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«TRAINING ACTIVITIES ON FOOD CONTAMINATION CONTROL AND MONITORING WITH SPECIAL REFERENCE TO MYCOTOXINS»

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MICOTOXICOSES IN MAN AND ANIMALS

(DIAGNOSIS AND BASIC CONTROL MEASURES)

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MICOTOXICOSES IN MAN AND ANIMALS

(Diagnosis and basic control measures)

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The group of micotoxicoses common to men and animals includes ergotism, stachybotryotoxicosis, fusariotoxicosis and alimentary toxic aliekia (ATA).

ERGOTISM

Ergotism is a serious disease caused by the ingestion of vegetable food and animal feed products contaminated with Claviceps purpurea. The disease has been known from the 10-12th centuries. Claviceps purpurea Tul.(Ascomycetes class) is a parasite of both cultivated (mainly rye) and wild cereals. It is the sclerotia of the fungus, known as spurred rye (Secale cornutum), which are toxic.

The sclerotia of Claviceps purpurea contain alkaloids, of which ergotoxin is the most active. Lysergine acid is the main toxic component of sclerotia alkaloids.

Freshly harvested sclerotia of Claviceps purpurea are the most toxic.

There are two forms of ergotism: convulsive and gangrenous.

With the convulsive form of the disease in man, the victim feels weak and loses his appetite. His whole body aches and he has a crawling sensation on his skin especially on his limbs. He is feverish, vomits and sometimes he has gastric and intestinal disorders. There is contraction of the arms and legs. This form is associated with a single ingestion of cereals with

a high ergot content.

With the gangrenous (chronic, lingering) form of the disease, 10-20 days following multiple ingestion of grain containing ergot in small quantities necroses occure on peripheral areas of limbs, accompanied by general weakness and sleepiness. The ends of the limbs grow cold, blacken, lose sensitivity. In serious cases the gangrenous areas are mummified, with separation of the muscles from the bones.

Ergot alkaloids enter the milk of nursing mothers afflicted with the disease and it becomes toxic (Fomina, 1933).

Ergotism in man is a disease of the past, although some outbreaks of the disease may still occur when spurred rye is not separated from the harvested grain.

The diagnosis was confirmed by the presence of ergot in cereal products consumed by the patients, who, for the most part, came from among the rural population.

There is still no known cure for this disease.

Ergotism in animals still occurs today. The disease afflicts all species of agricultural animals and poultry, with horses and pigs considered to be the most susceptible. After a single ingestion of a large quantity of spurred rye, the convulsive form of ergotism develops in the affected animals. Clinical manifestations of toxicosis appear within the first day following ingestion of the contaminated feed. A short period of excitation gives way to depression, vomiting, excessive salivation. Movement is charachterized by the loss of stability and by tremor. Flexion contraction is finally develops into convulsions. Pregnant animals have miscarriages.

With the gangrenous form of ergotism the skin becomes dry,

"testaceous", and cool to the touch. Necroses develop. The horse loses its mane and tail, digestion is disturbed. Cracks form on the nipples of lactating cows, and the nipples may fall off. In pigs gangrenous foci appear on the snout, the helix, and tip of the ears, on the back and along the backbone; sows have agalactia, miscarriages, or the young are stillborn. Gangrene and fall-off of the hoof horn is often observed in all animals, while in birds there is fall-off of the comb, beak and tongue. Acute cachexia develops. The body temperature drops below normal. The timely detection of ergot sclerotia in the cereal (mixed feed) and the immediate cessation of its consumption may halt the further progress of the disease. It is assumed that feedstuffs containing 1 per cent of ergot by weight produce toxicoses in animals (Young, 1979), although the degree of ergot toxicity varies considerably in relation to the period of harvesting.

TOXICOSES INITIATED BY CAP FUNGI.

Cases of micotoxicoses in patients poisoned by the cap fungus Amanita phalloides, in some cases fatal, have been recorded recently (1979-1981).

Bastien P. was the first (1980) to treat the patients using a complex therapy including vitamin C neomicyn with nifuroxacido taken orally. 98 of the 100 people affected recovered, and two died.

