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La Troisième conférence internationale mixte FAO/OMS/PNUE sur les mycotoxines

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Le mois de mars 1999 a vu se dérouler à Tunis la Troisième conférence internationale sur les mycotoxines. Cet événement a été parrainé par la FAO, en collaboration avec l'Organisation mondiale de la santé (OMS) le Programme des Nations Unies pour l'environnement (PNUE) et il perpétue une tradition initiée il y a plus de 20 ans. En effet, en 1977, pour la première fois, 42 pays et 10 organisations internationales se sont réunis à Nairobi, sous l'égide de la FAO, de l'OMS et du PNUE, sur le thème des mycotoxines. Cela a été l'occasion de se concerter sur les actions à mener pour limiter la contamination des denrées alimentaires par ces toxines naturelles. Cette conférence a été jugée très utile et, 10 ans plus tard, la communauté internationale a jugé bon de se réunir à nouveau, cette fois à Bangkok. Trente-trois pays et six organisations internationales ont débattu du suivi et des progrès réalisés en 10 ans, donnant ainsi les éléments pour les stratégies à appliquer au cours des années à venir.

Tout cela résume l'historique ayant abouti à la tenue de la troisième conférence, près de 12 ans plus tard en 1999. Durant ce laps de temps, de nouvelles mycotoxines, les fumonisines, ont été étudiées plus en détail par les chercheurs. D'autres informations plus récentes – concernant l'importance sur le plan de la santé humaine de mycotoxines déjà connues ainsi que les progrès réalisés dans les techniques d'échantillonnage et d'analyse – ont permis d'envisager d'une manière différente la problématique de la contamination des denrées alimentaires par les mycotoxines. En effet, les programmes de surveillance instaurés il y a plusieurs dizaines d'années commencent à porter leurs fruits et les derniers développements en matière de réglementation, de contrôle et de procédures de décontamination ont accéléré ce besoin de concertation internationale. C'est ainsi que cette dernière conférence a pu réunir 38 pays et 10 organisations internationales afin de débattre et de s'accorder sur les priorités des activités à mener dans le futur.

L'organisation des contrôles, la finesse des méthodes d'analyse étant en constante amélioration, et le cadre de la réglementation des mycotoxines dans les denrées destinées à la consommation humaine et animale étant de plus en plus complet (plus de mycotoxines, dans une plus grande variété de produits et dans un plus grand nombre de pays), les problèmes posés par les mycotoxines sont plus nombreux, et mieux cernés. Les dommages économiques créés par les refus et l'écartement de nombreux lots du marché ne peuvent plus être ignorés. Parallèlement, les progrès de la recherche en toxicologie, le développement de concepts tels que l'analyse des risques permettent de mieux évaluer quels peuvent être les risques pour la santé, à court et à long terme. Il est capital que ces connaissances, liées à la fois à l'aspect santé et à l'aspect économique, soient connues des décideurs pour que les orientations prises en termes de moyens accordés à la prévention et au contrôle soient raisonnées et correctement dimensionnées.

Cette conférence avait donc pour but immédiat d'offrir un forum d'échanges d'informations scientifiques et techniques, et de porter ces informations à la connaissance des fonctionnaires ayant une influence sur les politiques publiques et l'administration des contrôles, dans le but d'une harmonisation de la réglementation et des programmes de renforcement de la prévention et du contrôle. L'objectif final était de garantir la santé du consommateur, tout en limitant les pertes en denrées alimentaires. Il ne faut en effet pas oublier, qu'outre le préjudice immédiat subi par le pays exportateur, dont l'économie nationale en dépend parfois dramatiquement, il semble absurde de gaspiller des ressources alimentaires à une époque où le concept de sécurité alimentaire est au centre des préoccupations mondiales.

La communauté internationale ayant convenu des orientations à respecter dans les travaux à venir, les institutions des Nations Unies participantes, en l'occurrence la FAO, l'OMS et le PNUE, ainsi que les comités d'experts indépendants tels que le Comité mixte FAO/OMS d'experts des additifs alimentaires (JECFA), ont pu bénéficier des indications précieuses quant à leur plan de travail et aux priorités à fixer pour les prochaines années.

Les débats ont débuté par un examen de la situation générale pour tenter de mesurer l'importance des dommages occasionnés par la contamination des denrées par les mycotoxines. Malgré les estimations considérables en termes économiques, cela reste un exercice difficile, étant donné le manque de données comparables au niveau mondial. On comprend donc l'importance de la prise de conscience du problème et de sa surveillance.

Afin de faire le point sur les connaissances acquises durant ces dernières années, quatre mycotoxines ou groupes de mycotoxines ont fait l'objet de présentations: les fumonisines, l'ochratoxine, la zéaralénone et les trichothécènes. On a jugé opportun de modifier la perspective en présentant trois études de cas concrets portant sur des produits tels que le maïs (voir article de Riley et Norred, p. 25), le café et les pistaches. Ces études présentaient les possibilités de prévention des contaminations des produits par les mycotoxines dont il avait été question auparavant et les options de décontamination. Tout cela a été précédé d'un document introductif (voir article de Lopez-Garcia, Park et Phillips, p. 38) présentant les systèmes intégrés de gestion des mycotoxines. Ces cas concrets, à la fois de contaminants et de produits contaminés, ont amené à aborder les concepts de l'analyse des risques dans la réglementation visant les mycotoxines, cela étant bien sûr un moyen de protéger la santé publique en procédant à une revue systématique des dangers, de l'exposition et donc du risque encouru, en n'oubliant ni la gestion de ces risques, ni une communication adéquate à ce sujet. Le premier document a présenté une vue d'ensemble du processus d'évaluation des risques concernant ces contaminants particuliers que sont les mycotoxines (voir article de Kuiper-Goodman, p. 10). Le second document s'est penché sur les processus spécifiques mis en œuvre par le JECFA (voir article de Herrman et Walker, p. 17). La conférence s'est ensuite intéressée à la réglementation concernant les mycotoxines et à ses modalités d'application. Le premier document a présenté un aperçu de la réglementation mondiale et le second (voir article de Park, Njapau et Boutrif, p. 49) a mis en évidence l'utilité du concept du Système d'analyse des risques – points critiques pour leur maîtrise (HACCP) dans la réduction des risques de contamination liés aux mycotoxines.

La Conférence a formulé différentes conclusions et recommandations, et a, en particulier, insisté sur le fait que les pays doivent tenir compte des méthodologies d'évaluation des risques développées par les organisations internationales, afin de baser leurs exigences en termes d'innocuité et de santé sur des fondements transparents et scientifiques. Cela ressort d'ailleurs de façon très claire des dispositions des Accords sanitaires et phytosanitaires (SPS) de l'Organisation mondiale du commerce (OMC). Il a été également rappelé que les effets sur la santé demeurent le souci principal, mais que les mesures de contrôle doivent tenir compte des conséquences socioéconomiques. C'est pour cette raison qu'une priorité élevée a été accordée aux travaux du JECFA dans ce domaine, et il a été recommandé que celui-ci se réunisse dès que les données nécessaires auront été rassemblées. Ces données devront de préférence s'appuyer sur des observations sur des êtres humains. On accordera une attention particulière aux enfants, et dans l'évaluation des apports, on veillera à l'harmonisation des méthodologies. Etant donné que certaines régions, telle l'Afrique subsaharienne, disposent d'informations limitées sur l'étendue des contaminations, il est fondamental d'encourager le partenariat entre pays développés et en développement pour combler cette lacune.

En ce qui concerne la prévention et le contrôle, il a été recommandé que des recherches sur le développement de variétés résistantes à l'infestation fongique soient menées. Les programmes intégrés de contrôle des mycotoxines doivent s'inspirer des principes du système HACCP. La Conférence s'est également penchée sur le problème des besoins en formation dans le domaine des principes et programmes HACCP, des bonnes pratiques agricoles et de fabrication, et du développement des stratégies pratiques de contrôle et de gestion. Enfin, la Conférence a tenu à préciser que, pour garantir la rentabilité, la réglementation et le contrôle devaient être axés sur les sources majeures de contamination, les ressources à y affecter étant limitées.

Des recommandations précises en ce qui concerne les aflatoxines, les fumonisines et les ochratoxines ont été formulées. La Conférence s'est également intéressée aux problèmes d'échantillonnage et d'analyse. Elle a insisté sur le besoin de développer la recherche tant au niveau de l'échantillonnage et des techniques d'analyse qu'à celui du matériel de référence pour couvrir une gamme de produits et de mycotoxines plus vaste. Elle a ajouté qu'un manuel explicitant les différentes méthodes et étapes de l'échantillonnage devrait être élaboré, et que des méthodes analytiques simples et solides devraient être développées à l'usage des pays en développement. La FAO, l'OMS et le PNUE pourraient apporter leur aide dans le transfert des technologies. Il reste également nécessaire de fournir des normes analytiques, en particulier pour des mycotoxines peu courantes, domaine dans lequel la FAO a un rôle important à jouer en termes de centralisation et de diffusion de l'information. Pour finir, la FAO, l'OMS et le PNUE devraient également promouvoir le développement de méthodes analytiques qui ne soient pas nuisibles à l'environnement ou au personnel de laboratoire. ◆

Third Joint FAO/WHO/UNEP International Conference on Mycotoxins

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The Third International Conference on Mycotoxins took place in March 1999 in Tunis, Tunisia. It was jointly organized by FAO, the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) and continued a tradition that stretches back for more than 20 years. The first such meeting took place in 1977 in Nairobi, under the sponsorship of FAO, WHO and UNEP, when 42 countries and ten international organizations met to reach consensus on actions that would restrict the contamination of food products by these natural toxins. This conference was considered very useful. Ten years later, the international community decided that a sequel was needed, this time in Bangkok where 33 countries and six international organizations discussed follow-up and progress during the ten-year interval, and shaped the strategies to be applied during subsequent years.

This is the brief historical background to the third conference which was held some 12 years later in 1999. During the intervening period, new mycotoxins, including fumonisins, were studied more closely by researchers. More recent additional information on, for example, the impact of already-known mycotoxins on human health, and progress in sampling and analysis techniques shed new light on food contamination by mycotoxins. The monitoring programmes initiated several years previously were beginning to bear fruit, and recent developments in regulation, control and decontamination procedures had emphasized the need for international coordination. Some 38 countries and ten international organizations met at this third conference to discuss and agree on future operational priorities.

The problems caused by mycotoxins are now more numerous and better defined, as analytical methods have become increasingly precise and the regulatory framework for mycotoxins in foods and feeds has become more comprehensive (covering greater numbers of mycotoxins in a wider range of products and an increased number of countries). The economic cost of having consignments rejected and withheld from markets can no longer be ignored. At the same time, advances in toxicological research and the development of concepts such as risk analysis make it easier to assess potential short- and long-term health risks. Decision-makers need to be made aware of the health and economic implications so that resource allocation policy for prevention and control can be measured and adequate.

The primary aim of this conference was, therefore, to serve as a forum for the exchange of scientific and technical information, and to make this information available to government officials responsible for policy-making and administering controls so that prevention and control regulations and programmes could be harmonized – the ultimate aim being to safeguard consumer health while, at the same time, limiting food losses. Quite apart from the immediate damage to the exporting country whose economy may be heavily dependent on exports, it seems absurd to waste food resources at a time when food security is a prime global concern.

The guidelines agreed by the international community for future work provide the participating United Nations agencies (FAO, WHO and UNEP) and independent expert committees, such as the Joint FAO/WHO Expert Committee on Food Additives (JECFA), with invaluable markers for their future plans of work and priorities.

The debate began with a situational overview to gauge the level of damage caused by mycotoxin food contamination – an exercise that was made difficult by the absence of comparable worldwide data, although there are many economic estimates. Awareness of the problem needs, therefore, to be raised and constant surveillance implemented.

