fusaric acid
Claviceps	Ergot alkaloids

Mycotoxicoses of pigs

Introduction

Mycotoxins cause illness and lethality in domestic animals fed mouldy feedstuffs. These acute intoxications can have devastating effects and are difficult to diagnose and treat because the suspect feed may be consumed before it can be tested. Because of the large number of structurally unrelated mycotoxins produced by the various fungi, it is difficult to pinpoint which toxin(s) is responsible for a particular outbreak, even if a mycotoxicoses is strongly suspected. The economic impact of lowered productivity, decreased weight gain and feed efficiency, increased disease incidence because of immune system suppression, subtle damage to vital body organs, and interferences with reproduction is many times greater than that of immediate morbidity and lethality. Diagnosis of naturally occurring mycotoxicoses, however, is difficult because there are a multiplicity of factors such as breed, sex, environment, nutritional status, and other toxic entities that can affect the intoxication.

In Table 2, the mycotoxin status of the SA maize crop for the last three seasons is given (SAGL data) as well as the guidelines for the maximum acceptable levels in animal feeds for Pigs by AFMA, (2003).

Class	**South African Maize Crop Quality Averages per season (SAGL 2008)**			**Guideline to Maximum Acceptable levels in animal feeds (AFMA)**		
Mycotoxins	**2004/2005**	**2005/2006**	**2006/2007**	**Nursing**	**Growing**	**Sow**
Total Aflatoxin, ppb(ug/kg) [max. value]	0 [0.00]	0 [0.00]	0.17 [9.00]	20	20	20
Fumonisin, ppm(mg/kg) [max. value]	1.06 [6.60]	0.97 [3.40]	0.64 [4.50]	10	10	10
Deoxynivalenol, ppm(mg/kg) [max. value]	0.53 [3.86]	2.74 [6.20]	0.53 [3.10]	0.3	0.3	0.3
Ochratoxin, ppb(ug/kg) [max. value]	0.04 [2.40]	0.03 [2.90]	0.50 [6.50]	0.2	-	-
Zearalenone, ppm(mg/kg) [max. value]	0.02 [0.44]	0.12 [0.39]	0 [<0.1]	0.2	0.2	0.1
No. of samples	**100**	**90**	**90**			

Aflatoxins

Aflatoxin is produced by *Aspergillus flavus* which can germinate at moisture levels of 15 to 17% but infection and growth require higher moisture (Cranshaw, 2008). The aflatoxins are potent liver toxins and most animal species exposed to these mycotoxins show signs of liver disease ranging from acute to chronic. These toxins may be lethal when consumed in large doses. Generally, young animals are more susceptible than older ones to the toxic effects of aflatoxins. Aflatoxin toxicity has been reported in suckling piglets, growing and finishing pigs, and breeding stock. Clinical and pathological signs include decreased rate of weight gain, decreased feed conversion efficiency, toxic hepatitis, nephrosis, and systemic hemorrhages (Hoerr and D'Andrea 1983; Miller et al. 1981, 1982). The effects of aflatoxins in pigs vary, depending on age, diet, concentration, and length of exposure. Swine appear to be resistant to dietary levels of aflatoxins up to 300 ppb fed from time of weaning to marketing (Monegue et al. 1977). However Cranshaw, (2008) mentioned that Aflatoxin at low levels (20 to 200 ppb) suppresses the immune system and makes pigs more susceptible to bacterial, viral, or parasitic diseases. Long term consumption of contaminated feed may cause cancer, liver damage, jaundice, and internal bleeding. Profits are reduced because of loss in feed efficiency, slower growth, and increased medical costs. High concentrations of aflatoxin (1,000 to 5,000 ppb) result in acute effects, including death (Cranshaw 2008). USA guidelines establish a maximum of 300 ppb for total aflatoxins (B1+B2+G1+G2) in swine feed, but specify limits of 200 ppb for finishing swine, 100 ppb for breeding swine, and 20 ppb for immature animals (Abramson, 2001). European Community guidelines specify an upper limit of 20 ppb aflatoxin B1 in swine feed (Smith, 1997). The guideline for maximum acceptable levels in animal feeds published by AFMA, (2003) also specifies 20 ppb as the maximum value for all classes of pigs (Table 2).

Aflatoxin M1 has been found in the milk of sows fed diets containing aflatoxin. Pigs nursing sows consuming feed with 500 to 750 ppb of aflatoxin had higher death rates and slower growth. Pigs were permanently stunted, and performance was reduced throughout the growing/finishing period, even though they were not exposed to aflatoxin after weaning (Cranshaw, 2008).

High Aflatoxins levels are not very common in the South African grain crop. During the 2006/2007 the SA grain Laboratory (SAGL) reported the detection of Aflatoxin in only three out of the 54 randomly selected samples of maize tested (Table 2). Stated values were between 0.25 and 9.0 parts per billion (ppb) which is way lower than levels that would affect pig production. Imported maize from Argentina and other African countries showed the same tendency. Although levels seem negligible, random testing is still needed as a warning system.