Cases of poisoning with A.phalloides have been recorded several times recently, and this should be taken into consideration by practical specialists and public health organisations.

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STACHYBOTRYOTOXICOSIS

The disease was first recorded in the Soviet Union in the Ukraine in 1931 and the cause was identified in 1938 (Drobotko, Iatel et al., 1946, 1949). It was established that toxic strains of Stachybotrys alternans developing mostly on roughage produced a highly toxic matter.

The disease was also observed in other countries (Hungary, Rumania) but remained undiagnosed. Stachybotryotoxicosis was considered to be an acute viral or bacterial infection or a serious form of avitaminosis. Complex investigations performed by large teams of Soviet research workers excluded the role of viruses and pathogenic bacteria in the etiology of this disease.

Stachybotrys alternans, a typical cellulose destructor, was known as a species from the genus Corda and was described by Bonorden H.F. as early as 1851.

The horse is most susceptible to this disease, but ruminant animals (cattle, sheep) and pigs can also be afflicted by stachybotryotoxicosis. The desease can be reproduced in all laboratory animals.

Toxic strains of S.alternans have also been found and described in countries in Europe, Asia and America, and this micromycete has been thorougly studied by Pydoplichko N.M. (1953).

Rural dwellers, particularly people who handle fodder or vegetable technical raw materials (cotton,etc.) contaminated with S.alternans frequently developed a toxicosis. The symptoms of the disease are irritation of the mucous membrane of the eyes, edema of the nose and mouth, lesion of the upper parts of the respiratory tracts. Bloody rhinitis is possible. The surface of

of the skin, particularly near sweat glands (groin, hands), is inflamed, acutely painful and itchy. Fatal outcomes have not been recorded (Lynnik F.A.).

The toxin of S.alternans has a pronounced necrotic effect on the skin of rabbits and other animals. The methods developed by us for determining the toxicity of S.alternans, and of food and feedstuffs contaminated with this fungus, were first published in 1944. At the present time these simple methods are applied everywhere. Crude non-purified stachybotryotoxin obtained by us in 1939 from straw infected with the fungus preserved its necrotic effect on the skin of a rabbit over the following 40 years.

Stachybotryotoxicosis may occur in either of two forms, the typical, which has been arbitrarily divided into three stages, and the atypical, which has one stage.

The typical form in the horse occurs in three stages. At first local lesions of the head are observed, as well as excessive salivation. Lesions of the mucous membrane of the oral cavity are similar to those which occur in stomatitis simplex and are accompanied by the appearance of fissures at the corners of the mouth. No particular abnormalities in the general condition of the horse are observed at this stage. If the animal continues to recieve toxic fodder the second (latent) stage begins, which is charachterized by stable changes in the blood reduction in the total number of leukocytes and trombocytes at normal temperature. A secondary necrosis symmetrically placed on the oral and lip mucous membranes appears. Outwardly the general condition of the horse still remains satisfactory. Duration from the second stage varies from 8 to 40 days.

The third, final stage is charachterized by a sharp rise in the body temperature, pronounced leuko-thrombocypetonia and the disappearance of granulocytes, and the complete inability of the blood to clot. Inorganic phosphorus of the blood serum diminishes sharply (five to eightfold) to 1.2-0.6 mg%.Necrotic areas are observed along the alimentary tract starting from the oral cavity and particularly in the large intestine, as well as large foci of hemorrhages. Under natural conditions the typical form is observed on the 20th-45th day after the ingestion of toxic fodder.

The atypical form has different manifestations. It develops in 5-10 hours after a single ingestion of large amounts of highly toxic fodder. Nervous disorders comprise the main visible syndrome. Loss of sensation, loss of reflex response or, on the contrary, hyper irritability are observed. The animal may become totally blind; it starts with legs apart, tries to move but cannot. It swallows with great difficulty, clonic spasms of the head muscles, contraction of the back of the head, and shortness of breath are observed. The pulse rate increases to 80-100 per minute. Animals afflicted with the atypical form do not display the blood changes observed with the typical form; leukocytosis is possible. The outcome of the atypical form and of the third stage of the typical form is often fatal.