Four mycotoxins or mycotoxin groups were reviewed to determine insights acquired in recent years: fumonisins, ochratoxin, zearalenone and trichothecenes. It was believed that taking three different perspectives might yield interesting results so case studies were presented on maize (see Riley and Norred on p. 25), coffee and pistachio. These suggested ways of preventing contamination from the mycotoxins under consideration and looked at decontamination options. A previous introductory paper

(Lopez-Garcia, Park and Phillips on p. 38) had addressed the issue of integrated mycotoxin management systems.

These concrete examples of contaminants and contaminated products triggered debate on the concept of risk analysis in mycotoxin regulation, the systematic review of dangers, exposure and, therefore, risk, clearly being one way of protecting human health, without however neglecting the management of risk and necessary communication. One of the papers presented at the Conference (Kuiper-Goodman on p. 10) looked at the risk assessment process for these very distinctive contaminants. Another dealt with the specific processes implemented by JECFA (Herrman and Walker on p. 17).

The Conference then looked at mycotoxin regulations and enforcement modalities. The first paper presented reviewed worldwide regulations, and the second (Park, Njapau and Boutrif on p. 49) drew attention to the usefulness of the Hazard Analysis and Critical Control Point (HACCP) concept in reducing the risk of mycotoxin contamination. The Conference concluded by examining the importance of analysis and sampling techniques in the control of mycotoxins.

Several conclusions and recommendations were made. In particular, the Conference insisted that countries take note of the risk assessment methodologies that had been developed by the international organizations, so that their safety and health requisites would be transparent and scientifically justified. This echoed the provisions of the World Trade Organization (WTO) Sanitary and Phytosanitary Agreements (SPS).

It also recalled that impact on human health remained the primary concern, although control measures should also take social and economic consequences into account. High priority was given to the work of JECFA which was urged to discuss the matter as soon as the necessary data – preferably based on observations with human beings – had been gathered. Particular attention would be paid to children and efforts would be made to standardize methodologies for input evaluation.

Some geographical areas such as sub-Saharan Africa have little information on the extent of contamination – a shortcoming that should be put right through partnerships between developed and developing countries. As regards the more specific question of prevention and control, it was recommended that research be directed towards developing varieties that are resistant to fungal infestation. The integrated mycotoxin control programmes should reflect HACCP principles. Training requirements were also stressed, on: HACCP principles and programmes; good agricultural and manufacturing practices; and the development of practical control and management strategies.

Finally, the Conference pointed out that regulation and control should concentrate on the principal sources of contamination to maximize returns from limited available resources. Specific recommendations for aflatoxins, fumonisins and ochratoxins were also made. The Conference examined the problems of sampling and analysis and identified a clear need to pursue research on sampling plans, techniques of analysis and reference materials to cover a wider range of products and mycotoxins. A manual explaining the different sampling methods and stages should be produced. At the same time, simple and robust analytical methods should be developed for use in developing countries, with FAO, WHO and UNEP providing assistance with technology transfer. Analytical standards are needed, particularly for the less common mycotoxins, and FAO could again play a key role here as a clearing-house for information. FAO, WHO and UNEP should also promote the development of analytical methods that are environmentally friendly and not harmful to laboratory staff. ◆

Tercera Conferencia Internacional FAO/OMS/PNUMA sobre micotoxinas

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En el mes de marzo de 1999 tuvo lugar en Túnez la Tercera Conferencia Internacional sobre Micotoxinas. Esta reunión fue organizada conjuntamente por la FAO, la Organización Mundial de la Salud (OMS) y el Programa de las Naciones Unidas para el Medio Ambiente (PNUMA), y perpetúa una tradición iniciada hace ya más de 20 años. En efecto, en 1977 se reunieron por primera vez en Nairobi 42 países y 10 organizaciones internacionales, bajo el patrocinio de la FAO, la OMS y el PNUMA, para tratar el tema de las micotoxinas. En esta ocasión se llegó a un acuerdo sobre las medidas que habían de tomarse para limitar la contaminación de los alimentos con esas toxinas naturales. La Conferencia fue considerada sumamente útil y 10 años después la comunidad internacional estimó que era necesario reunirse de nuevo, esa vez en Bangkok. Treinta y tres países y seis organizaciones internacionales examinaron el seguimiento y los progresos realizados en 10 años, proporcionando con ello los elementos para las estrategias que habrían de aplicarse en los años sucesivos.

Estos son los antecedentes históricos de la Tercera Conferencia, celebrada unos 12 años más tarde, en 1999. Durante ese período de tiempo, los investigadores han estudiado más detenidamente nuevas micotoxinas, como las fumonisinas. Otras informaciones más recientes, relativas por ejemplo a la importancia para la salud humana de micotoxinas ya conocidas y los progresos realizados en las técnicas de muestreo y análisis, han arrojado nueva luz sobre el problema de la contaminación de alimentos con micotoxinas. Los programas de vigilancia establecidos hace varias decenas de años comienzan a dar fruto y las últimas novedades en materia de reglamentación, control y procedimientos de descontaminación han acentuado la necesidad de una colaboración internacional. Este es el motivo de que en esta Conferencia se hayan reunido 38 países y 10 organizaciones internacionales para debatir y acordar las actividades prioritarias que han de llevarse a cabo en el futuro.

Teniendo en cuenta la constante mejora de la organización del control y de la precisión de los métodos de análisis, y el marco cada vez más amplio de la reglamentación de las micotoxinas presentes en los alimentos y los piensos (que se aplica a más micotoxinas, en productos más diversos y en un número mayor de países), los problemas que plantean las micotoxinas son más numerosos y, sobre todo, están mejor delimitados. No se puede seguir pasando por alto los daños económicos ocasionados por el rechazo y el descarte de numerosos lotes en el mercado. Paralelamente, los progresos en la investigación toxicológica y la elaboración de conceptos como el de análisis de riesgos permiten evaluar mejor los riesgos para la salud a corto y largo plazo. Es preciso que estos conocimientos relativos a la economía y la salud estén a disposición de los encargados de tomar decisiones, para que las medidas adoptadas respecto de los medios destinados a la prevención y al control estén fundamentadas y respondan a las necesidades.

El objetivo inmediato de esta Conferencia era, por consiguiente, ofrecer un foro para el intercambio de información científica y técnica y facilitar esta información a los funcionarios públicos de los que dependen las políticas oficiales y la administración del control, con miras a armonizar los reglamentos y los programas de prevención y control. La finalidad que se perseguía era garantizar la salud del consumidor limitando al mismo tiempo las pérdidas de alimentos. En efecto, no hay que olvidar que, además del perjuicio inmediato que sufre el país exportador, en ocasiones considerable para la economía nacional, parece absurdo desperdiciar recursos alimentarios en una época en que la atención mundial se centra en el concepto de seguridad alimentaria.

Las orientaciones convenidas por la comunidad internacional para las actividades futuras proporcionan a los organismos participantes de las Naciones Unidas, a saber, la FAO, la OMS y el PNUMA, así como el Comité Mixto FAO/OMS de Expertos en Aditivos Alimentarios (JECFA), valiosas indicaciones en cuanto al plan de trabajo y a las prioridades que han de establecerse para los próximos años.

Los debates se iniciaron con un examen de la situación general para tratar de calcular la importancia de los daños ocasionados por la contaminación de alimentos con micotoxinas. A pesar de las numerosas estimaciones económicas, ese cálculo sigue siendo difícil dado que faltan datos comparables a nivel mundial. Por consiguiente, es necesario tener conciencia de estos problemas, y llevar a cabo una acción de vigilancia constante.

Para hacer un balance de los conocimientos adquiridos en los últimos años, las exposiciones se centraron en cuatro micotoxinas o grupos de micotoxinas: las fumonisinas, la ocratoxina, la zearalenona y los tricotecenos. Pareció conveniente modificar la perspectiva presentando tres estudios de casos concretos, relativos a productos como el maíz (véase el artículo de Riley y Norred en este mismo número, pág. 25), el café y los pistachos. En estos estudios se indicaban las posibilidades de prevención de la contaminación de productos con micotoxinas que se habían examinado anteriormente y las opciones para su descontaminación. Todo ello estuvo precedido de un documento introductivo (véase el artículo de López García, Park y Phillips, pág. 38) en el que se presentaban sistemas integrados de gestión de micotoxinas. Estos casos, tanto de contaminantes como de productos contaminados, sirvieron para abordar los conceptos de análisis de riesgos en la reglamentación sobre micotoxinas, como medio para proteger la salud pública mediante un examen sistemático de los peligros de la exposición, sin olvidar la gestión de esos riesgos y su comunicación adecuada. En el primer documento se presentó una visión de conjunto de los procesos de evaluación de riesgos relativos a esos contaminantes particulares que son las micotoxinas (véase el artículo de Kuiper-Goodman, pág. 10). El segundo documento trataba de los procesos aplicados por el Comité Mixto FAO / OMS de Expertos en Aditivos Alimentarios (véase el artículo de Herrman y Walker, pág. 17).

A continuación la Conferencia se interesó por la reglamentación sobre las micotoxinas y sus modalidades de aplicación. En el primer documento se presentaba un resumen de la reglamentación mundial y en el segundo (véase el artículo de Park, Njapau y Boutrif, pág. 49) se señalaba la utilidad del concepto de Análisis de peligros y de puntos críticos de control (HACCP) en la reducción de los riesgos de contaminación asociados con las micotoxinas. Por último, se examinó la importancia de las técnicas de análisis y muestreo en las actividades de lucha contra las micotoxinas.

La Conferencia formuló diversas conclusiones y recomendaciones. En particular, insistió en que los países debían tener en cuenta las metodologías de evaluación de riesgos elaboradas por las organizaciones internacionales con el fin de que sus requisitos en materia de inocuidad y salud se basaran en principios científicos y transparentes. Por lo demás esto se desprendía claramente de las disposiciones del Acuerdo sobre la Aplicación de Medidas Sanitarias y Fitosanitarias (SPS) de la Organización Mundial del Comercio (OMC). También se recordó que los efectos sobre la salud seguían siendo la preocupación principal, aunque las medidas de control debieran tener en cuenta las consecuencias socioeconómicas. Por este motivo se concedió gran prioridad a las actividades en este sector del JECFA, y se recomendó que éste se reuniera rápidamente, una vez que hubieran podido recogerse los datos necesarios. Estos datos deberían basarse preferiblemente en observaciones en seres humanos. Se concederá especial atención a los niños y, al evaluar las ingestas, se tratará de armonizar las metodologías. Algunas zonas geográficas, como por ejemplo el África subsahariana, disponen de información limitada sobre la amplitud de la contaminación, por lo que debe alentarse la colaboración entre países desarrollados y en desarrollo para colmar esa laguna. Por lo que concierne a la prevención y el control, se recomendó que se realizaran investigaciones sobre la obtención de variedades resistentes a la infestación por hongos. Los programas integrados de lucha contra las micotoxinas debían inspirarse en los principios del sistema HACCP. También se subrayaron las necesidades de capacitación en principios y programas de HACCP, en buenas prácticas agrícolas y de fabricación y en la formulación de estrategias prácticas de lucha y de gestión. Por último, la Conferencia señaló que, para garantizar la rentabilidad, la reglamentación y el control deberían orientarse hacia las fuentes principales de contaminación, dado que los recursos disponibles eran limitados. Se formularon recomendaciones precisas con respecto a las aflatoxinas, las fumonisinas y las ocratoxinas. La Conferencia se interesó también por los problemas del muestreo y el análisis. Indicó la necesidad de fomentar la investigación sobre planes de muestreo, técnicas de análisis y material de referencia para abarcar una gama más amplia de productos y de micotoxinas. Debería prepararse un manual en el que se explicaran los diferentes métodos y fases del muestreo. Además deberían establecerse métodos de análisis sencillos y adecuados a las condiciones de los países en desarrollo. La FAO, la OMS y el PNUMA podrían prestar ayuda en la transferencia de tecnologías. Será también necesario proporcionar normas analíticas, para micotoxinas poco corrientes, ámbito en el que la FAO tendría que desempeñar, una vez más, una importante función de coordinación y difusión de la información. La FAO, la OMS y el PNUMA deberían fomentar la elaboración de métodos analíticos que no fueran nocivos para el medio ambiente ni para el personal de laboratorio. ♦

Approaches to the risk analysis of mycotoxins in the food supply

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A number of cereal and other crops are susceptible to fungal attack, either in the field or during storage. The fungi involved may produce mycotoxins as secondary metabolites. The level of mycotoxins in foods can fluctuate widely and vary significantly from year to year. These fluctuations depend on many factors, including adverse conditions that favour fungal invasion and growth either in the field or during storage. Mycotoxins are a diverse group of chemical substances. When present at high enough levels in the diet, many have caused acute and / or chronic adverse health effects in animals and humans. Mycotoxins can affect many target organs and systems, notably the liver, the kidney and the nervous, endocrine and immune systems. There is much concern about chronic effects brought about by low levels of exposure, and several mycotoxins have been classified by the International Agency for Research in Cancer (IARC) as human carcinogens or potential human carcinogens (IARC, 1993).