Trichothecenes (DON; T-2 toxin and DAS)

The **trichothecenes** are potent inhibitors of protein biosynthesis and most effects in animals have this basic attribute.

Deoxynivalenol (DON)

Deoxynivalenol (DON) is the most common of the trichothecene group causing animal disease, and effects range from feed refusal and vomiting to immunosuppression and loss of productivity. DON is common in cereal grains, and of the trichothecenes, poses the greatest problems to animal health (reviewed by Miller et al., 2001; Rotter et al., 1996). Although DON can be acutely lethal when ingested in large quantities, moderate- to low-level ingestion of the toxin can cause poor performance and altered immune function (Pier et al., 1980a, b). Monogastric animals, particularly swine, exhibit

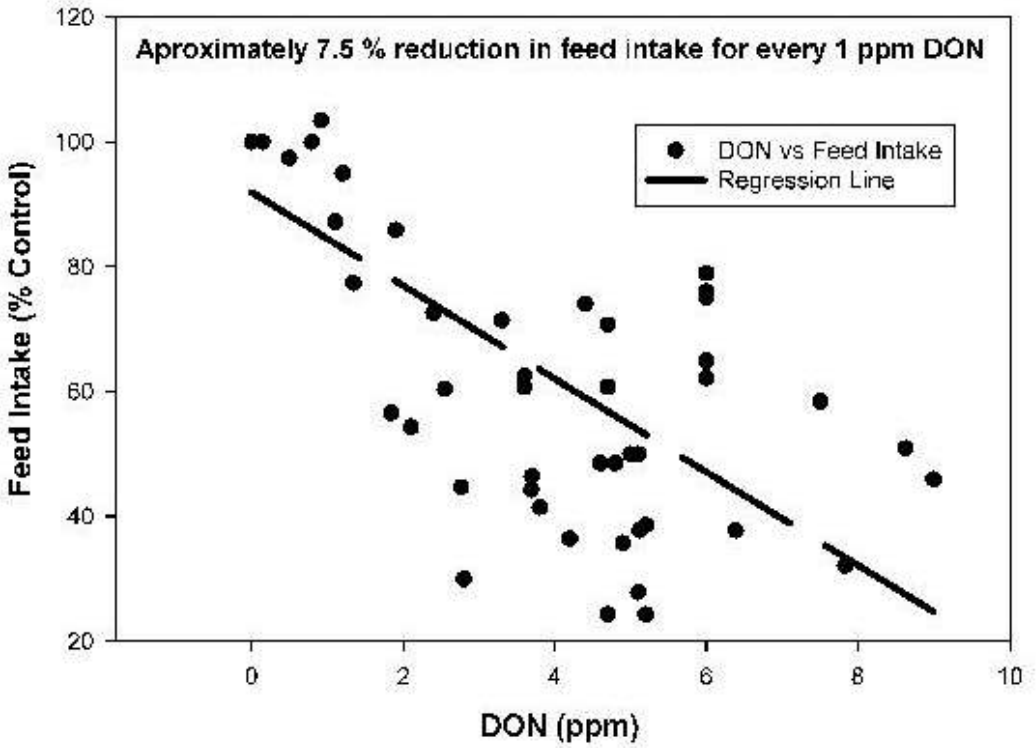
the greatest sensitivity to DON, while chickens and turkeys, followed by ruminants, appear to have higher tolerance (Prelusky et al., 1994b).

Diminished feed consumption and lower weight gain are the principal clinical effects seen in pigs that have eaten DON in naturally contaminated feeds (2 ppm feed) (Friend et al., 1982; Rotter et al., 1994b; Trenholm et al., 1984). At 1.3 ppm DON in diet, feed intake by growing pigs is significantly decreased, followed by complete feed refusal at 12 ppm and vomiting at 20 ppm (Abbas et al., 1986; Forsyth et al., 1977; Young et al., 1983). The most common signs of acute DON exposure are abdominal distress, increased salivation and malaise; however, vomiting has been reported at higher dietary concentrations (Vesonder and Hesseltine, 1981; Young et al., 1983). In fact, the observation that DON consumption caused swine to vomit led to the use of the term vomitoxin to describe this compound (House, 2003). Extensive lesions are not typically documented in field cases, because pigs regulate toxin ingestion by adjusting their feed intake (Chavez and Rheaume, 1986; Friend et al., 1986; Harvey et al., 1989b). Although pigs fed DON exhibit altered blood parameters, these effects cannot be easily separated from nutritional status, i.e., weight loss as a result of significantly decreased feed intake (Lun et al., 1985; Young et al., 1983). Nevertheless, altered stomach condition and serum protein status do indicate a specific effect of *Fusarium* toxins/DON (Prelusky et al., 1994a; Rotter et al., 1994b, 1995b). DON is considered one of the least toxic trichothecenes with regard to mortality.