Clinical manifestations and pathoanatomical findings in cattle, sheep and pigs affected by stachybotryotoxicosis basically coincide with those found in the horse, but are muted (Povazhenko, 1964). The complete shedding of wool was observed in sheep.

An indispensable condition for controlling stachybotryotoxi-

cosis is the immediate elimination of the suspected roughage from the feed.

In the first stage of the disease horses do not need any medication but should be released from work. Symptomatic treatment is recommended for the second stage. In the third stage antibiotics (penicillin, streptomycin, tetracycline) should be administered in therapeutic doses to suppress the sepsis which appears in connection with the necrobiotic process.

FUSARIOTOXICOSIS

Micromycetes of the genus Fusarium are abundant naturally, and many of them are saprophytes and semiparasites of plants.

Illness in humans and animals caused by cereal products infected with one of the fungi from genus Fusarium, namely F. graminearum, was first recorded in the Far East in 1882 by Palchevsky N.A., and was described under the name of "intoxicated corn", "intoxicating rye" (Taumelreggen), "toxic barley" (Giftgerste). Outbreaks of this disease were recorded in Sweden in 1883 (Erikson G.), in Finland, in North America and in Western Europe (Germany) due to large amounts of imported American grain infected by Fusarium fungi.

In 1888 Voronin M.V., having studied the microflora of the intoxicated grain, established that its toxicity was due to infection of the grain by F.graminearum and other species.

The disease in humans. After ingestion of food, usually bread baked from "intoxicated grain" infected by F.graminearum, symptoms of poisoning soon appear, the first of which are weakness and heaviness in the limbs, followed by trembling, difficulty in walking and loss of the capacity to work. Severe

headache and dizziness are observed, together with vomiting, abdominal pain and diarrhoea. In serious cases there is loss of consciousness or fainting. A day late the general condition of the patient is similar to that after heavy alcoholic intoxication, which explains why this disease was described as poisoning with "intoxicated bread"

The active agent of this mycotoxicosis is choline or acetylcholine, ether of choline (Gabrilovitch, 1906). The toxin is not destroyed at high temperatures and food prepared from contaminated grain preserves its toxicity.

It has been established that grain infected by this fungus is toxic to horses, pigs, dogs and, to a lesser extent, to cattle. After ingestion of oats or barley infected by this fungus, horses become excited, coordination is disturbed and the animals seize nearby inedible objects, imitating the clinical picture of rabies. Then depression, weakness and trembling are observed. Reflex response is weak, thirst is increased. Development of resistance to this toxin has never been observed.

Over the last ten years it has been established that Fusarium graminearum, F.moniliforme and some other species of the genus Fusarium may produce methabolite zearalenone (F_2) in cereal crops and this has an estrogenic effect. Zearalenone is most frequently found in corn (maize) and less frequently in rye, millet and oats.

Pigs are especially susceptible to this mycotoxin. In young pigs zearalenone induces hyperestrogenism, in newborn piglets-deformities, in sows- infertility (Kurtz et al.,1980).

Symptoms of estrogenism in young pigs have been recorded

(Joung, Vesonde, 1979; Aucock et al., 1980) with diets containing zearalenone at a rate of 1.0, 2.5, 3.8 and 10 mg/kg. Clinical manifestations may appear after 4-7 days following the ingestion of the infected fodder (Perlini, 1982), depending on the amount of the toxin.

When lactating sows were fed mixed feed containing zearalenone the latter was found in the milk. In cattle it may produce infertility. Egg-laying in poultry is affected by this toxin. The estrogenic effect of the toxin has been demonstrated in monkeys.

There still exists a potential menace to human health associated with this toxicosis in some regions of the world where cereals heavily contaminated with zearalenone may be used for food purposes.

FUSARIOTOXICOSIS FROM OVERWINTERED GRAINS
ALIMENTARY TOXIC ALEUKIA (ATA)

ATA in men is an extremely serious disease caused by ingestion of snow-covered overwintered grain. ATA has not been recorded in the Soviet Union since 1945, when the etiology of this disease was established and effective control measures were developed. The first cases of ATA were recorded in 1932. In the war and postwar years (1941-1945) the disease was again recorded among the rural population of some regions where grain had been left in the field and had passed the winter under snow.