Although there are geographic and climatic variations in the production and occurrence of mycotoxins, exposure to these substances occurs all over the world and much of the world's food supply is contaminated to some extent. Monitoring of mycotoxins is needed in areas where high levels cause problems that could have adverse effects on health. Although these toxicants can never be completely removed from the food supply, risk analysis based on sound scientific knowledge makes it possible to define the levels in food (tolerances, guideline levels and maximum residue levels) that are unlikely to be detrimental to health. This will aid the harmonization of mycotoxin regulations and control procedures, and facilitate international trade in food. Considerable efforts have already been made to assess the health risks posed by just a few of these chemicals. In terms of exposure and the severity of the chronic lesions (especially cancer) they cause, mycotoxins appear, at present, to pose a higher risk than anthropogenic contaminants, pesticides and food additives (see Table). In addition, the implications of exposure to several mycotoxins at once may need to be considered.

Rating health risks from foods

Acute		Chronic
	High	
Microbiological		Mycotoxins
Phycotoxins		Anthropogenic contaminants
Some phytotoxins		Some phytotoxins
Mycotoxins		Unbalanced diet
Anthropogenic contaminants		Phycotoxins
Food additives		Microbiological
Pesticide residues		Food additives
		Pesticide residues
	Low	

Source: Kuiper-Goodman, 1998.

RISK ANALYSIS

At the time of two previous meetings on mycotoxins – held by FAO, the World Health Organization (WHO) and the United Nations Environment Programme (UNEP) in Bangkok in 1987 and Nairobi in 1997 – the application of risk analysis to mycotoxin problems was not well developed. The lack of a unified approach among countries resulted in a wide variety of guidelines and regulations regarding mycotoxins. During the last ten years, much progress has been made in the approaches to risk analysis for all of the chemicals that may cause concern for food safety, including mycotoxins, and a leading role has been taken by international organizations such as WHO and FAO (especially through the Codex Alimentarius Commission [CAC] and the Joint Expert Committee on Food Additives [JECFA]), the International Agricultural Research Centres, the Organisation for Economic Co-operation and Development (OECD) and the International Life Sciences Institute (ILSI), as well as several national agencies (CAC,1998; JECFA, 1996, IARC,1991; IPCS, 1990). Although it has been recognized that common approaches and common terminology are essential for harmonization, this goal has not yet been achieved.

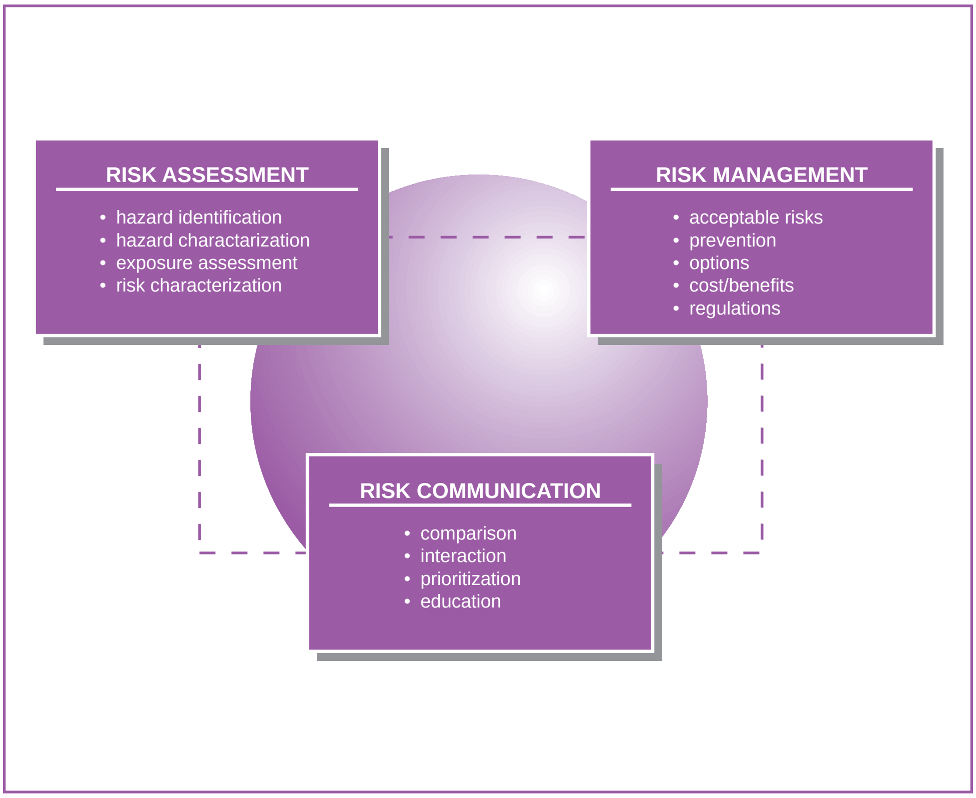
In dealing with the problems associated with mycotoxins, a framework of risk analysis similar to that recently proposed by FAO and WHO (FAO / WHO, 1995) needs to be used. According to this framework, risk analysis is made up of three parts: risk assessment, risk management and risk communication (see Figure). Each of these major spheres of influence overlaps with the others. Such an approach considers scientific principles related to human and animal health, including comparisons with other risks (as part of risk communication), as well as socio-economic factors (as part of risk management). The aim is to achieve practical solutions, such as guidelines regarding maximum residue levels, procedural guidelines aimed at preventing the problem (e.g. Hazard Analysis and Critical Control Point [HACCP]) or a combination of both. Ideally, such guidelines are acceptable to the countries that produce food commodities as well as to the countries that receive them.

Since the last FAO / WHO / UNEP meeting, new mycotoxins have been discovered (fumonisins) and for some of the other mycotoxins important new data related to toxicology, epidemiology and human exposure have become available (as a result of improved detection methods and the use of biomarkers). This has resulted in new and updated evaluations by IARC (IARC,1993) and JECFA (JECFA,1996), as well as national agencies (Kuiper-Goodman, 1985; Kuiper-Goodman, Scott and Watanabe, 1987; Kuiper-Goodman and Scott, 1989; Olsen *et al.*, 1991; Bowers *et al.*, 1993; Kuiper-Goodman, 1996; Kuiper-Goodman *et al.*, 1996). Scientific evaluations have become the basis for recommendations regarding the international regulation of mycotoxin levels (aflatoxins, ochratoxins, patulin, zearalenone) made by the Codex Committee on Food Additives and Contaminants (CAC, 1999) and the European Union (EU).

Several factors make it difficult to use a harmonized approach. One of these factors relates to the conflict between national interests and trade interests. Countries need to be autonomous and serve their own interests. However, the interests of producing countries do not necessarily coincide with those of recipient countries and the presence of mycotoxins in food commodities could lead to trade barriers, unless all parties agree on the approach for deriving safe levels and can see that their own interests have been addressed. Other impeding factors relate to data interpretation and analysis and differences in food intake patterns among countries. These are discussed later in this article.

RISK ASSESSMENT

Ideally, risk assessment involves a complete toxicological assessment, an epidemiological assessment, an exposure assessment and a risk characterization. However, in the risk management of mycotoxins it may be necessary to take action before all this information is available. In this article, “hazard” is defined as the intrinsic property of a biological, chemical or physical agent to cause adverse health effects under specific conditions. This definition implies some certainty that, under similar conditions, the agent will cause similar adverse health effects. “Risk” is defined as the



Risk analysis framework for food safety

estimated likelihood of an adverse health effect, weighed for its severity, occurring in humans as a result of exposure to a biological, chemical or physical agent in food.

Hazard identification

Many economically important mycotoxins have carcinogenic properties that affect several organs. They may also cause developmental effects, including birth defects, and affect the immune system; some also exhibit hormonal activity or are neurotoxic. In addition to these diverse organ- or site-specific actions, a disturbance of the gastrointestinal system, skin irritation and haematological effects have been observed. These studies usually determine empirically the "no-observed-adverse-effect level" (NOAEL), which can be regarded as a "threshold".

Several of the carcinogenic mycotoxins appear to have both initiating and promoting properties and also contribute to tumour progression, as reflected in both tumour pathology and genotoxicity test results. It has been presumed that there is no threshold for this process. Other mycotoxins seem to exert predominantly tumour-promoting activity, a mode of action for which it is presumed that a threshold does exist. Under hazard characterization, these two types of carcinogens are treated differently and this has an impact on how safe levels are determined. However, the distinction between the two groups of carcinogens is not always clear. Thus, mycotoxins have a wide spectrum of toxicological effects, and may affect many diverse cellular processes. This diversity of biological effects demands a case-by-case evaluation and may require a variety of extrapolation techniques (see next section, Hazard characterization).

The widespread occurrence of mycotoxins has made them a cause of human as well as animal mycotoxicoses (ergotism, liver cancer, yellow rice disease, alimentary toxic aleukia [ATA], turkey-X-disease). Risk assessment, therefore, also uses information from epidemiological studies of exposed humans.

Hazard characterization

Hazard characterization is the extrapolation phase of risk assessment. Its aim is to make a predictive characterization of the hazard to humans, based on animal studies (species extrapolation) under low exposure conditions (extrapolation from high to low dose). The endpoint of hazard characterization is the estimation of a "safe dose" such as a provisional tolerable daily intake (PTDI) or equivalent – the word "tolerable" indicates that, generally, mycotoxins do not serve a useful purpose to humans. In general, (P)TDIs are determined only when there is likely to be a threshold in the relationship between dose and effect, based on knowledge of the mechanism and mode of action. To derive a TDI for humans, it has been common practice to divide the NOAEL by a safety factor of 100 when extrapolating from animals to humans. This takes into consideration a factor of 10 for interspecies differences and another factor of 10 for intra-species (in this case, intra-human) variation. When there are significant irreversible effects for which thresholds have been established (as is the case for non-genotoxic carcinogens) or insufficient data, additional uncertainty factors may be added. Sometimes the setting of a (P)TDI is deferred until sufficient data are available. Alternatively, and as an interim measure, a margin of safety approach is sometimes used, as in the interim risk assessment for fumonisins.

For genotoxic carcinogens the default position has been that there is no threshold dose below which effects, such as initiation of the carcinogenic process, will not occur, and a TDI is generally not determined. Non-threshold carcinogens are not allowed as food additives. When such chemicals cannot be completely avoided (as is the case for some mycotoxins), a variety of approaches have been used. Mathematical models, most of which presume that the effects of low doses are linear, have been used to extrapolate the possibility of adverse effects at low doses. The dose corresponding to a risk level of 10^{-5} or 10^{-6} has, in some jurisdictions, been considered as posing a negligible risk. Other jurisdictions consider that, for genotoxic carcinogens or even genotoxic agents (e.g. patulin) for which the carcinogenic potential has not been established, the most appropriate method of regulation is to determine levels that are "as low as is reasonable" (ALAR) or as low as is technologically achievable. Alternatively, regulation can be based on biological factors, such as mode of action and weight of evidence, which examine the severity of the resulting lesion. This information can be combined with an estimate of tumour potency such as the TD_{05}. Dividing the TD_{05} by an uncertainty factor of 5 000 gives a value that is equivalent to a risk level of 1:100 000 and provides estimates of safe intake that are similar to those derived using low-dose linearized models (Kuiper-Goodman, 1990). This approach can, therefore, be used for both genotoxic and non-genotoxic agents, which is especially useful when there is some uncertainty regarding the mode of action (threshold versus non-threshold, e.g. ochratoxin A) (Kuiper-Goodman, 1996). The value of 5 000 for the uncertainty factor can be decreased when additional biological information indicates that there is less cause for concern. Estimates for a "safe dose" may also be derived from appropriate epidemiological studies, such as for aflatoxins, when they are available. Efforts need to be made to establish more international harmonization in dealing with mycotoxins for which a non-threshold mode of action is postulated.