The extent to which DON affects pigs relates to age and sex as well as to the contamination source (Trenholm et al., 1984; Foster et al., 1986; Prelusky et al., 1994b). Initial studies reported that detrimental effects can be observed when purified DON is added at a level of 5 ppm (Trenholm et al., 1984); however, the situation with naturally contaminated diets is more complex. Because *F. graminearum* produces many metabolites besides DON (Miller 1995), mycotoxicoses may be caused by multiple toxins. Unidentified/bound toxins, conjugated mycotoxins, or toxic agents of other origin might contribute substantially to the animal response (Foster et al., 1986; Prelusky et al., 1994b).

Figure 1 depicts data derived from a number of studies that were conducted to examine the impact of dietary DON on feed intake, measured during the first few weeks of exposure. Each point represents a treatment mean value and the line of best fit has been plotted. On the basis of simple regression analysis, an estimated 7.5% reduction in feed intake is expected for every 1 ppm DON found in the diet.

Figure 1. The impact of dietary DON concentration on feed intake in swine. Data represent mean values derived from published literature (Referred by House, 2003).



The fact that a substantial proportion of the data available comes from research conducted in Eastern Canada raises the questions as to whether regional differences in mycotoxin profiles and grain utilization (maize vs. wheat and barley) could influence the responses observed (House, 2003)

In Canada two studies with 144 Cotswold pigs (72 barrows, 72 gilts), with a starting weight of 22 kg, were done in order to establish the effect of DON on feed intake and performance. The presence of DON in the diet at 2 ppm resulted in a 7.6% reduction in feed intake relative to the 0 ppm DON diet, with pigs consuming the 1 ppm diet having intermediate levels of feed refusal. Despite the reduction in feed intake, average daily gain was not affected (approx. 820 g/d). Because the animals were not split sex fed, it was not possible to determine the impact of DON on feed intake for the sexes, but gilts were more sensitive to the presence of DON than were barrows, as judged by the time required to reach market weight.

The presence of DON in the diet at 1 and 2 ppm increased the median time required to reach market weight by 5.2 and 14.1 days, respectively, relative to the 0 ppm treatment ($P<0.05$). To summarize the first trial, DON at levels of 2 ppm were well tolerated by barrows, however gilts showed a higher sensitivity to the presence of this mycotoxin in the diet.
In a second trial with grain grown in another season, the presence of up to 4 ppm DON in the diet had no adverse effects on swine over the entire grower -finisher period. Therefore, unlike the previous study, gilts did not seem to be sensitive to the presence of DON in the diet. The reason for the different results between the two trials is not readily apparent, but may be *different sources of DON-contaminated grain* -Therefore, the possibility exists that, even though the DON content of the experimental diets were set (and confirmed), other mycotoxins might be present that could influence the results. *Seasonal effects* must thus not be ruled out, as the first trial was conducted in the late fall-early winter and the second trial was conducted in the summer. The possibility exists that temperature, ventilation rates, disease pressure, or other factors may have influenced the data obtained.

On the basis of the above findings, both starter and grower-finisher pigs, of modern genotype, are able to tolerate DON in the diet when present at levels above 1 ppm. Barrows appear able to tolerate levels of DON up to 4 ppm in the grower-finisher stage. Producers using split-sex feeding programs may be able to channel DON-contaminated grains to the feeding of male pigs. However, on the basis of the results from the first grower-finisher trial, care must be taken when formulating diets for gilts, and guidelines (maximum 1 ppm DON) should be adhered to. While data on the impact of DON on the reproductive herd is minimal (Authors quoted by House, 2003).), the observed sensitivity of gilts to DON provides some justification for ensuring that the DON content of gestation and lactation diets is as low as possible.

Tolerance to DON may provide some clues about the toxin's mode of action. At lower dietary DON concentrations, reduction in food intake is transitory in several species, e.g., pigs, mice, lasting only a few days before animals begin to compensate for initial losses (Côté et al., 1985; Friend et al., 1982; Rotter et al., 1992, 1994a). With increased DON levels in feed, animals may not return fully to control intake but the extent of feed refusal diminishes with time. Several lines of evidence suggest that tolerance development occurs with most anorexic compounds that rely on a central serotoninergic mechanism (Silverstone 1992).

For the South African situation it is an open question how the different breeds and the additive effects of DON and the cumulative effect of other mycotoxins would influence intake and production. DON is probably one of the mycotoxins that we need to be aware of in our grains if we look at the SAGL data (Table, 2). The SAGL analyses for maize during the 2006/2007 season detected DON in 47 % of the samples tested with an average of 0.5 ppm with a maximum of 3.1 ppm (SAGL, 2008). Average values per season are higher than the maximum acceptable levels for all classes and especially the 2005/2006 season showed a high average value of 2.74 ppm that is way higher than the maximum acceptable values of 0.3 ppm.

