Introduction

There are many reports on toxicoses caused by mycotoxins contaminated in feeds\(^1,2\). Mycotoxins exhibit a variety of toxic effects in animals such as liver and kidney toxicity, estrogenic effects, suppression in immune system and carcinogenisity. These undesirable effects bring economic losses in animal industry through impairment of animal health and production of mycotoxin contaminated animal products. The Ministry of Agriculture, Forestry and Fisheries of Japan (MAFF) has established guidelines for aflatoxin, deoxynivalenol and zearalenon in animal feeds for the prevention of mycotoxicoses and mycotoxin carry over to animal products (Table 1).

Sometimes mycotoxins occur in feeds at concentrations high enough to cause acute toxicoses in animals. However, there is only one report strictly diagnosed as acute mycotoxicosis, ryegrass staggers cases reported by us\(^3\), during last decade in Japan. According to the Statistical Year Books of Mutual Aid for Livestock (Kachiku Kyosai Tokei)\(^4\), about 300 cattle were affected mycotoxicoses every year (Table 2). These reports indicate the low incidence of acute mycotoxin poisoning of livestock in Japan.

On the other hand, subclinical losses in performance or increases in incidence of disease induced by lower level mycotoxins in feeds are suggested\(^2\). These suspected subclinical losses might be greater economic problem than damages brought by acute effects. But these cases, if exist, are difficult to diagnose. Therefore, the significance of mycotoxin problems in animal industry is not clear.

### Table 1. MAFF guideline for mycotoxins in feeds

<table>
<thead>
<tr>
<th>Mycotoxin</th>
<th>Feed</th>
<th>Concentration (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflatoxin B(_1)</td>
<td>Formula feeds (for cattle, pig, chicken and quail)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Formula feeds (for suckling calf, milking cow, suckling pig and chick)</td>
<td>0.01</td>
</tr>
<tr>
<td>Deoxynivalenol</td>
<td>Feeds for cattle older than 3 months</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Feeds except above</td>
<td>1</td>
</tr>
<tr>
<td>Zearalenone</td>
<td>All feeds</td>
<td>1</td>
</tr>
</tbody>
</table>
In this paper, present state and future tasks of researches on mycotoxicoses in livestock are briefly overviewed.

**Mycotoxin Contamination in Feeds**

The Fertilizer and Feed Inspection Services, Japan (FFIS) is monitoring mycotoxin contamination of commercial feeds in Japan and announcing the results on their website (http://www.ffis.go.jp/). According to their survey, mycotoxin contamination of grains or formula feeds high enough to induce acute effects on livestock is uncommon. However, feeds easily get moldy during storage under Japanese hot, humid climate. There is little information on the concentrations of mycotoxins in feeds actually fed to animals.

Some mycotoxins have been found in forages in the field or in storage as hay or silage in USA\(^2\). On the other hand, there is little information on the contamination of Japanese forages and silages. FFIS is monitoring mycotoxins produced by fungal endophytes in imported ryegrass and fescue straws. But local roughages are out of their coverage. Round bale wrapped silage system has been coming into wide use because of its convenience. However, wrapped silage easily gets mould with its low anaerobicity. Therefore, it is necessary to make clear the current conditions of mycotoxin contamination in local roughage to assess the risk of mycotoxins on animal industries.

**Immunotoxicity of Mycotoxins**

Although many works have been confirmed immunotoxicity of some mycotoxins\(^5\), there has been no report for the field infectious disease cases induced by immunomodulatory effects of mycotoxins. Even though mycotoxins may induce opportunistic infection through their immunotoxicity, the actual clinical phenomenon is the occurrence of infectious disease. Therefore, it is needed to diagnose the cause of opportunistic infection with consideration of the involvement of mycotoxins as one of the inducers.

Immunological adverse effects elicited from high level contamination of mycotoxins in feeds might be submerged with the other clear acute toxic effects of toxins. For example, deoxynivalenol (DON) induces feed refusal and vomit in pigs. If such level of DON affects immune system of the pig, the farmer can easily notice the presence of DON without the symptom of infection. It is important to make clear whether low level mycotoxins could be the inducer of the opportunistic infections without inducing any other clinical signs.

Details of the mechanism of action of mycotoxins on animal immune systems have not been clear. Further investigations including cellular and molecular approach should be performed for systematic understanding on immunomodulatory effects of mycotoxins.

<table>
<thead>
<tr>
<th>Year</th>
<th>1999</th>
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<th>2001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affected</td>
<td>342</td>
<td>244</td>
<td>323</td>
</tr>
<tr>
<td>Dead</td>
<td>40</td>
<td>23</td>
<td>41</td>
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</table>
Synergism of Mycotoxins

Detection of multiple mycotoxins in a single feed grain source is not uncommon. Furthermore, common formula feeds are consisted of multiple grain sources. Therefore, it sometimes happens that animals consume multiple mycotoxins at a time.

Some workers demonstrated that pure mycotoxin added to feeds was less toxic than diets with same amount of mycotoxin supplied from naturally contaminated materials\textsuperscript{6, 7). These observations are suggesting the participation of other mycotoxins in naturally contaminated feed materials.