Although difficult to determine, the TDI can be viewed as an intrinsic property of mycotoxins, which takes into consideration both the potency of the effects measured and the biological factors regarding the severity, relevance and significance of the effects for humans.

Exposure assessment

Reliable and validated analytical methods are currently available for only a few mycotoxins. Improved methods have recently been established with the development of specific antibodies for use in enzyme-linked immunosorbent assays (ELISAs) and the utilization of immuno-affinity columns for sample clean-up. Problems are caused by the non-homogenous distribution of mycotoxins in food commodities, which therefore require appropriate sampling.

Exposure to mycotoxins depends on the level of these substances in different foods and on the intake of those foods. There can be large national and regional differences in the intakes of foods, so exposure assessments are country-specific and this is an impediment for harmonization. For mycotoxins, the monitoring data for food commodities of concern collected over several years usually provide the input for data on levels. Estimates may then be refined by considering further modifications to the levels of mycotoxins, in the food that is actually consumed, by including information on manufacturing and processing both by industry and in the home. In Canada, exposure estimates can be based on the average intakes of the total population, of the 90th percentile value of the total population, or of only those persons who actually consume the food being assessed. They may be made for different age or target groups, depending on the scenario being investigated (i.e. acute intake versus chronic intake). Exposure varies according to age, with young children, generally, being exposed at a much higher rate in terms of body weight for commodities such as milk (up to sevenfold) and peanut butter (up to fourfold) that may contain aflatoxins or their metabolites. Exposure assessments can sometimes also be based on measurements of biomarkers in humans (aflatoxins, ochratoxins), and the intake can then be estimated on the basis of pharmacokinetic relationships.

It is also necessary to address the potential hazards to human health that arise from the presence of mycotoxins in animal food products. At high levels in feed, mycotoxins may cause illness or death of farm animals through the development of such animal toxicoses as aflatoxicosis. Carry-over studies in livestock have only been conducted for major mycotoxins, and more information on bioavailability to humans of the parent compound and its metabolites, including bound metabolites (conjugates, protein-bound), is needed. At lower levels in feed, mycotoxins may have no apparent effect on livestock production, but their residues and related substances might move up the food chain. This indirect intake of mycotoxins and related substances from the consumption of animal food products may pose a health hazard to humans. In a previous review it was found that the risk to humans associated with indirect exposure from animal-derived food products is generally somewhat lower than that from direct exposure from cereal and other food crops that may contain mycotoxins (Kuiper-Goodman, 1991).

Since mycotoxins affect mainly staple foods, exposure in market-based economies, where different sources are mixed, tends to be lower but is usually of long duration. In farming communities, high exposure of shorter duration may sometimes occur. Little is known about the differences in associated long-term risks between these two types of exposure. Probabilistic exposure assessments have recently been introduced and help to visualize the distribution of exposure under diverse scenarios. International agreement on how to derive appropriate parameters is needed.

Risk characterization

Risk characterization is the qualitative and / or quantitative estimation, including the attendant uncertainties, of the severity and probable occurrence or absence of known and potential adverse health effects on an exposed population. It is based on hazard identification, hazard characterization and exposure assessment. Risk characterization can also be the establishment of levels of daily exposure at which the risk is insignificant over a lifetime (i.e. exposure needs to be below the TDI or other measure of safe dose). This latter definition may be more relevant, bearing in mind the uncertainties that have already been discussed. For substances for which a TDI cannot be determined, the safety margin between human exposure and adverse effects seen in animal species may serve as an indication of the likelihood of ill effects occurring in humans, and this may be used in risk management. This was the case in the recent evaluation of fumonisins (Kuiper-Goodman *et al.*, 1996). As well as considering the average population, risk characterization also needs to consider those groups that are most vulnerable to exposure, such as children (because of their lower body weight), and other groups for which there may be differences in bio-availability, metabolism or genetic disposition, such as the elderly. In this regard, the adequacy of a tenfold safety factor to address differences in human susceptibility arising from human variability needs to be examined.

Detailed risk assessments have been performed for only a few mycotoxins (aflatoxins, deoxynivalenol, ochratoxin A, zearalenone, fumonisins) (Kuiper-Goodman, 1985; Kuiper-Goodman, Scott and Watanabe, 1987; Kuiper-Goodman and Scott, 1989; Olsen *et al.*, 1991; Bowers *et al.*, 1993; Kuiper-Goodman, 1996; Kuiper-Goodman *et al.*, 1996) and these evaluations need to be re-examined from time to time taking into account new information on both exposure and basic toxicology as well as improved understanding of the mechanism of action.

RISK MANAGEMENT

With regard to mycotoxins, there are a variety of risk management options that help to ensure a safe food supply. These range from prevention of mould growth and setting of regulatory limits, to diversion into alternate uses. Enormous economic costs are associated with all of these options.

One impediment to harmonization in trade relates to the setting of maximum residue limits (MRLs) for mycotoxins. MRLs are now generally based on scientific evaluations. They cannot be exceeded in traded goods, but levels of mycotoxins somewhat above these levels can be tolerated on a low-incidence basis. A large percentage of incidences of mycotoxin occurrence are well below the MRL. The export of commodities is a continuous process, so it is not possible to base allowable levels on the weighted average of the actual levels, adjusted for several commodities, or to revise the allowable levels for various commodities on a yearly basis. However, in the final risk assessments, exposure assessments for mycotoxins can be based on actual residue levels (and not on the MRL) as a worst case scenario. The concern of regulators is that, if a higher MRL were to be allowed, it would become the acceptable level for industry and blending upwards to this level would occur, thus increasing exposure. For this reason blending is not allowed in many jurisdictions.

CONCLUSIONS

There have been a wide variety of regulations pertaining to mycotoxins. Initially, many of these were not based on sound scientific evaluation. As yet, there is a lack of agreement among countries, but in recent years the Codex Committee on Food Additives and Contaminants (CCFAC) has been moving towards harmonization by inviting position papers on proposed regulatory limits for several mycotoxins (aflatoxins, ochratoxins, patulin and zearalenone) and, based on comments from its member countries, it is hoped that a consensus can be reached. The ultimate aim is to achieve optimal regulations for human safety which do not become trade barriers. ◆

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Approaches to the risk analysis of mycotoxins in the food supply

Mycotoxins are fungal metabolites that are present in a large part of the world's food supply. They pose a potential threat to food safety. At lower levels, the possible chronic toxicity of many mycotoxins (aflatoxins, ochratoxins, fumonisins, zearalenone) is usually of greater concern than acute toxicity, since some of these substances are very potent carcinogens and exposure to them is widespread. While the complete elimination of mycotoxins from foods would be an impossible goal, it is important to ensure that their levels do not threaten health. In recent years, a variety of interrelated approaches have been developed to assess the hazards, monitor exposure and determine the associated risks. These processes need to be transparent so that the hazards and the need for risk management and intervention are clear. Risk assessments provide the scientific background and understanding for sound policy decisions that protect the public at an affordable cost and allow for public/international discussion, scrutiny and harmonization. Because there are differences in the significance of biological effects and in the available data, there is at present no single approach that can be used for all problems regarding mycotoxins, and a case-by-case approach is needed.

Méthodes d'analyse des risques liés aux mycotoxines dans les approvisionnements en produits alimentaires

Les mycotoxines sont des métabolites fongiques qui sont présents dans une grande partie des produits alimentaires dans le monde entier. Ils constituent une menace pour ce qui est de l'innocuité des produits alimentaires . A une teneur moindre, on s'inquiète davantage de la possible toxicité chronique de nombreuses mycotoxines (aflatoxines, ochratoxines, fumonisines, zéaralénone) que d'une toxicité aiguë, étant donné que certaines de ces substances ont un effet cancérigène très important et l'exposition à ces produits est largement répandue. Même si l'élimination complète des mycotoxines des aliments serait un objectif impossible à atteindre, il importe d'assurer que leur teneur ne constitue pas une menace pour la santé. Ces dernières années, toute une variété de méthodes interdépendantes ont été mises au point pour évaluer le dangers, déterminer l'exposition et définir les risques associés. Ces méthodes doivent être transparentes afin que les dangers et la nécessité d'une gestion des risques et d'une intervention soient clairs. L'évaluation des risques fournit une base scientifique qui permet de prendre des décisions judicieuses visant à protéger le consommateur, à un coût abordable, et permet d'examiner, d'analyser et d'harmoniser les politiques au niveau international. Etant donné qu'il existe des différences dans les effets biologiques et dans les données disponibles, on ne dispose pas à l'heure actuelle d'une méthode unique pouvant être utilisée pour tous les problèmes concernant les mycotoxines, et c'est pourquoi une approche au cas par cas est nécessaire.

El análisis de riesgos de micotoxinas en los suministros alimentarios

Las micotoxinas son metabolitos fúngicos que están presentes en una gran parte de los suministros alimentarios mundiales, y pueden representar una amenaza potencial para la inocuidad de los alimentos. La posible toxicidad crónica de muchas micotoxinas (aflatoxinas, ocratoxinas, fumonisinas, zearalenona) en dosis inferiores suele suscitar mayor preocupación que la toxicidad aguda, dado que algunas de esas sustancias son carcinógenos muy poderosos y la exposición a ellas es muy amplia. Aunque sería imposible eliminar por completo las micotoxinas de los alimentos, es importante asegurarse de que sus niveles en los alimentos no representen una amenaza para la salud. En los últimos años se han elaborado varios enfoques relacionados entre sí para evaluar los peligros vinculados a la exposición a micotoxinas y determinar los riesgos asociados. Es necesario que este proceso sea transparente a la hora de declarar los peligros y la necesidad de una gestión de los mismos y de una intervención. La evaluación de riesgos proporciona el fundamento y los conceptos científicos necesarios para adoptar decisiones normativas acertadas que protejan al público con un costo asequible, y permitan asimismo un debate, una supervisión y una armonización internacional. Teniendo en cuenta las diferencias de los efectos biológicos y los datos disponibles, no hay en la actualidad un único enfoque que pueda aplicarse a todos los problemas relacionados con las micotoxinas, por lo que es necesario examinar cada caso por separado. ◆

Risk analysis of mycotoxins by the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

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The Joint FAO/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) has been meeting regularly since 1956 to evaluate food additives, contaminants, naturally occurring toxicants and residues of veterinary drugs in food. To date, the Committee has evaluated more than 1 200 chemicals, including more than 20 contaminants.

JECFA provides scientific advice to the Codex Alimentarius Commission (CAC), primarily through two of its general subject committees, the Codex Committee on Food Additives and Contaminants (CCFAC) and the Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF). JECFA also provides FAO and WHO member countries with scientific advice on chemicals in food. Because its primary client is CAC, its priorities are generally established by CCFAC and CCRVDF.

To date, JECFA has evaluated three mycotoxins: aflatoxins B, G, and M; patulin and fumonisins. However, governments and CAC are becoming increasingly concerned about the presence of mycotoxins in foodstuffs, as evidenced by the presence of several additional mycotoxins on the CCFAC priority list: fumonisins, trichothecenes and zearalenone for evaluation, and ochratoxin A for re-evaluation. Zearalenone will be evaluated at JECFA's fifty-third meeting in June 1999, but the others are awaiting further data before they are placed on the agenda for evaluation.[1] As with nearly all contaminants, the lack of relevant toxicological and epidemiological data is the primary impediment to the evaluation of most mycotoxins.