T2 and DAS

Pigs are sensitive to T-2 toxin and very sensitive to DAS (Lewis & Southern, (2000). The levels of T-2 toxin and DAS in feed that will exert negative effects on pig performance, reproduction and health are less well documented. Friend et al. (1992) reported a tendency for lower feed intake and gain when T-2 toxin was included in the diet at 0,4; 0,8; 1,6 and 3.2 ppm. Although negative effects were observed at the lower levels, they concluded that a reduction in performance may occur at approximately 3 ppm. The AFMA guideline for T-2 toxin is however 0.2 ppm for all pigs.

The T-2 toxin consumption over time by breeding sows has caused drastically decreased conception rates and weak piglets. High levels of T-2 toxin can also cause dermatitis of the skin on the snout, dorsal part of the nose, behind the ears, around the prepuce as well as on the mucous membrane of the oral cavity and the tongue. T-2 toxins are not analysed as part of the SAGL program, but other Trichothecenes such as DON, can most probably serve as a marker toxin for the group.

Ochratoxin A

Ochratoxin is the most important of the *Penicillium* mycotoxins. It is particular serious for the poultry and swine industries because monogastric animals lack the ability to degrade ochratoxin rapidly, as compared to ruminants (Abramson, 2001). Ochratoxin A, a nephrotoxic mycotoxin produced by several *Aspergillus* and *Penicillium* species, primarily affects the kidneys in animals exposed to naturally occurring levels (Krogh, 1977). Changes in the renal function of pigs exposed to ochratoxin A include impairment of proximal tubular function, altered urine excretion, and increased excretion of

urine glucose (Krogh, 1976). Extra renal effects may have occurred in animals exposed to levels of Ochratoxin A in feed greater than 5 to 10 ppm. These effects included enteritis, necrosis of lymphoid tissue, and fatty change in liver (Szczech et al., 1973).

A major renal disease in swine known as porcine nephropathy that occurs in certain European countries, particularly Denmark, is associated with the consumption of ochratoxin-contaminated barley (Hald, 1991). Affected pigs show signs of pain in the kidney area, consume excessive amounts of water, appear depressed, urinate almost continuously, and have decreased feed consumption. The impaired renal function results in glucosuria and proteinuria, with casts evident in the urine. Pathologically, the kidneys are bilaterally affected, showing enlargement and paleness with large amounts of connective tissue evident in the cortex when viewed on a cut surface. Histopathologically, there is tubular degeneration and atrophy, interstitial fibrosis, and, perhaps, hyalinization of the glomeruli (Hald ,1991).

According to Krogh (1991) ochratoxin is hazardous to swine at low levels, typically 0.2 ppm. If ingested over a long enough period of time by swine, this toxin can contaminate most of the edible tissues, and can produce enough kidney damage to result in condemning the carcass. As ochratoxin residues in animal products are transmissible to consumers, some national governments have taken stringent measures to allay consumer fears regarding their pork products. In Denmark, for example, an entire swine carcass is considered contaminated, and is condemned, if 25 μg/ml ochratoxin is detected in the blood.

Ochratoxin contaminates a variety of plant and animal products, and is particularly likely to appear in stored cereal grains. This mycotoxin is a worldwide problem, and its impact is greatest in temperate climates where much of the world's grain is produced and stored. Ochratoxin is found in meat products from monogastric animals, and has been frequently detected in pork products from Europe.

Ochratoxin tested positive in thirteen maize samples for the 2006/2007 season in the SAGL analysis report. Positive samples tested between 0.97 ppb and as high as 6.5 ppb. These values are way higher than the 0.2 guideline given by AFMA (2003) for piglets and the same value quoted by Krogh (1991)

Fumonisins

Tests in the USA involving intubation with pure fumonisins, or feeding highly contaminated feed (200 ppm), resulted in pulmonary oedema, accompanied by liver damage and pancreatic lesions (Abramson, 2001). Some cases of pulmonary oedema were observed in weaned pigs at lower contamination concentrations, between 10 and 40 ppm, but with longer feeding periods of 28 days (Hascheck et al., 2001). Several symptoms of pulmonary oedema were detected in a group of 20 weaned pigs which received contaminated feeds with Fumonisins in concentrations of 10, 20 and 40 ppm during a four week period; three animals had minor lesions at 10 ppm; two pigs had minor lesions and two pigs presented serious lesions in the group receiving 20 ppm; but five pigs showed serious lesions in the group which received the higher contamination of 40 ppm (Zomborszky et al., 2000).