Large teams of research workers from the Ministry of Public Health of the USSR, the Institute of Nutrition of the Academy of Medical Sciences of the USSR, the Cereals Research Institute,

the Chkalov Institute for Epidemiology, the Academies of Sciences of the USSR and the Ukrainian SSR, and the All-Union Toxic Fungi Research Laboratory took part in identifying the etiology of ATA and developing control measures under extremely difficult war conditions.

Extensive mycological and toxicological investigations performed by us in 1941-1944 established that the etiology of ATA is associated with F.sporotrichiodes. The results of these complex investigations were summarized in a collection of articles "Overwintered cereals" published in 1948.

Man is highly susceptible to toxic overwintered grain, and its ingestion during 5-15 days as bread, porridge or in other forms, may result in alimentary toxic aleukia. The complete complex of ATA symptoms was reproduced by us in cats in 1943-44. We could not reproduce the typical picture of ATA in man in all other species of small laboratory animals and big animals, although they were all found to be susceptible to toxic grain and toxic fungi cultures.

According to Olifson L.E. (1955) he isolated from toxic strains of Sporotrichiella a pure mycotoxin which he named sporofusariogenine.

Bamburg J.R. (1976), Smalley B.B. and Strong F.M. (1976) isolated a toxin of a trichotecenic nature which recieved the name of T_2-toxin. Further research and investigations are required to determine the nature and the structure of the toxin. The range of susceptibility of various animals to T_2 varies. Among laboratory animals, cats are the most susceptible to the toxin. J.Lutsky et al. (1978) demonstrated that the symptoms of ATA may be experimentally reproduced in cats by administering

them per os T_2-toxin at a rate of 0.08-0.1 mg/kg. For T_2-toxin LD_{50} of rats amounts to 3 mg/kg of the body mass (Perlini, 1982).

Under natural conditions cattle, pigs, horses, sheep and poultry may be infected.

FUSARIOTOXICOSIS IN ANIMALS FROM OVERWINTERED CEREALS

Large and small horned livestock. The charachteristic symptoms of this disease appear in livestock very soon after the ingestion of the toxic grain, sometimes on the first day. The symptoms include loss of appetite, lack of muscular co-ordination as well as tremor and moaning, laboured breathing, cessation of rumination and atony of the rumen. Paresis and paralysis may develop. Postmortem dissection shows hemorrhagic diathesis and massive hemorrhages of the heart under the epicardium, and also catarrhal hemorrhagic inflammation of the digestive tract. In acute cases the blood picture shows leukocytosis and, after lengthy illness, leukopenia.

Weather conditions, particularly a snowy, mild winter, contribute to active toxin production by the fungus in grain that was left in the field and passed the winter under snow cover. In 1952 an early winter prevented the cereal harvest in a number of regions of the Central zone of the USSR from being completed, and a part of the crop was left in the fields under snow. When the snow had melted the fields were used as pastures for cattle and sheep and this resulted in mass outbreaks of illness and the death of animals.

Pigs. Pigs are highly susceptible to trichothecene T_2. The clinicohematologic and pathomorphological pictures are similar to those of fusariotoxicosis in cattle. The disease is accompanied by vomiting, convulsions, edema of the head, necrosis of the snout, gums and tongue, hemorrhages on the skin. Sows have abortions. Fatal outcomes are frequently observed. Weaver G.A. and Kurtz H.J. (1980) demonstrated that T_2 at a dose of 1 ppm did not affect the pigs, though at a concentration of 16 ppm it caused the death of the infected animals.

Horses. Infection causes hyperemia, edema of the oral cavity and necrosis of the tongue; the lips are edematic and covered with fissures. There is excessive salivation. Leukopenia develops and blood retraction diminishes. The development of fusariotoxicosis resembles that of stachybotrytoxicosis. Necrobiotoc lesions are observed along all parts of the digestive tract.

It is known that germinating oats are given to pedigree horses as a source of vitamin E. It has been established that oats infected by F.sporotrichioides become toxic if they germinate in conditions of high humidity,and if introduced into the feed ration cause mass outbreak of illness among pedigree horses. The elimination of toxic grain from the feed leads to recovery.