OCHRATOXIN A AND PATULIN

The contaminants ochratoxin A and patulin have both been evaluated twice by JECFA. They were re-evaluated at the forty-fourth meeting in 1995, when the previous provisional tolerable weekly intake (PTWI) of 0.1 mg per kilogram of body weight for ochratoxin A was confirmed and a provisional maximum tolerable daily intake (PMTDI) of 0.4 mg per kilogram of body weight was established for patulin. A traditional approach was used in these assessments in that no-observed-effect levels (NOELs) and lowest-observed-effect levels (LOELs) were identified and safety factors were applied to both.

Expression of the tolerable intake on a weekly basis is considered to be appropriate for contaminants that may accumulate within the body over a period of time, as is the case with ochratoxin A. On any particular day, consumption of food containing above-average levels of the contaminants may exceed that day's proportionate share of the weekly tolerable intake. The weekly assessment takes into account such daily variations, with the primary concern being prolonged intake of the contaminant. By contrast, a PMTDI was established for patulin because it does not accumulate in the body and only occasionally is apple juice (the primary route of intake) heavily contaminated.

Levels of ochratoxin A and patulin contamination of foodstuffs and potential intakes of these contaminants were considered by the Committee during their evaluations. However, this information was not included as an integral component of the risk assessment because it was assumed that there is no appreciable risk when intake is below the PTWI or PMTDI.

AFLATOXINS

Aflatoxins were first evaluated at the thirty-first JECFA meeting in 1987. The Committee recognized that aflatoxin B_1 is a well-known potent hepatocarcinogen in all the mammalian species studied, with a wide range of sensitivities. While good data were available on the relationships among aflatoxin levels, duration of exposure and carcinogenicity in animals, the available data on the association between aflatoxin exposure and primary liver cancer in humans were difficult to evaluate because of the large number of uncertainties in these studies, including inadequate data on the dietary intake of aflatoxins, the

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[1] JECFA reports are posted on the FAO Web site (www.fao.org/waicent/faoinfo/economic/esn/jecfa.htm).

contribution of hepatitis B virus to the etiology of cancer, and cultural and dietary status and habits. The Committee concluded that the available scientific information was insufficient for determination of the extent to which exposure to aflatoxins contributed to the increased incidence of primary liver cancer in the populations that were studied.

In view of these uncertainties, the Committee was unable to establish a figure for a tolerable intake level. It urged that the intake of dietary aflatoxin be reduced to the lowest practicable levels so that the potential risk could be minimized, and it recommended that efforts should be made to limit the presence of aflatoxins in food to irreducible levels. An earlier Committee meeting had defined an irreducible level as “that concentration of a substance which cannot be eliminated from a food without involving the discarding of that food altogether, severely compromising the ultimate availability of major food supplies”.

Subsequent to this evaluation, CCFAC began working on standards for aflatoxin levels in food and feed products, but it has been exceedingly difficult to reach consensus on the maximum levels that should be included in these standards. A major impediment to consensus is that the levels of contamination of foodstuffs vary widely around the world and, with the “irreducible level” recommendation, decisions are made solely on trade grounds.

With respect to trade, the perspectives of delegations differ profoundly. Delegations from countries in which aflatoxin contamination is not prevalent want standards that are based on low maximum levels because they do not wish to see the quality of their food supply degraded. Delegations from countries in which the climatic conditions make aflatoxin contamination a problem naturally wish to have standards in which higher levels of contamination are permitted so that they can trade their products on world markets. In addition, when stringent international standards are used, the populations of these countries are placed at higher risk because products with low levels of contamination are exported, leaving the more contaminated, lower-quality products for domestic consumption.

After a number of years of little progress, CCFAC asked JECFA, at its Twenty-sixth Session in 1994, to provide estimates of the toxicological potency of aflatoxins and to derive estimates of the potential risks for different human populations. In response to this request, aflatoxins B, G, and M were considered at the forty-sixth meeting of the Committee in 1996. However, the evaluation could not be completed at that meeting and it was carried over to the forty-ninth meeting in 1997, when a detailed evaluation was completed (WHO, 1998).

Health risks

The Committee reviewed a wide range of studies, in both animals and humans, that provided qualitative and quantitative information on the hepatocarcinogenicity of aflatoxins. It evaluated the potencies of these contaminants, linked potencies to intake estimates and considered the impact, and overall risks, of hypothetical standards on sample populations.

It was recognized that aflatoxins are among the most potent mutagenic and carcinogenic substances known. Extensive experimental evidence from test species shows that aflatoxins are capable of inducing liver cancer in most of the animal species studied. Most epidemiological studies also show a correlation between exposure to aflatoxin B_1 and an increased incidence of liver cancer, although there is some evidence suggesting that humans are at substantially lower risk from exposure to aflatoxins than test species are. Some epidemiological studies suggest that the intake of aflatoxins poses no detectable independent risk and others suggest that it poses risks only in the presence of other risk factors such as hepatitis B infection.

A number of factors influence the risk of primary liver cancer, most notably carriage of hepatitis B virus which is determined by the presence of hepatitis B surface antigen in serum. The potency of aflatoxin B_1 appears to be significantly enhanced in individuals with simultaneous hepatitis B infection. This interaction makes it difficult to interpret the epidemiological studies and determine the extent to which aflatoxins act as independent risk factors.

The identification of hepatitis C virus is an important recent advance in understanding the etiology of liver cancer. Two studies have investigated interactions among hepatitis C infection, aflatoxins and liver cancer but, so far, the results have been inconclusive. It is estimated that between 50 and 100 percent of cases of liver cancer are associated with persistent infection with hepatitis B and / or hepatitis C.

The Committee considered that the weight of scientific evidence, which includes epidemiological data, studies in laboratory animals and *in vivo* and *in vitro* studies of metabolism, supports the conclusions that aflatoxins should be treated as carcinogenic food contaminants and that their intake should be reduced to levels as low as reasonably achievable.

CARCINOGENIC POTENCY

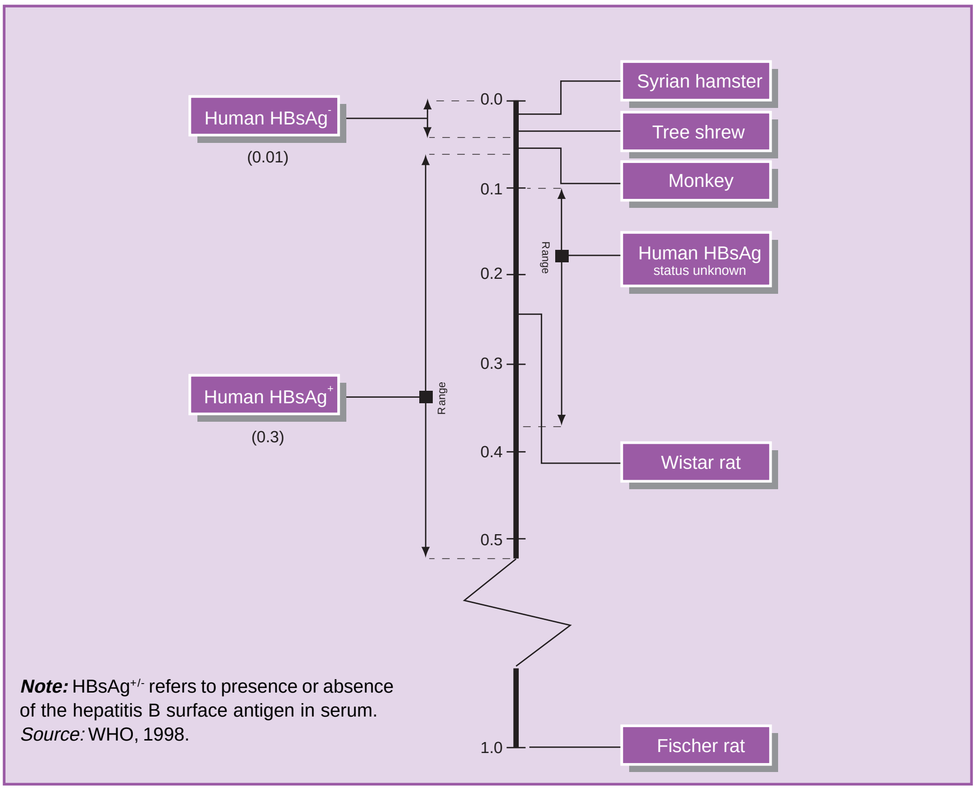
A number of dose-response analyses have been performed on aflatoxins. However, all of these analyses have limitations, the most important of which are the following:

- All of the epidemiological data from which a dose-response relationship can be determined are confounded by concurrent infection with hepatitis B. The epidemiological data are from geographical areas where the prevalence both of individuals carrying hepatitis B surface antigen and of contamination with aflatoxins are high; the relationship between these risk factors in areas where both of them are low is unknown.
- It is not known how reliable and precise the estimates of exposure to aflatoxins are in the relevant study populations. For example, aflatoxin biomarkers in humans do not reflect their long-term intake.
- The shape of the dose-response curve is also unknown, and this introduces an additional element of uncertainty when choosing mathematical models for interpolation.

Observations relating to the interaction between hepatitis B infection and aflatoxins suggest two separate aflatoxin potencies; one is apparent in populations in which chronic hepatitis infections are common, the other in populations in which chronic hepatitis infections are rare. In analyses based on toxicological and epidemiological data, potency estimates for aflatoxins were divided into two basic groups, potencies applicable to individuals without hepatitis B infection and those applicable to individuals with chronic hepatitis B infection. As can be seen from the Figure, extrapolations of animal data to estimate potencies in humans generally fall within the range of potency estimates derived from the epidemiological data.

In deriving the potency estimates of 0.01 and 0.3 cases per year per 100 000 people, per ng of aflatoxin B_1 per kilogram of body weight per day for hepatitis B surface antigen negative and positive individuals, respectively, the Committee used only those potency estimates from the epidemiological studies that showed a positive association between aflatoxins and liver cancer. Studies in which no association was detected, or in which the association was negative, were not used, leading to an overestimate of aflatoxin potency. Other potential biases included:

- When current levels of intake (measured using biomarkers or dietary surveys) are related to current levels of liver cancer (which is presumed to have a long induction period), historical levels of intake are ignored and, since intakes are likely to have been higher in the past, aflatoxin potency will be overestimated.
- Owing to limitations in the methods used to detect hepatitis B virus, the earliest studies systematically underestimated the prevalence of hepatitis B infection in patients with liver cancer by as much as 20 to 30 percent. This also leads to an overestimation of the relative potency of any other factor, including aflatoxins.
- Histological confirmation of cases of liver cancer is limited in most epidemiological studies, allowing the



Note: HBsAg$^{+/-}$ refers to presence or absence of the hepatitis B surface antigen in serum.
Source: WHO, 1998.

Potency estimates for human liver cancer resulting from exposure to aflatoxin B_1 derived from epidemiological and toxicological studies (cancers per year per 100 000 people per ng per kilogram of body weight per day)

possibility that cases of non-primary liver cancer have been included and this too could lead to an under- or overestimation of the aflatoxin potency.

When these biases are taken into account, the values shown in the figure should be viewed as overestimates of the potency of aflatoxins, and it is possible that humans are less sensitive to aflatoxins than the animal species tested in laboratory experiments. Differences in the carcinogenic potency of aflatoxins among species can be partially attributed to differences in metabolism. However, there was insufficient quantitative information available about the competing aspects of metabolic activation and detoxification of aflatoxin B_1 in various species to identify an adequate animal model for humans and to explain the apparent differences in potency among species.