Screenings and broken kernels contain higher levels of mycotoxins. Fumonisins tested positive in most of the SAGL samples for the 2006/2007 season, and levels were on average 0.64 ppm with a maximum of 4.5 ppm. Imported maize from other African countries and Argentina showed slightly

higher levels with an average of 1.66 ppm and a maximum of 5.3 ppm. All these levels are lower than the maximum 10 ppm guidelines for all classes of pigs by AFMA (2003).

Zearalenone and Ergot alkaloids.

Two of the most prominent mycotoxins that can cause reproductive effects are Zearalenone and Ergot alkaloids.

Zearalenone

The major effects of zearalenone are estrogenic and primarily involve the urogenital system. Swine are the most commonly affected animals, although cattle, poultry, and laboratory rodents also are affected (Hagler et al., 2001). Hyperestrogenism in female swine may be manifested as swelling of the vulva and enlargement of the mammary glands, especially in prepubescent gilts. Dietary concentrations of 1.0 ppm zearalenone or more may produce hyperestrogenism in pigs (Kurtz and Mirocha, 1978). Zearalenone has been associated with feminization in young male swine, including testicular atrophy, swollen prepuce, and mammary gland enlargement; decreased libido may be a variable consequence but mature boars apparently have enough testicular reserve to avoid decreased spermatogenesis. In severe cases, this syndrome may progress to rectal and vaginal prolapse. Other effects related to higher concentrations include anoestrus, nymphomania, and pseudo pregnancy.

The mode of action of zearalenone and its derivatives involves displacement of estradiol from its uterine binding protein (Hidy et al., 1977), elucidating an estrogenic response (Hagler et al., 2001). The South African grain crop for the last three seasons had lower average Zearalenone levels than the guideline minimum acceptable levels by AFMA (2003). Maximum analysis values were however higher than these maximum acceptable levels for the 2004/2005 and 2005/2006 seasons and warrant attention in order to be aware of any toxicity signs.

Ergot Alkaloids

Abortion may be a variable and controversial sequel to ergot ingestion, depending on species affected and alkaloid content of sclerotia. Ergot-contaminated diets of pregnant swine are associated with decreased piglet birth weights and increased stillborn rates; gestation time may be shorter or longer than normal. Ergot also inhibits prolactin secretion in pregnant swine, resulting in diminished udder development and agalactia at farrowing. Severity of effects is directly related to dietary concentrations; feeds containing at least 0.3% ergot sclerotia have definite detrimental effects on overall reproductive performance (Burfening, 1973; Loveless, 1967). Altered reproduction patterns and reproductive failures in swine are associated with ergot (Bailey et al., 1973).

Individual versus multiple mycotoxin contamination.

The scientific literature is replete with information on the effects of individual mycotoxins in various livestock species. Multiple mycotoxin contamination is an area that has recently become of greater concern to the livestock industry. The concern arises from the fact that concentrations of individual mycotoxins associated with poor livestock performance and/or disease syndromes in commercial operations usually are lower than those reported to cause toxic effects in controlled laboratory studies. Additionally, in some of these reports the feed contained more than one mycotoxin. For example, aflatoxin and fumonisin B1, and vomitoxin and zearalenone commonly occur together in the same grain. Many fungal species also are capable of simultaneously producing several mycotoxins. Therefore, an individual grain may be naturally contaminated with more than one mycotoxin (Trenholm et al., 1989), or the incorporation of numerous grain sources, which are each contaminated with a different mycotoxin(s), into a single feed may result in a diet that contains a number of

different mycotoxins. Poor livestock performance and/or disease syndromes, reported in commercial operations, may be due to synergistic interactions between multiple mycotoxins. When mycotoxins are fed in combination, interactive effects can be classified as additive, less than additive, synergistic, potentiative, or antagonistic (Klaasen and Eaton, 1991; Kubena et al., 1988). Mycotoxin interaction studies published in refereed journals reported in all cases that the interactive effects of only two mycotoxins were studied.

Results of these studies should be interpreted with some caution. Many of the studies involved acute or sub-acute levels of mycotoxins, whereas syndromes reported in the field occur with much lower concentrations of mycotoxins. Also, only pairs of mycotoxins were evaluated in these studies, whereas under commercial conditions contaminated feeds may contain two or more mycotoxins. Finally, studies were conducted under laboratory conditions where animals generally are not exposed to many of the environmental stressors (heat, ammonia, disease, etc.) that occur under commercial conditions. Future research in the area of mycotoxin interactions should include combinations of two or more mycotoxins at concentrations that commonly occur in the field. These data suggest that mycotoxin synergism may be less of a concern than had been suggested by field outbreaks where multiple mycotoxins had been implicated as possible intoxicants. Further research that evaluates lower concentrations of multiple mycotoxins under commercial environmental conditions is warranted.

Preventing Mycotoxin formation

The prevention of mould growth, mycotoxin production and the detoxification/binding of mycotoxins is quite diverse and a topic that can be elaborated on substantially.

Preventive actions can start before harvesting and initial storage, over which many pig producers have little control.