Poultry. Depression is observed, together with complete refusal to eat, and sleepiness. Feathers become dishevelled, the comb and wattles turn cyanotic. The mucosa of the oral cavity has catarrhal hemorrhagic inflammation. A charachteristic feature is the appearance of necroses, together with the presence of blood in the faeces and suppression of the immune system. Prolonged illness results in cachexia and death.

The minimum concentration of T_2 in the feed capable of inducing pathological changes constitute about 1 µg/g for hens, about 0.5 µg/g- for turkey and geese and 0.25 µg/g- for ducks (Kotik, Trifanova, 1980).

At the present time outbreaks of the disease in agricultural animals and poultry are most frequently caused by feedstuffs contaminated with toxic species of the genus Fusarium, Sporotrichiella section.

Shuh H. (1981) described 13 field cases of the disease in cattle, pigs and poultry due to feedstuffs contaminated with searalenone and the trichothecene toxin- deoxynivalenol.

ASPERGILLOTOXICOSES

A number of Aspergillus species have toxigenic properties and cause toxicoses in animals. The role of many of them as the etiological factor of micotoxicoses has not been finally established. The following species are considered to be the most toxigenic: Aspergillus fumigatus, A.flavus, A.parasiticus, A. clavatus, A.ochraceus.

AFLATOXICOSES

Aflatoxicoses are mycotoxicoses caused by the ingestion of vegetable products infected with Aspergillus flavus. The toxic action of Aspergillus flavus on pigs was established in 1957 (Burnside et al.) Extensive research in this field started when an acute outbreak of a lethal disease in turkey poults occured in England in 1960, causing an estimated loss of at least 100 000 birds (Sargeant et al., 1961). The disease was caused by

aflatoxin B_1 contained in a batch of groundnut meal infected with A.flavus. The concentration of aflatoxin B_1 in the original groundnut meal was later estimayed to be about 10mg/kg. Further research on rats showed that continuous feeding on such groundnut meal induced hepatomas. Later on it was established that an other species- A.parasiticus- also produces aflatoxins (B_1 and B_2, G_1 and G_2). The disease in turkey poults was charachterized by rapid deterioration in the condition of the birds, subcutaneous haemorrhages and death. A postmortem revealed that the livers of the birds were pale, fatty and showed extensive necrosis. Similar manifestations appeared in chickens (Lanza et al., 1981) when they were fed a diet containing aflatoxin B_1 at a level of 5 µg/g. With a concentration of 1.25 µg/g enlargement of the liver and pancreas was observed in Japanese quails, at 5 µg/g the growth was suppressed, the LD_{50} constituted 20 µg/g (Chang et al., 1982).

Detroy et al. (1970) noted that groundnut meal contaminated with aflatoxins might be the cause of mycotoxicoses in pigs, calves, oxen, poultry chicks, fur bearers (minks, nutrias). All species of agricultural animals, especially poultry and pigs, fed on vegetable feedstuffs containing aflatoxin developed signs of acute or chronic poisoning with liver lesion.

It has been established that aflatoxin B_1 has strong carcinogenic and teratogenic effects,

Some cases of poisoning in children associated with the ingestion of food containing aflatoxins have been recorded. Considering the high concentrations of aflatoxins in groundnut and groundnut products imported from tropical countries, a number of countries have sharply reduced their import of ground-

nuts and groundnut meal in the last few years; many countries have adopted strict measures limiting the level of aflatoxin contamination of food products, the maximum permissible concentration of the toxin being 5-20 µg/kg. The maximum permissible concentration of aflatoxin in animal feedstuffs is 50 µg/kg.

So far there is no direct evidence of aflatoxicosis in man.

MICOTOXICOSES IN ANIMALS

Aspergillotoxicosis

Aspergillotoxicosis is a serious disease in farm animals which can occur at any season of the year and is associated with the ingestion of cereal waste and feeding meal infected by toxic strains of Aspergillus fumigatus. The toxic action of A.fumigatus strains on laboratory animals was established as early as 1902-1938 (Gemi, Besta, Bodin, Lenorman, Henrichi).