POPULATION RISKS

In a population, the fraction of the total incidences of liver cancer that is attributable to intake of aflatoxins was derived by combining estimates of aflatoxin potency (risk per unit dose) and estimates of aflatoxin intake (dose per person). The frequency and amount of aflatoxin contamination in a number of products were available, and the Committee concentrated on groundnuts, cereals and maize. Many of the data on levels of aflatoxin contamination were derived from non-random samples that appeared to be biased upwards because monitoring studies focus on products that are thought to be contaminated. Some of the data on levels of contamination are not likely to be based on current CAC sampling recommendations for aflatoxins. Accordingly, data on levels of contamination should be interpreted with caution and used only to infer patterns of importance in setting standards and not to provide exact contamination estimates.

Dietary intakes

Mean dietary intakes of aflatoxins for various regions were estimated using regional diets from the Global Environment Monitoring System – Food Contamination Monitoring and Assessment Programme combined with data on levels of aflatoxin contamination.

The Committee considered the possible impact of applying two hypothetical standards to aflatoxin contamination – 10 and 20 mg per kilogram. These should not be construed as recommended standards; they were chosen for illustrative purposes only. Governments and CAC should perform this type of analysis for particular standards that are being considered, basing it on their own data on contamination, dietary patterns and prevalence of hepatitis B.

Two examples using these hypothetical standards were developed. In the first example, it was assumed that the level of contamination of food by aflatoxins is low and the proportion of the population that is hepatitis B surface antigen positive is small. Monitoring data from Europe on aflatoxin B_1 levels in groundnuts, maize and their products were used and it was assumed that 1 percent of the population is hepatitis B surface antigen positive. Assuming that these foods are ingested according to the "European diet", the mean estimated intakes of aflatoxins are 19 ng per person per day when a standard of 20 mg per kilogram is applied and 18 ng per person per day with a standard of 10 mg per kilogram. Using the potency estimates shown in the Figure, these intakes translate into estimated population risks of 0.0041 and 0.0039 cancers per year per 100 000 people when standards of 20 and 10 mg per kilogram, respectively, are applied. Thus, reducing the hypothetical standard from 20 mg to 10 mg per kilogram yields a reduction in the estimated population risk of approximately two cancers per year per 1 000 million people.

The second example pertains to areas with higher levels of aflatoxin contamination and a larger percentage of the population carrying the hepatitis B virus. Monitoring data from China on aflatoxin B_1 levels in groundnuts, maize and their products were used, and it was assumed that 25 percent of the population is hepatitis B surface antigen positive. Assuming that these foods are ingested according to the "Far Eastern diet", the mean estimated intakes of aflatoxins are 125 ng per person per day when a standard of 20 mg per kilogram is applied and 103 ng per person per day with a standard of 10 mg per kilogram. Using the potency estimates in the Figure, these intakes translate into estimated population risks of 0.17 and 0.14 cancers per year per 100 000 people when standards of 20 mg and 10 mg per kilogram, respectively, are applied. Thus, reducing the hypothetical standard for this population from 20 mg to 10 mg per kilogram yields a reduction in the estimated population risk of approximately 300 cancers per year per 1 000 million people. These calculations, and the basis for them, are explained in more detail in WHO, 1998 and WHO, 1999.

The differences in population risks between these hypothetical standards are lower than might be expected on a first analysis. However, the results are not surprising when it is considered that, in both cases, the most highly contaminated samples are eliminated, thus greatly reducing average estimated intakes of aflatoxins. The use of standards by all countries should, therefore, be encouraged.

CONCLUSIONS

After reviewing and analysing the data, the Committee came to the following conclusions:

- Aflatoxins are considered to be human liver carcinogens, aflatoxin B_1 being the most potent. Aflatoxin M_1 has a potency approximately one order of magnitude lower than that of B_1.
- The potency of aflatoxins in individuals who carry hepatitis B is substantially higher than in those who do not carry it. Thus, reduction of the intake of aflatoxins in populations with a high prevalence of hepatitis B will result in a greater reduction in liver cancer rates than reduction of the intake of aflatoxins in populations with a low prevalence of hepatitis B.
- Vaccination against hepatitis B will reduce the number of carriers of the virus. The present analysis suggests that reducing the number of carriers would reduce the potency of aflatoxins in vaccinated populations and, consequently, reduce the risk of liver cancer.
- Analyses of the application of hypothetical standards for aflatoxin contamination in food (10 mg or 20 mg per kilogram) to model populations indicate that:
  - populations in which the prevalence of hepatitis B surface antigen positive individuals is low and / or in which the mean intake of aflatoxins is low (less than 1 ng per kilogram of body weight per day) are unlikely to exhibit detectable differences in population risks;
  - populations in which both the prevalence of hepatitis B surface antigen positive individuals and the intake of aflatoxins are high would benefit from reductions in aflatoxin intake.
- Reductions in the intake of aflatoxins can be achieved through avoidance measures such as improved farming and proper storage practices and / or through enforcing standards for levels of contamination in food or feed within countries and across borders.
- When two alternative standards for aflatoxin contamination in food are considered, the higher standard will yield essentially the same risk as the lower standard if the fractions of samples excluded under the two standards are similar. When a substantial fraction of the current food supply is heavily contaminated with aflatoxins, reducing the levels of contamination may result in a detectable reduction in rates of liver cancer. Conversely, when only a small fraction of the current food supply is heavily contaminated, reducing the standard by an apparently substantial amount may have little appreciable effect on health.

FAO and WHO encourage governments and CAC to make use of this evaluation in deciding on the appropriate standards to apply to aflatoxins. Significant resources are required, however, as use of the evaluation requires a significant amount of information at the national level, including monitoring data and information on dietary patterns and the prevalence of hepatitis B in the population. A comforting factor is that risks are significantly reduced when the most highly contaminated samples are eliminated. This can be done without a detailed analysis of the risk, and governments are encouraged at least to take this step if they are lacking the information necessary to make full use of the evaluation carried out by JECFA. ◆

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Risk analysis of mycotoxins by the Joint FAO/WHO Expert Committee on Food Additives (JECFA)

The Joint FAO/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) evaluates food additives, contaminants, naturally occurring toxicants and residues of veterinary drugs in food and provides scientific advice to the Codex Alimentarius Commission (CAC). To date, JECFA has evaluated three mycotoxins: aflatoxins B, G, and M; patulin and fumonisins. Trichothecenes and zearalenone are listed for evaluation at the next JEFCA sessions; and ochratoxin A will be re-evaluated.

In this article, the scientific evidence regarding mycotoxins and liver cancer is assessed and the JECFA conclusions are provided. Aflatoxins are considered to be human liver carcinogens, aflatoxin B_1 being the most potent. Aflatoxin M_1 has a potency approximately one order of magnitude lower than that of B_1. The potency of aflatoxins in individuals who carry hepatitis B is substantially higher than in those who do not carry it. Thus, reduction of the intake of aflatoxins in populations with a high prevalence of hepatitis B will result in a greater reduction in liver cancer rates than reduction of the intake of aflatoxins in populations with a low prevalence of hepatitis B. Vaccination against hepatitis B will reduce the number of carriers of the virus. The present analysis suggests that this would reduce the potency of the aflatoxins in vaccinated populations and, consequently, reduce the risk of liver cancer. Analyses of the application of hypothetical standards for aflatoxin contamination in food (10 mg or 20 mg per kilogram) to model populations indicate that: populations in which the prevalence of hepatitis B surface antigen positive individuals is low and/or in which the mean intake of aflatoxins is low (less than 1 ng per kilogram of body weight per day) are unlikely to exhibit detectable differences in population risks; while populations in which both the prevalence of hepatitis B surface antigen positive individuals and the intake of aflatoxins are high would benefit from reductions in aflatoxin intake.

Reductions in the intake of aflatoxins can be achieved through avoidance measures such as improved farming and proper storage practices and/or through enforcing standards for levels of contamination in food or feed within countries and across borders. When two alternative standards for aflatoxin contamination in food are considered, the higher standard will carry essentially the same risk as the lower standard if the fractions of samples excluded under the two standards are similar. When a substantial fraction of the current food supply is heavily contaminated with aflatoxins, reducing the levels of contamination may result in detectable reductions in rates of liver cancer. Conversely, when only a small fraction of the current food supply is heavily contaminated, reducing the standard by an apparently substantial amount may have little appreciable effect on health. FAO and WHO encourage governments and CAC to make use of this evaluation in deciding on the appropriate standards to apply to aflatoxins. However, this requires a significant amount of information at the national level including monitoring data and information on dietary patterns and the prevalence of hepatitis B in the population.

L'analyse des risques des mycotoxines par le Comité mixte FAO/OMS d'experts des additifs alimentaires (JECFA)

Le Comité mixte FAO/OMS d'experts des additifs alimentaires (JECFA) évalue les additifs alimentaires, les contaminants, les substances toxiques d'origine naturelle et les résidus de médicaments vétérinaires dans les aliments, et donne des avis scientifiques à la Commission du Codex Alimentarius (CAC). A ce jour, le JECFA a évalué trois mycotoxines – les aflatoxines B, G et M – la patuline et des fumonisines; il est prévu que les trichothécènes et la zéaralénone seront évaluées lors des prochaines sessions du JECFA; et l'ochratoxine A fera l'objet d'une réévaluation.

Dans cet article, les preuves scientifiques concernant les mycotoxines et le cancer du foie sont évaluées, et on pourra lire les conclusions du JECFA. Les aflatoxines sont considérées comme des carcinogènes du foie chez l'homme, l'aflatoxine B_1 étant le plus virulent d'entre eux. La virulence de l'aflatoxine M_1 est d'environ un ordre de grandeur inférieur à celui de l'aflatoxine B_1. La virulence des aflatoxines chez les individus porteurs d'hépatite B est nettement plus élevée que chez ceux qui ne le sont pas. Ainsi, la réduction de l'ingestion d'aflatoxines chez les populations qui ont une prévalence élevée d'hépatite B permettra de réduire davantage les taux de cancer du foie qu'une réduction de l'ingestion d'aflatoxines chez des populations qui ont une faible prévalence d'hépatite B. La vaccination contre l’hépatite réduira le nombre de porteurs du virus. Selon cet article, cela réduirait la virulence des aflatoxines chez les populations vaccinées et donc le risque de cancer du foie. Des analyses de l’application de normes théoriques concernant la contamination des aliments par les aflatoxines (10 mg/kg ou 20 mg/kg) à des populations hypothétiques indiquent ce qui suit: dans les populations où la prévalence d’individus ayant une réaction positive à l’antigène de surface de l’hépatite B est faible et/ou l’ingestion moyenne d’aflatoxines est faible (moins de 1 ng/kg de poids corporel par jour) il est peu probable qu’apparaissent des différences notables du point de vue des risques; alors que chez les populations où la prévalence d’individus ayant une réaction positive à l’antigène de surface de l’hépatite B est forte et où l’ingestion d’aflatoxines est élevée, il y aurait intérêt à réduire l’ingestion d’aflatoxines.

Pour ce faire, on peut prendre des mesures préventives telles que de meilleures pratiques de culture et un entreposage correct et/ou appliquer des normes visant les concentrations de la contamination dans les produits d’alimentation humaine ou animale à l’intérieur des pays et au-delà des frontières. Lorsque deux normes possibles pour la contamination des produits alimentaires par l’aflatoxine sont examinées, la norme supérieure entraînera pour l’essentiel le même risque que la norme inférieure si les fractions des échantillons exclus dans le cadre des deux normes sont similaires. Lorsqu’une part importante des approvisionnements alimentaires courants est fortement contaminée par des aflatoxines, la réduction des niveaux de contamination peut entraîner une baisse sensible des taux de cancer du foie. Inversement, lorsqu’une petite part seulement des approvisionnements alimentaires courants est fortement contaminée, l’abaissement apparemment sensible de la norme peut ne guère avoir d’effet appréciable sur la santé. La FAO et l’OMS encouragent les gouvernements et la CAC à utiliser cette évaluation pour décider de normes appropriées à appliquer aux aflatoxines. Toutefois, cela nécessite de disposer d’une quantité suffisante d’informations au niveau national, y compris des données de surveillance, et des informations sur les schémas alimentaires, et sur la prévalence de l’hépatite B dans la population.