Pre-harvest control

To lower pre-harvest contamination, treatment of field crops with fungicides used to be the traditional technique (Mesterházy and Bartók, 1996). However, environmentally more friendly alternatives have been sought recently. Damaged feedstuffs are readily available food sources for mould growth. Any time the grain kernel is cracked and the endosperm is exposed, the probability of mould growth increases. During harvest, equipment should be adjusted to lessen kernel damage and remove foreign matter.

Resistance breeding

Plant breeding is traditionally used to improve the resistance of the host plants to fungal infection. Such attempts are promising e.g. in the case of *Fusarium* infection of wheat and maize (for a review, see Munkvold, 2003).

Biocompetitive exclusion

There are also promising results for lowering fumonisin contents of maize, and for controlling deoxynivalenol levels in wheat using biocompetitive exclusion (Cleveland et al., 2003).

Genetic engineering

Genetic engineering can either be used to modify plant genes to become less susceptible to fungal infection or mycotoxins, or genes responsible for detoxification can be introduced to the plant. The identification of microbial species that metabolize fumonisins to CO_2 has opened up the possibility of engineering maize that detoxifies fumonisins (see below; Duvick, 2001).

Postharvest control

Although the prevention of mycotoxin contamination in the field is the main goal of agricultural and food industries, the contamination of various commodities with *Fusarium, Aspergillus, Alternaria* and *Penicillium* fungi and mycotoxins is unavoidable under certain environmental conditions. For postharvest control, storage conditions should be improved to minimize the mycotoxin content of foods and feeds. Mycotoxin production is dependent on a number of factors, e.g. water activity of the stored product, temperature, gas composition, the presence of chemical preservatives and microbial interactions. An integrated approach for controlling several of these factors could give much more effective control of deterioration without requiring extreme control of any one factor.

Decontamination/detoxification procedures are useful in order to recuperate mycotoxin contaminated commodities. While certain treatments have been found to reduce levels of specific mycotoxins, no single method has been developed that is equally effective against the wide variety of mycotoxins which may co-occur in different commodities. Several strategies are available for the detoxification or decontamination of commodities containing mycotoxins. These can be classified as physical, chemical and (micro) biological approaches

On farm control

Storage conditions are important. The critical point for controlling fungal growth in storage is grain moisture content. Grain that is dry when placed in storage and kept dry (less than 14 % moisture) is unlikely to support growth of fungi that produce mycotoxins. Grain storage bins should be kept clean and in good repair. Condensation, which sets the stage for mould growth and toxin production, should be avoided. Feed and grain storage bins should be cleaned frequently to prevent feedstuffs from bridging and forming hot spots.

Consider treating the grain before storing with an insecticide to reduce insect damage. Fungal inhibitors, such as propionic acid, may help prevent fungal growth in stored grains. However, fungal inhibitors have no effect on mycotoxin already present in the maize at the time of application. They only prevent further growth of fungi.

Ground feed is an ideal source of food for fungal growth. During periods of high humidity and heat, ground feedstuffs and/or swine diets should not be stored for more than 10-14 days. Maize screening is an excellent medium for fungal growth and has been associated with Fumonisin toxicity. If feed ingredients or completely mixed diets appear to have mould growth, then it is best to sample the ingredients or mixed diets before feeding to livestock.

Less well understood, perhaps, is the fact that the geographic distributions of some toxins may be localized down to the farm level. Producers need to establish their own historical record of mycotoxin exposure and monitor for deviations from that pattern (Doerr, 2003). The producer, then, needs to be in a position to monitor for one or more ‘marker’ toxins that will allow some reasonable conclusions to be drawn as to the overall mycotoxicological quality of the feeds and forages in use. A marker toxin derives from the fact that since many moulds produce more than one toxin, and that some toxins are far easier to assay than others, using simple means to deduce the extent of contamination is most efficient.

Troubleshooting also raises the issue of what actions to take once a problem is detected. A first approach recommended is to make maximum use of steps likely to reduce the risk of serious mould

infestation and subsequent mycotoxin formation such as listed in Table 3. It needs to be realized that application of all preventive measures does not provide for foolproof protection. “Breaks” will occur and even the most diligent producer should expect to have a problem now and then. Furthermore, what appears to be a uniform environment is often far from it. Pig feeds in an on-farm storage tank might seem like a relatively constant product. However, just within the tank, temperature differentials created by rise and fall of the sun create very discreet microenvironments, some of which change moisture contents sufficiently to support germination and growth of mould spores.