Aspergillotoxicosis in farm animals has acute and subacute forms. The disease afflicts pigs, sheep, horses and poultry. The acute form of aspergillotoxicosis in animals is charachterized by muscular trembling, uncertain gait, followed with loss of muscular coordination, convulsions in the limbs and paralysis. Excessive salivation, laboured breathing and dyspnea are also observed. Body temperature remains normal. Animals refuse to eat. Pigs assume the pose of a sitting dog, and are liable to bouts of vomiting. Horses have abdominal pain, cattle-atony of the proventriculus. With the sub-acute form the affected animals suffer from depression and paresis of the limbs. Appetite varies. Leukopenia and agranulocytosis occur in the blood. Postmortem dissection showes inflammation of the gastrointestinal tract, weakly pronounced hemorrhagic diathesis, degenera-

tive processes in parenchymatous organs, particularly in the liver. Ether extracts from the culture produce an acute dermal inflammatory reaction when applied topically on the skin of a rabbit. Several indole tremorgens (fumitremorgens A, B, C), the products of A.fumigatus metabolism, cause acute forms of toxicosis in agricultural animals. The toxin of A.fumigatus is destroyed by high temperatures (100° C) and this is used for detoxifying feed grain.

DENDRODOCHIOTOXICOSIS

This disease, which affects horses, develops extremely rapidly and has a fatal outcome. It has been observed for the most part during fall-winter-spring in stabled horses, and is caused by feeding horses on straw and chaff infested by Dendrodochium toxicum molds (Pidopl. et Bilai). Dendrodochiotoxicosis was first recorded in the South of the Ukraine. The etiology was established by Pidoplichko N.M. and Bilai V.I. et al. in 1947. Data indicate that there was a mass outbreak of this illness among sheep fed on teff contaminated with this fungus.

The clinical picture. The animals die within 16-24 hours following the ingestion of roughage infected with Dendrodochium toxicum without the development of a distinct clinical picture. The horses that died were predominantly aged 3-8 years, thick-fleshed, used for work. No mortality was recorded among suckling foals. The rapid development of the disease made it impossible to obtain detailed data on the clinical picture, although the toxin evidently seriously affects the activity of the central nervous system.

Direct experiments on horses performed by Borisevitch V.I., Ponomarenko F.M., Petrovsky G.I. showed that shortly before death they suffered from depression, disturbances in cardiac action and in the alimentary tract. There was a sharp increase in the content of hemoglobin, as well as in the number of erytrocytes and leukocytes. Necropsy findings showed pronounced cyanosis of the conjunctiva and of the mucous membrane of the nose. The tissues and organs of the front part of the animal's body were filled with blood. The lungs were edematous, there were hemorrhages in the parenchyma of the lungs and on the heart epicardium. In contrast, the organs of the abdominal cavity are anemic. Weak catarrhal inflammation was observed in the intestine. Consumption of barley infected with the culture of Dendrodochium toxicum resulted in the death of yelts and postmortems showed well-pronounced necrotic changes in the mucosa of the oral cavity (Djilavjan H.A., Chernov K.S.). Ether extracts have necrotic and acute resorptive effects which, in a number of cases, resulted in the death of rabbits when dendrodochiotoxin had been applied to the skin of the animals. Now that the etiology of the disease has been established and control measures introduced:elimination of straw infected with D.toxicum from the rations,there are only rare cases of this disease in horses.

CLAVICEPSTOXICOSIS

Clavicepstoxicosis is an alimentary toxicosis of animals associated with the ingestion of wild grasses of the genus Paspalum containing toxic sclerotia of Claviceps paspali. The disease

has been recorded in regions with a humid subtropical climate, predominantly during the pasturing period in the fall, when the fungus sclerotia are ripening. Clavicepstoxicosis may also occur during stall feeding if the animals are fed on hay from regions where Paspalum grasses are infected with the fungus C. paspali and contain its sclerotia. Most susceptible to this toxicosis are horses and, among poultry- geese. The disease may also effect (to a lesse extent) cattle, including oxen, sheep and, exceptionally, pigs.(during pasturing). The disease manifests itself as an infection of the central nervous system.

Cases of clavicepstoxicosis were investigated in the Transcaucasian region in 1943-1944.