Análisis de riesgos de micotoxinas por el Comité Mixto FAO/OMS de Expertos en Aditivos Alimentarios (JECFA)

El Comité Mixto FAO/OMS de Expertos en Aditivos Alimentarios (JECFA) evalúa aditivos alimentarios, contaminantes, sustancias tóxicas naturales y residuos de medicamentos veterinarios en los alimentos y proporciona asesoramiento científico a la Comisión del Codex Alimentarius (CAC). Hasta la fecha, el JECFA ha evaluado tres micotoxinas –las aflatoxinas B, G y M–, la patulina y las fumonisinas; los tricotecenos y la zearalenona serán evaluados en los próximos períodos de sesiones del JECFA; la ocratoxina A será objeto de una reevaluación. En este artículo, se examinan los datos científicos disponibles sobre las micotoxinas y el cáncer de hígado y se ofrecen las conclusiones a que ha llegado el JECFA. Se considera que las aflatoxinas son carcinógenos para el hígado humano, siendo la aflatoxina B$_1$ la más potente. La aflatoxina M$_1$ tiene una potencia de un orden de magnitud aproximadamente inferior a la de la aflatoxina B$_{1.}$ La potencia de las aflatoxinas en individuos que son portadores de la hepatitis B es considerablemente mayor que en los individuos no portadores. Por consiguiente, la reducción de la ingesta de aflatoxinas en poblaciones con una prevalencia alta de la hepatitis B redundará en una reducción de las tasas de cáncer de hígado mayor que la reducción de la ingesta de aflatoxinas en poblaciones con una baja prevalencia de la hepatitis B. La vacunación contra la hepatitis B reducirá el número de portadores del virus. El presente análisis sugiere que si se reduce el número de portadores se reducirá la potencia de las aflatoxinas en las poblaciones vacunadas y por consiguiente el riesgo de cáncer de hígado. Estudios sobre la aplicación de normas hipotéticas para la contaminación de alimentos con aflatoxinas (10 mg/kg o 20 mg/kg) a modelos de población indican que las poblaciones en las que la prevalencia de individuos positivos al antígeno superficial de la hepatitis B es baja y/o en la que la ingesta media de aflatoxinas es baja (inferior a 1 ng/kg de peso corporal al día) no mostrarán probablemente diferencias detectables en los riesgos para la población; las poblaciones en las que tanto la prevalencia de individuos positivos al antígeno superficial de la hepatitis B como la ingesta de aflatoxinas son altas resultarían beneficiadas si se redujera la ingesta de aflatoxinas. La reducción de la ingesta de aflatoxinas puede conseguirse mediante medidas preventivas como por ejemplo sistemas de cultivo mejorados y prácticas de almacenamiento adecuadas o mediante la aplicación de normas relativas a los niveles de contaminación en los alimentos o los piensos dentro de los países y entre ellos. Cuando se examinan dos normas alternativas para la contaminación de alimentos con aflatoxinas, la norma más rigurosa dará esencialmente el mismo resultado en lo que respecta al riesgo que la norma menos rigurosa si la fracción de muestras excluidas en las dos normas es análoga. Cuando una parte considerable del suministro de alimentos está altamente contaminada con aflatoxinas, la reducción del nivel de contaminación puede dar lugar a una reducción detectable de las tasas de cáncer de hígado. Por el contrario, cuando sólo una pequeña parte del suministro de alimentos está altamente contaminada, puede que la reducción del nivel en una cantidad aparentemente considerable tenga pocos efectos apreciables sobre la salud. La FAO y la OMS instan a los gobiernos y al CAC a que utilicen esta evaluación para decidir las normas apropiadas que han de aplicarse a las aflatoxinas. Sin embargo, ello requiere un volumen considerable de información a nivel nacional, incluidos datos de seguimiento, información sobre hábitos alimentarios y prevalencia de hepatitis B en la población. ◆

Mycotoxin prevention and decontamination – a case study on maize

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Numerous reviews and publications have summarized the approaches already in use and being developed to minimize mycotoxin contamination of maize (Agricultural Research Service, 1997a and 1997b; CAST, 1989; Robens, 1990; Jackson, DeVries and Bullerman, 1996; Sinha and Bhatnagar, 1998; Scott, 1998). Many of the strategies used for other commodities can generally also be applied to maize (McMullen, Jones and Gallenberg, 1997). In this article, "prevention of mycotoxin production in maize" encompasses prevention of toxin biosynthesis and metabolism in the field (pre-harvest) or in storage (post-harvest). "Mycotoxin detoxification" refers only to post-harvest treatments designed to remove, destroy (decontaminate) and ultimately reduce the toxic effects of mycotoxins (detoxify). The potential ability of a plant to detoxify mycotoxins *in situ* is treated as a prevention strategy.

HEALTH AND TRADE EFFECTS

Clearly the pre- or post-harvest prevention of mycotoxin contamination is the preferred strategy for minimizing mycotoxins in foods and feeds. Failure to prevent fungal invasion and toxin formation in the field or in storage will inevitably lead to an increased risk of adverse health effects and economic loss. However, if chemical monitoring is successful, maize consumption should not be a significant source of increased health risk from mycotoxins. Early identification of mycotoxin-contaminated grains provides the opportunity to direct the most highly contaminated grains into uses that minimize consumption by sensitive species. Nonetheless, the lower economic value of contaminated maize can result in large monetary losses for the farmer. In addition, regulatory limits that are inappropriately stringent can effectively remove large amounts of maize from the market. For example, in a year of high fumonisin contamination in maize-producing countries (in the absence of careful monitoring), an action limit set too low could result in a significant loss of food from the market. Thiel *et al.* (1992) reported that 35 percent of the commercial maize products that they sampled from the United States contained more than 1 part per million (ppm) of total fumonisins. Worldwide, total fumonisins in maize meal range from < 50 parts per billion (ppb) to several ppm (Shephard *et al.*, 1996). Thus, an action limit set at 1 ppm could result in a significant loss of maize meal from the world market. In a time of dwindling food supplies, this is clearly an unacceptable loss.

PREVENTION STRATEGIES

Some prevention strategies that are currently in use or under development are summarized in Box 1. An integrated multipronged approach is the preferred strategy (CAST, 1989). However, some specific strategies are more practical and timely than others. For example, the strategies listed as "known to be effective" are labour-intensive and relatively low-cost. The specifics of these approaches vary from fungus to fungus and mycotoxin to mycotoxin. The pre- or post-harvest strategy that should be emphasized in a particular year will depend on the climatic conditions of that year. Unfortunately, humans cannot usually avoid weather that favours fungal infection, and the combination of high temperature and drought often precludes increased irrigation and, consequently, adequate mineral nutrition. Conversely, reducing the moisture level in the field at critical periods is equally impossible. Nonetheless, understanding the environmental factors that promote infection, growth and toxin production is the first step in developing an effective plan to minimize mycotoxins in foods and feeds.

Prevention or reduction in the incidence of pre- and post-harvest infection is clearly a critical factor in reducing mycotoxin accumulation, since the concentrations of aflatoxins, deoxynivalenol or fumonisins have been shown to be greater in symptomatic than in non-symptomatic maize ears or kernels (Desjardin *et al.*, 1998; Reid, Mather and Hamilton, 1996; Scott and Zummo, 1995). Environmental factors that favour *Aspergillus flavus* infection include high soil or air temperature, drought stress, nitrogen stress, crowding of plants and conditions that aid dispersal of conidia during silking (CAST, 1989;

BOX 1
STRATEGIES FOR PREVENTION OF MYCOTOXINS IN MAIZE

Pre-harvest strategies

Known to be effective

- Reduction in plant stress through irrigation, mineral nutrition, protection from insect damage.
- Avoidance of environmental conditions that favour infection in the field.
- Minimization of crop residues and other point sources of inoculum.

Potentially effective

- Breeding for maize cultivars resistant to fungal infection.
- Use of crop protection chemicals that are antifungal agents.

Developmental

- Development of transgenic maize plants resistant to fungal infection.
- Development of transgenic maize cultivars capable of catabolism/interference with toxin production.
- Development of maize genetically engineered to resist insect damage.
- Development of maize seeds containing endophytic bacteria that exclude toxigenic fungi.
- Exclusion of toxigenic fungi by pre-infection of plants with biocompetitive-non-toxigenic fungal strains.

Post-harvest strategies

Known to be effective

- Harvesting when water content is optimal to prevent saprophytic development of toxigenic fungi.
- Removal of damaged maize and drying of kernels to the optimal moisture content before storage.
- Control of insect and rodent activity and maintenance of appropriate moisture levels and temperature.
- Frequent cleaning of feed delivery systems and short-term storage areas.

Potentially effective

- Use of antifungal agents such as propionic and acetic acids.

Note: The authors would like to acknowledge the expert advice from and valuable discussion with A.E. Desjardin, United States Department of Agriculture, Agricultural Research Service (USDA-ARS).

Robens, 1990). The growth of *A. flavus* and *A. parasiticus*, and subsequent aflatoxin production in storage, are favoured by high humidity (> 85 percent), high temperature (> 25° C) and insect or rodent activity (CAST, 1989).

Typically, infections with *Fusarium graminearum* are localized, sporadic, favoured by cool, moist conditions during silking (Munkvold and Yang, 1995; Park, Smalley and Chu, 1996) and most common in wetter summers (Sutton, 1982; Vigier *et al*., 1997). Epidemics are usually associated with wet conditions late in the growing season. Storage of maize that is wet and at cool to moderate temperatures has been associated with outbreaks of oestrogenic syndrome and feed refusal (CAST, 1989) owing to the presence of zearalenone and deoxynivalenol, respectively.

Fusarium moniliforme is the most common pathogen of maize (Munkvold and Desjardin, 1997). Because *F. moniliforme* is a seed-borne, symptomless endophyte in maize, its elimination is very difficult (Agricultural Research Service, 1997a). Maize ear rot associated with *F. moniliforme* and *F. proliferatum* is accompanied by significant fumonisin levels. In the United States, warm, dry years have resulted in greater fumonisin accumulation than cooler years (Shephard *et al.*, 1996), whereas maize grown in cooler areas usually contains low amounts of fumonisin (Doko *et al.*, 1995; Miller, 1994). However, dry weather early in the growing season followed by wet weather during silking and later has been associated with severe ear rot (Munkvold and Desjardin, 1997). Moisture on the silks clearly promotes infection (Munkvold, McGee and Carlton, 1997). *F. moniliforme* and *F. proliferatum* kernel rot of maize is also an important ear disease in hot maize-growing areas (De Leon and Pandey, 1989; King and Scott, 1981; Ochor, Trevathan and King, 1987) and is associated with warm, dry years and / or insect damage (Shurtleff, 1980). High incidence of European corn borer damage increases *F. moniliforme* disease and fumonisin concentrations (Lew, Adler and Edinger, 1991), while high levels of thrip (*Frankliniella occidentalis*) infestation are correlated with increased disease incidence (Farrar and Davis, 1991). Ear rot is reduced in maize that has been genetically engineered for resistance to the European corn borer (Munkvold, Hellmich and Showers, 1997). Hybrids with thin kernel pericarp and increased incidence of kernel splitting (aggravated by drought) are more susceptible to kernel rot (Hoenisch and Davis, 1994; Odvody, Spencer and Remmers, 1997). As with aflatoxins, fumonisin production in the field is promoted by environmental stress, as evidenced by the fact that maize hybrids grown outside their range of adaptation or under cool but drought-stressed conditions, had higher fumonisin concentrations (Shelby, White and Burke, 1994; Doko *et al*., 1995; Miller, 1994; Visconti, 1996).

Tillage practices, crop rotation, weed control, late seasonal rainfall, wind and pest vectors can all affect the amount and source of fungal inoculum that maintains the disease cycle in maize (Munkvold and Desjardin, 1997). Any action that interrupts the cycle should reduce the probability of silk and kernel infection. For example, elimination of waste maize deposits will reduce the incidence of *A. flavus* in kernels and soil beneath the piles (Olanya *et al.*, 1997). Not surprisingly, nitidulid beetles (vectors for *A. flavus*) living under or near waste maize deposits were found to be highly contaminated with *A. flavus*. In the same study, it was reported that soil-borne *A. flavus* was greatly increased when soil temperatures were 35° to 40° C. So, in drought years with high temperatures, when increased irrigation is not practical, steps to reduce inoculum may be one of the few practical strategies for reducing the probability of an aflatoxin (or other mycotoxin) epidemic.