Table 3. Preventive Measures (Doerr, 2003)	
Minimize moisture	General rule of thumb for feeds and ingredients is to control moisture to about 12 - 12.5 % moisture[a]
High quality feed ingredients	Cracks, fines, damage, off-colour, low protein, foreign material, etc. all tend to correlate with mycotoxin risk
Sanitized equipment	Storage tanks, trucks, mixers, feed troughs, etc.
Short feed residence time on-farm	The longer a rich nutrient source remains in storage, the greater the toxin risk
Crop selection	Seek appropriate cultivars. Caution: Some varieties bred to resist one mould may be more susceptible to another.
Prevent insect damage	
Use appropriate anti-fungal compounds at sufficient application rates	As a rule, a given amount of mould inhibitor buys a given amount of preservation time. That protection is subject to variation due to moisture and other factors.
[a] Over drying of grains results in damage which can increase risk of mould infestation.	

Sampling and Analysis

Commercial enzyme immunoassay kits (ELIZA) are available to screen commodities for DON, T-2 toxin, fumonisin B1 and zearalenone (Abramson, 2001). These TLC and HPLC measurements by contract laboratories can perform the tests within a reasonable time. It is important to have assurance that such methods have been thoroughly validated. The most critical part of any analytical procedure for mycotoxins is sampling the commodity in a truly representative manner (Whitaker, 2000). For example, published studies of aflatoxins in peanuts have shown that only 6 % of the total testing error is due to the analytical method, while 94 % is due to sampling and sub-sampling problems. It is strongly advised to employ well-validated protocols in obtaining representative samples of grain for mycotoxin testing. This would ensure that end-use decisions regarding the commodity tested are based on valid results.

Strategies to control mycotoxins in feeds

Broadly speaking, the aim of detoxification is to inactivate or remove the mycotoxin, while leaving no chemical residues from the process. Furthermore, the palatability and nutritional value of the commodity should be maintained. The low market price of feed ingredients such as cereal grains requires that detoxification be cost-effective (Abramson, 2001).

For lowering mycotoxin contamination of feeds and foods, several strategies have been investigated. These can be divided into biological, chemical and physical methods (Varga et al., 2004).

Physical methods

Mechanical separation, density segregation, colour sorting, removal of the fines or screenings from grains significantly reduces the mycotoxin content of these grains. Simple washing procedures, using water or sodium carbonate solution, result in some reduction in concentrations of DON, zearalenone and fumonisins in grains or maize cultures. Gamma irradiation has successfully been used to control ochratoxin levels in feeds

Physical/mechanical methods are available for removing infected grains or screenings, involving washing procedures and eradiation (Refai et al., 1996). These methods might be impractical and not cost effective.

In-feed adsorbents and binders

There are a number of products available that target specific mycotoxins by adsorbing, binding or detoxifying by bio-transformation.It is of utmost importance when using such products to identify the type of mycotoxin/s and apply the correct product. In the 80's, Phillips et al. (1988) showed that hydrated sodium calcium aluminosilicates (HSCAS) have high affinity for aflatoxin B1 after screening 38 different adsorbents that were representative of the major chemical class of aluminas, silicas and aluminosilicates (activated carbon, sodium bentonite, calcium bentonite and zeolites). HSCAS are phyllosilicate clays which are very effective with regard to preventing aflatoxicosis in a variety of animals (Huwig et al., 2001). The efficacy of HSCAS was quite limited against zearalenone and ochratoxin A and totally ineffective for trichothecenes such as T-2 toxin, diacetoxyscirpenol and DON. Beneficial effects of activated carbon have been shown in rats intoxicated with T-2 toxin, and showed *in vitro* the capacity to adsorb fumonisin B1 and ochratoxin A from aqueous solutions although it was ineffective in reducing the toxic effects of fumonisins in *in vivo* experiments (Huwig et al., 2001).

Dried whole yeast cell mass, yeast cell wall extracts and wall components of *Lactobacillus rhamnosus* have also been observed to be able to bind mycotoxins (Turbic et al., 2002; Lahtinen et al., 2004). The yeast cell walls harbouring polysaccharides (glucan, mannan), proteins and lipids exhibit numerous different and easily accessible adsorption centres including different adsorption mechanisms, e.g. hydrogen bonding, ionic, or hydrophobic interaction. Therefore, it was possible to bind 2.7 mg zearalenone per gram of cell wall (Huwig et al., 2001). A modified yeast glucan could also be used to adsorb T-2 toxin and zearalenone efficiently (Freimund et al., 2003). A polymeric glucomannan adsorbent prepared from yeast cell wall has also been used successfully to overcome *Fusarium* mycotoxicoses in swine (Swamy et al., 2002).

Chemical methods

A wide variety of chemicals have been found to be effective (to different extents) against several mycotoxins. The chemicals used fall into the categories of acids, bases (e.g. ammonia, sodium hydroxide), oxidizing reagents (e.g. hydrogen peroxide, ozone), reducing agents (e.g. bisulfite, sugars), chlorinating agents (e.g. chlorine), salts and miscellaneous reagents such as formaldehyde. Ammoniation is the method that has received the most attention for detoxification of aflatoxin- or ochratoxin-contaminated feeds and has been used successfully in several countries (Chelkowski et al., 1982).