The clinical picture. The disease develops rapidly and manifests itself at the end of the first day or on the second day, depending on the amount of toxic feed consumed by the animal. One of the first signs is the appearance of muscular tremor in the body, particularly in the muscles of the hind limbs, followed by severe disruption of coordination in the form of an uncertain, stumbling ("drunken") gait. If the animal is seriously infected, it falls. If the feed is quickly changed the outcome is favourable. The pathoanatomical picture is not characteristic.

It has been established that Claviceps paspali parasitizing on Paspalum digitaria produces tremorgen toxin-paspalinine.

Gallagher et al. (1980) determined the chemical nature of the toxin, which is a derivative of indole ($C_{27}H_{37}O_4$):
In mice, intraperitoneal injection of the toxin at a dose of 80 mg/kg produces tremor. The typical clinical syndrome of the toxicosis appeared in sheep after intravenous administration of

paspalinine at a dose of 1 mg/kg (Mantle, Penny, 1981). The disease may be experimentally reproduced in all agricultural and laboratory animals. The toxin contained in sclerotia is not destroyed in storage. The primary and most important step in the prevention and control of clavicepstoxicosis is the elimination of hay containing sclerotia of Claviceps paspali from the ration and the non-admission of animals to pastures contaminated with this fungus.

MYROTHECIOTOXICOSIS

Myrotheciotoxicosis is an alimentary disease which occurs among sheep and is associated with the ingestion of straw and cereal waste infected with the fungus Myrothecium verrucaria.

The disease was first recorded and investigated by Djilavjan H.A., Karpova-Benua E.I., Koroleva V.P., Vertinsky K.I. in 1953. At the beginning of the outbreak, the disease develops in the acute form with high mortality. The disease affects both young and adult animals.

Animals fall ill on the first or second day following the ingestion of feed infected with the fungus M.verrucaria. They suffer from depression and do not wish to move. At the beginning the body temperature remains within normal limits, later on it drops to subnormal. Hyperemia of the mucous membranes and serous nasal secretions are observed. There is loss of appetite and cessation of rumination; atony appears. Breathing becomes laboured and the pulse quickens. There may be diarrhea with bloody stools. Uncertain gait is observed in some animals. The affected animals lie down, groan, grind their teeth; profuse salivation appears. Dyspnea increases, there are signs

of asphyxia and clonic convulsions. The affected animals with the above clinical manifestations die within 1-5 days of the onset of the illness.

With the subacute form of the disease, only weakly pronounced clinical signs are observed to begin with. The elasticity of the skin and muscles deteriorates, the wool of the coat may be pulled out or drops out. The disease is charachterized by the appearance of inflammatory infiltrates in the form of a swelling, large hemorrhages and hematomas at the place of medical injections. The affected animals are unsteady on their feet, lie and cannot stand up. Response to surroundings is suppressed. The body temperature remains within normal limits. Nevertheless, the animals die after 10-15 days or have to be destroyed for sanitary reasons.

The postmortem examination reveals multiple or single necrotic foci with hemorrhages, catarrhal inflammation of the intestine and dystrophic processes in the parenchymatous organs. Pronounced hyperemia is observed and the lymph nodes are edematous. Myrotheciotoxicosis has been experimentally reproduced in sheep. M.verrucaria destroys cellulose. It rarely occurs in vegetable substrata and soil, and for this reason the disease is observed only sporadically. Under culture conditions the fungus develops well in ground barley and maize. Toxic products are extracted by organic solvents and produce a necrotic reaction in rabbits when applied to the skin. It is assumed that the toxin is not homogeneous and consists of several toxic products. There is a report (Jorvis et al., 1981) that a new macrocyclic trichothecene toxin- verrucarin- has been isolated during fermentation of Myrothecium verrucaria. Additional studies are

needed on myrotheciotoxicosis.

SPORODESMIOTOXICOSIS (FACIAL ECZEMA)

The disease has been recorded predominantly in sheep, rarely in cattle, and is associated with the ingestion of dead plants infected with the toxic fungus Pithomyces chartarum (syn. Sporodesmius bakery Syd.) found in pastures. Outbreaks of the disease have been recorded in Australia and New Zealand. The first mention of the disease appears as early as the last century (1880) in New Zealand. The etiology was establsihed in 1958 (Persivalet a.Tornton). At first it was named "facial eczema" due to the appearance in the clinical picture of exudative epidermatitis on the facial skin of sheep and cows. The disease has never been recorded in the USSR.