The bulk of our knowledge on adverse effects of mycotoxins are obtained by investigating the biological functions of purified mycotoxins in experimental animals. In contrast, little is known about the toxicities of combinations of mycotoxins. Therefore, more data are needed about synergistic toxicological effects of mycotoxins.

New Diagnostic Approach for Mycotoxicoses

Estimation of the amount of mycotoxins ingested by animals is essential for diagnosis of the suspected mycotoxicosis. In these years, commercial enzyme-linked immunosorbent assay (ELISA) kits are prevalent for the determination of mycotoxin concentration in feeds. Although the ELISA kits are convenient for assay, determination of mycotoxin concentration in feeds is not enough to estimate exact amount of mycotoxins consumed by animals. Namely, mycotoxin contamination of feeds is not homogeneous and intake of moldy feeds is often uncertain.

It should be useful for the diagnosis of mycotoxin poisoning, if actual mycotoxin intake can be estimated by measuring concentrations of mycotoxins in biological samples such as blood, urine or tissue. Ochratoxin A (OTA) is persistent in blood stream of animals and blood OTA concentration is a useful marker for the extent of human or animal exposure to OTA\textsuperscript{8). Meky et al.\textsuperscript{9) reported that urinary DON metabolites could be a biomerker for DON in both animals and humans. As for fungal endophyte mycotoxin, lolitrem B, we showed that loitrem B concentration in fat tissue could be a maker for the amount of this mycotoxin consumed by cattle\textsuperscript{10).}

Establishment of convenient analytical methods of mycotoxins or their metabolites in biological samples is expected for the estimation of mycotoxin intake. These methods should also be applied to confirm whether low level mycotoxins can induce opportunistic infection in the field.

Public Health Problems

It is well known that dairy cows consuming rations contaminated with aflatoxin B\textsubscript{1} excrete aflatoxin M\textsubscript{1} in their milk. The most effective way of controlling aflatoxin M\textsubscript{1} in milk is to reduce contamination with aflatoxin B\textsubscript{1} of feeds for dairy cows. Specific regulations exist in many countries (Table 1). A newer approach is use of oltipraz (5-(2-pyrizinyl)-4-methyl-1,2-dithiol-3-thione), that inhibits aflatoxin B\textsubscript{1} metabolism by inhibiting the activity of cytochrome P-450 isoenzymes\textsuperscript{11). No aflatoxin M\textsubscript{1} formation was found in bovine hepatocytes incubated with aflatoxin B\textsubscript{1} and oltipraz. The
findings suggest that oltipraz is highly effective in inhibiting aflatoxin M₁ contamination of milk from dairy cows exposed to aflatoxin B₁-contaminated feeds.

Ochratoxin A distributes mainly to the kidneys in a number of species, especially in pigs. However, contribution of pig kidney to human total ochratoxin A intake should be very low under standard dietary habitat. Transfer to milk has been demonstrated in rats, rabbits and humans, but little is transferred to the milk of ruminants owing to metabolism of ochratoxin A by the rumen microflora to non-toxic ochratoxin α.

We determined lolitrem B concentrations in several organs and tissue of the Japanese Black cows fed endophyte-infected perennial ryegrass straw. As shown in Table 3, lolitrem B was not detected in muscle, liver, kidney, lung and cerebrum of the cattle showing the symptoms of ryegrass staggers. In contrast, perirenal fat tissue contained 210 µg/kg of lolitrem B. This observation indicates that lolitrem B will not accumulate in major edible parts of beef cattle. Therefore, the neurotoxic effect of lolitrem B to human through beef is unlikely.

In this short review, problems on risk assessment of mycotoxins in animal industries are discussed. Researches on control practices of mycotoxins in feeds and treatments of contaminated feeds are also important to minimize the undesirable effects of mycotoxins.

### References


<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Muscle</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Cerebrum</th>
<th>Fat</th>
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<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>ND*</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
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</tr>
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<td>2</td>
<td>1</td>
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<td>ND</td>
<td>ND</td>
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<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>NT</td>
<td>144</td>
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</tbody>
</table>

Group 1 received 6.5 kg of ryegrass straw containing 1200 µg/kg of lolitrem B every day.
Group 2 received 3 kg of ryegrass straw a day.
*ND = not detected
**NT = not tested
家畜に対するマイコトキシンの影響に関する—考察

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飼料を汚染するマイコトキシンが家畜に中毒を起こして生産性を低下させたり、場合によっては家畜を死亡させることは広く知られている。しかし、わが国における家畜のマイコトキシン中毒発生状況調査は行われておらず、その実態は明らかではない。ただ、我々が入手している断片的な情報から判断して、かつて多く見られたようなマイコトキシンによる家畜の急性中毒事例はさほど多くないように思われる。一方、種々のマイコトキシンが免疫毒性を示すことが明らかになり、急性中毒量以下のマイコトキシン摂取による免疫機能の低下が、家畜の生産性阻害要因になるのではないかと指摘されている。しかし、野外での家畜の感染症発症にマイコトキシンが関与していることを明確に立証した報告はない。このような背景をふまえ、飼料を汚染するマイコトキシンが家畜におよぼす影響について、研究の現状を紹介しながら、今後検討すべき問題点について考察する。