Sodium bisulfite has been shown to react with aflatoxins and trichothecenes to form sulfonate derivatives while peroxide and heat enhance the destruction of aflatoxin B1 by sodium bisulfite. Since DON-sulfonate appeared to be nontoxic to pigs, this treatment has been proposed for decontaminating DON contaminated maize destined for use in pig feeds

Biological methods

Biological detoxification can be defined as the enzymatic degradation or biotransformation of mycotoxins that can be obtained by either the whole cell or an enzyme system. Microorganism can be used successfully to metabolize certain mycotoxins and thus remove it. It differs between specific mycotoxins, but a variety of microorganisms, including bacteria, yeasts and fungi are able to convert certain toxins to other non- or less toxic forms or to detoxify it. All of these forms may however have effects on the animals such as estrogenic effects of converted Zearalenone.

Detoxification of Feed Ingredients

So far the only successful chemical deactivation process has been ammonia treatment of aflatoxin-contaminated maize (Smith, 1997). Other chemical treatments are either too expensive, or degrade the finished product to unacceptable levels. The same appears to be true for physical methods such as sieving or heat treatment.

Conclusion

If we accept that grains (and for the South African pig producer, maize) is one of the biggest contributors to mycotoxin contamination of pig feeds, the data available from the SAGL serve as a good indicator of potential trouble to be incurred. Aflatoxins and Fumonisins seem to be of less danger to the producer than DON and Ochratoxin and perhaps Zearalenone. However, troubleshooting mycotoxicological problems on pig farms starts with a fundamental approach to quality assurance at the farm level. This can be achieved by having the fundamental procedures of prevention and detection in place. Thereafter, the responsibility at the farm level should include basic preventive measures such as storage management, turnaround time of feeds and the development of a unit's history of marker toxin exposure and animal performance. If the responsible, or at least major, toxin is known, then a reasonable decision can be made with respect to an appropriate feed additive. Finally, success comes usually to those who recognize that no single approach will solve all mycotoxin problems. Fungal infestation, metabolism, and synthesis of toxic products go on all the time. Those who are aware of this, and have a regular program to control it, will ultimately make a greater success in animal productivity and economic return than those who choose to wait until disaster strikes.

Research Needs

The task force report by the Council for Agricultural Science and Technology in the USA (2003) lists a number of research needs that are globally inclined, but we need to be aware of the potential areas. The breakdown areas are as follows:

Public Policy

1. Develop uniform standards and regulations for mycotoxin contamination.
2. Support joint international cooperation (FAO/ WHO/UNEP) to adopt standardized regulations.
3. Develop a safe food supply for local populations.

Mycotoxin Detection

1. Develop new technologies for mycotoxin analysis, including multiple-toxin analyses, and improve detection (with specificity) of mycotoxins in prepared foods.
2. Develop biomarkers for human and animal exposure to mycotoxins, including multipanel arrays that can detect exposure to multiple toxins.

Human and Animal Interactions

1. Assess mycotoxins as virulence factors. Research the effect of mycotoxins as immunosuppressors.
2. Evaluate toxicological interactions of toxins with the host (activation and detoxification of mycotoxins by host metabolism).
3. Examine population variation for sensitivity to mycotoxins
4. Assess interactions among mycotoxins and with drugs, diet, and nutrition.
5. Assess role of fumonisins on humans and their involvement in oesophageal cancer.
6. Assess risks of ochratoxin exposure due to its occurrence in a variety of foods and, perhaps, environmental loci.

Plant and Fungus Interactions

1. Establish a better understanding of the factors affecting mycotoxin formation in the field and in storage.
2. Improve understanding of the ecology and epidemiology of mycotoxin-producing fungi.
3. Develop sound agronomic-management practices to decrease mycotoxin contamination.
4. Develop host-plant resistance to mycotoxin-producing fungi and to mycotoxin occurrence.
5. Develop models to better forecast the potential of mycotoxin contamination.
6. Research the genetic regulation and biosynthesis of mycotoxins by the producing organisms.

Indoor Air Quality

1. Determine mycotoxins responsible for indoor air quality problems.
2. Develop sound sampling protocols for assessing fungal populations.
3. Establish limits for respiratory exposure to mycotoxins.

Economics of Mycotoxin Contamination

1. Develop accurate loss estimates for mycotoxin contamination.

Bioterrorism

1. Assess potential for use of mycotoxins as bioterrorism agents.
2. Assess mycotoxin-producing fungi as bioterrorism-agent candidates.

On the South African scene, a concerted effort by the industries involved with Grain SA is crucial in order to be aware of contamination in our grain crops. However information on the grain by-products (which possibly contain high levels of contamination) and other feed ingredients also need to be gathered to determine their mycotoxin status and factors that influence this.

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