The clinical picture. Manifestations of the initial stage of the toxicosis in sheep are hyperexcitability, itching, salivation, edema of the ears and of the scalp. Later the toxin (sporodesmine) induces lesion of the liver (cholangitis) and in this connection there are disturbances in the release of phyloerythrin by the gall. This results in an increase in the light sensitivity of the animal and the appearance of solar burns on the head and other parts of the body not protected by wool together with edema and necroses.

The final stage of the disease is charachterized by the development of jaundice, cachexia and photophobia in the affected animals. Sporodesmiotoxicosis has been experimentally reproduced in sheep, rabbits, rats and guinea pigs (Perrin,1957; White, 1959; Mortimer, Taylor, 1962, etc.)

The administration of sporodesmin to sheep at a dose of 35 mg per animal results in acute toxicosis and death.

MICOTOXICOSES INDUCED BY OTHER TOXIC FUNGI

There are different opinions on the toxication of smut fungi of the genus Ustilago and rust fungi of the genus Uredinales on animals. Early publications spoke of the pathogenic action of loose and covered smut of oats (caused by Ustilago avenae, U.levis) and barley on agricultural animals. This resulted in the rejection of large amounts of fodder grain. Further publications (Reinfeld, 1934; Colosnitsky, 1948) and direct experiments carried out by us in 1968-79 on feeding smut infected cereals to animals, established that the smut of barley, millet and oats does not affect agricultural animals. In this connection the decision to reject smut infected cereals should be taken with circumspection. There are no reliable data on diseases in animals caused by rust fungi.

PENICILLOTOXICOSES

The pathogenic action of some species of Penicillium on animals has been established by direct experiments and observations carried out predominantly by Japanese research workers. There are some data on diseases in men caused by toxic strains of Penicillium islandicum, Penicillium rubrum, Penicillium viridicatum, Penicillium citreo-viridi and Penicillium urticae.

It is believed that pigs are particularly susceptible to vegetable feeds infected with toxic penicilles.

OCHRATOXICOSIS

Aspergillus ochraceus and some other species of Penicillium produce mycotoxines classified as ochratoxins (A and B) (Merwe, Steyne, etc., 1965). Producers of ochratoxins are widely spread, particularly in the moderate climatic zone. Turner W.B. (1971) refers these mycotoxins to pentaketides within the group of polyketydes. Ochratoxin A has been found in maize, wheat, oats and barley in a number of European countries and in the USA. Residues of ochratoxin have been detected in pig tissues as long as a month after the contaminated fodder had been withdrawn from the feed ration. The data on ochratoxicosis in farm animals (pigs, poultry) show that this disease is first manifested by nephropathy, nephritis. Direct experiments on rats and pigs have shown that a low dose of 200 µg/kg has a nephrotoxic effect. The teratogenicity of ochratoxin has been established.

Considering the extensive distribution of natural ochratoxin producers and the consequent contamination of food and feed stuffs, WHO and FAO in their detailed general review "Environmental Health Criteria-Mycotoxins" (1979) recommend that national public health organisations keep a constant check on food and animal feed-stuffs for ochratoxins.

CONCLUSION

The data presented here force us to pay the most serious attention to the potential menace to the health of humans and animals associated with toxin producing microscopic fungi so little known to us until quite recently. Scientists in many

countries have started extensive research of the problems connected with mycotoxicoses.

Specialised international organisations-WHO and FAO of the UNO- are paying some attention to mycotoxicoses and its prevention, and are enlisting the cooperation of national public health institutes and agricultural institutes in many countries in an attempt to solve this problem.

In our opinion, the primary and most important step in the prevention and control of mycotoxicoses is the elimination of the conditions which contribute to a high moisture content in vegetable food and feed stuffs at every stage, starting from harvesting and transportation up to storage and the preparation of food products and animal feeds..

This is at the present level of science and technology the most important and most practical task for research workers and specialists around the world.

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