Breeding for resistance to toxin production has met with limited success (McMullen, Jones and Gallenberg, 1997; Munkvold and Desjardin, 1997; Robens, 1990). Maize cultivars that are resistant to aflatoxin production have been reported (Windham and Williams, 1998; Campbell, Hamblin and White, 1997; Russin *et al.*, 1997). However, breeding to control aflatoxins, fumonisins, deoxynivalenol and zearalenone production *in planta* has yet to meet with any real success since the occurrence of these, the most common mycotoxins in maize, is clearly quite unpredictable and often quite high. If productive, resistant varieties of maize were readily available, they would preclude concern about detoxification and animal and human disease. However, they are clearly not available.

The use of chemicals is a very attractive strategy to prevent mycotoxin production. Some chemical treatments will prevent mould growth and, potentially, reduce mycotoxin production in the field and in storage (Wegulo *et al.*, 1997). However, with regard to maize and mycotoxins, the economic and ecological hurdles seem to be quite high (McMullen, Jones and Gallenberg, 1997), as evidenced by the fact that few of these approaches are being marketed widely.

Many new and exciting pre-harvest prevention strategies that involve new biotechnologies are being explored. These new approaches involve the design and production of maize plants that reduce the incidence of fungal infection, restrict the growth of toxigenic fungi or prevent toxin accumulation. Biocontrols using non-toxigenic biocompetitive agents are another potentially useful strategy in maize (Agricultural Research Service, 1997a and 1997b; Robens, 1990). However, the possibility of recombination with toxigenic strains is a concern (Geiser, Pitt and Taylor, 1998). In the case of *F. moniliforme* in maize, the use of bacterial biocompetitive agents and non-toxigenic *F. moniliforme* isolates is under development (Agricultural Research Service, 1997a). One interesting approach is the engineering of maize plants to catabolize fumonisins *in situ* (Munkvold and Desjardin, 1997). Typically, these approaches require considerable research and development but offer the potential of ultimately producing low-cost and effective solutions to the mycotoxin problem in maize.

Post-harvest prevention of mycotoxin production is primarily dependent on good management practices before and after harvest (Box 1). Aflatoxins are potentially serious post-harvest problems, unlike fumonisins, since *F. moniliforme*, like other Fusaria, does not grow in maize at less than 18 to 20 percent moisture (Munkvold and Desjardin, 1997). Nonetheless, animal health problems associated with the consumption of poorly preserved (mouldy) maize contaminated with fumonisins are not uncommon. As a last resort, chemical treatment with antifungal agents is a possibility. However, the cost-effectiveness of this approach is questionable. Chemical treatments that prevent mould growth and / or toxin production include the treatment of stored maize with propionic or acetic acid (CAST, 1989).

DETOXIFICATION STRATEGIES

Strategies currently in use and under development for detoxification of mycotoxin-contaminated maize are summarized in Box 2. Not surprisingly, the mycotoxins in maize that are of the greatest concern (aflatoxins, deoxynivalenol, zearalenone, ochratoxin A, fumonisins) are also quite stable and, therefore, difficult to degrade. Fumonisins, for example, are relatively stable molecules that do not react readily with macromolecules (although they bind quite specifically to the enzyme ceramide synthase) and are not mutagenic. Their lack of reactivity creates a challenge to anybody aiming at detoxifying maize. Conversely, fusarin C (a *Fusarium* mycotoxin detected in mouldy maize) is very unstable, reacts readily with macromolecules and is mutagenic. Because of its reactivity, it breaks down rapidly and would therefore be easy to detoxify if it caused food safety problems.

Detoxification and decontamination are not always the same thing. The fact that a toxin cannot be detected in a food or feed by analytical chemistry does not mean that the product has been detoxified. In Box 2, detoxification strategies have been arbitrarily divided into those that are primarily dependent on physical, chemical or microbiological processes that detoxify by destroying, modifying or absorbing the mycotoxin so as to reduce or eliminate the toxic effects. One promising method is the use of selective high-affinity hydrated sodium calcium aluminosilicates to bind aflatoxin in feeds and foods. However, some commonly used non-selective silico-aluminates do not completely protect, and may enhance toxicity of aflatoxin (Mayura *et al.*, 1998). Dietary

BOX 2
STRATEGIES FOR DETOXIFICATION OF MYCOTOXINS IN MAIZE

Physical methods

Cleaning: screening out fine materials reduces fumonisins and other mycotoxins – simple but incomplete.

Segregation and sorting: “black light” test for aflatoxins – simple but misleading; colour sorting technology – unproven with maize, but promising.

Density segregation and washing: of fumonisins, deoxynivalenol, zearalenone – non-specific and incomplete, but suitable for wet milling and alkaline processing of maize.

Thermal degradation: incomplete for most mycotoxins.

Microwave treatment: high levels destroy trichothecenes.

Solar degradation: of aflatoxins – results in maize oil encouraging.

Extrusion cooking: of fumonisins – temperature- and screw speed-dependent destruction – very promising (Katta *et al.,* 1998).

Wet milling: produces starch free, or almost free, of zearalenone, fumonisins and aflatoxins, but T-2 toxin is increased in maize germ.

Chemical methods

Thermal treatment plus reducing sugars: of fumonisins – promising but toxicology and stability uncertain.

Nixtamalization/alkaline hydrolysis: reversible degradation of aflatoxins and partial degradation of fumonisins, but toxicity remains – not an effective method for detoxification of fumonisins or aflatoxin; reduced zearalenone and deoxynivalenol.

Bisulphite: destroys aflatoxin B1, reduces deoxynivalenol in maize – bisulphite is a common food additive (the DON sulphonate is unstable in alkali).

Ammoniation: approved method for aflatoxin in maize in Mexico, South Africa and several states in the United States – may not be effective in detoxifying fumonisins in maize.

Hydrogen peroxide/sodium bicarbonate: destroys fumonisin in maize.

Ozonation: degrades and detoxifies aflatoxins in naturally contaminated maize – promising.

Hydrated sodium calcium aluminosilicates: bind aflatoxins with high affinity and capacity – demonstrated efficacy *in vivo* when added to diets; non-selective aluminosilicates may pose significant risks and should be avoided (Mayura *et al.,* 1998).

Activated charcoal: reduces dietary conversion of aflatoxin B_1 to aflatoxin M_1 in cows.

Microbiological methods

Ethanol fermentation: does not break down aflatoxin B_1, zearalenone or fumonisin B_1; toxins may actually be increased in spent grain used in animal feeds.

Probiotic mixtures: Lactobacillus and *Propionibacterium* may reduce bio-availability of dietary aflatoxin (Ahokas *et al.,* 1998).

Dietary interventions

Choline, methionine, vitamins, protein, dietary fat, antioxidants and inducers of metabolizing enzymes: addition to animal feeds can lower toxicity caused by mycotoxins in maize.

Sources: Except where indicated the information is summarized from CAST, 1989; Jackson, DeVries and Bullerman, 1996; Scott, 1998; T.D. Phillips, Texas A&M University, personal communication.

interventions intended to reduce toxicity after a mycotoxin has been absorbed are another detoxification strategy.

RECOMMENDATIONS

In view of the research carried out to date, the following recommendations can be made:

- Maize grown for human consumption in areas where conditions are frequently favourable to fungal invasion and mycotoxin production in the field should be tested for mycotoxin contamination before use.
- Additional research is needed to develop the ability to predict when and where environmental conditions may make mycotoxin contamination probable and to develop the means to disseminate warnings to farmers and processors.
- If invasion in the field is probable and environmental conditions are favourable for mycotoxin production in the field, care should be taken to reduce sources of inoculum and to minimize plant stress and insect damage.
- Once it is determined that field contamination is likely, care should be taken to minimize the growth of the fungus after harvest and while in storage. Planning should begin for decontamination and include the diversion of contaminated maize away from human consumption or consumption by sensitive species.
- Maize cultivars that are resistant to drought stress, insect damage and fungal infection need to be developed.
- Easy and economical decontamination procedures need to be developed. ◆

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Mycotoxin prevention and decontamination – a case study on maize

Prevention of mycotoxins in maize encompasses prevention of toxin biosynthesis and metabolism in the field or in storage. Mycotoxin detoxification refers to post-harvest treatments to remove, destroy or reduce the toxic effects. Failure to prevent mycotoxin formation in the field or in storage will inevitably lead to increased health risks and economic loss. However, successful monitoring should prevent mycotoxins from becoming a significant source of increased health risks. An integrated multi-pronged approach is the preferred strategy for controlling mycotoxin contamination. The pre- or post-harvest strategy that is most appropriate will depend on the climatic conditions of that particular year. Understanding the environmental factors that promote infection, growth and toxin production is the first step towards an effective plan to minimize mycotoxins in foods and feeds.

Fusarium moniliforme is the most common pathogen of maize. In maize, *F. moniliforme* is a seed-borne endophyte without symptoms, so its elimination is difficult. Tillage practices, crop rotation, weed control, late-season rainfall, wind and pest vectors can all affect the amount and source of the fungal inoculum that maintains the disease cycle in maize. Many of the new and exciting pre-harvest prevention strategies that are being explored involve production of genetically engineered resistant maize. Biocontrols using non-toxigenic biocompetitive agents are also a potentially useful strategy in maize. Post-harvest prevention of mycotoxin production is primarily dependent on good management practices before and after harvest. Detoxification strategies that are physical, chemical or microbiological can detoxify maize by destroying, modifying or absorbing the mycotoxins so as to reduce or eliminate the toxic effects.

Prévention des mycotoxines et décontamination – une étude de cas sur le maïs

La prévention des mycotoxines dans le maïs englobe la prévention de la biosynthèse et du métabolisme des toxines dans le maïs sur pied ou stocké. Par détoxication des mycotoxines, on entend les traitements après récolte visant à supprimer, détruire ou réduire les effets toxiques des mycotoxines. L'échec des tentatives faites pour prévenir la formation de mycotoxines dans le maïs sur pied ou stocké conduira inévitablement à une augmentation des risques sanitaires et à des pertes économiques. Toutefois, un suivi attentif devrait empêcher les mycotoxines de devenir une source importante de risques sanitaires. Une approche intégrée à multiples facettes semble la meilleure stratégie pour lutter contre la contamination par les mycotoxines. La stratégie, préalable ou postérieure à la récolte la plus appropriée à appliquer, dépendra des conditions climatiques de l'année considérée. Une bonne compréhension des facteurs écologiques qui favorisent l'infection ainsi que la croissance et la production de toxines est un préalable indispensable à la mise au point d'un plan efficace de réduction des mycotoxines dans les aliments, qu'ils soient destinés à l'alimentation humaine ou animale.

Fusarium moniliforme est le pathogène le plus commun du maïs. Dans la mesure où il s'agit d'un endophyte du maïs transmis par les semences et non accompagné de symptômes, son élimination sera difficile. Les façons culturales, la rotation des cultures, la lutte contre les adventices, les précipitations de fin de campagne, le vent et les vecteurs sont autant de facteurs déterminant la quantité et la source de l'inoculum fongique qui entretient le cycle de la maladie dans le maïs. Bon nombre des nouvelles stratégies de prévention préalables à la récolte qui sont actuellement à l'étude impliquent la production de maïs résistant génétiquement modifié. Les contrôles biologiques utilisant des agents biocompétitifs non toxicogènes constituent une autre stratégie potentiellement utile pour le maïs. La prévention après récolte de la production de mycotoxines dépend essentiellement de bonnes pratiques de gestion avant et après la récolte. Les stratégies de détoxication de nature physique, chimique ou microbiologique peuvent détoxiquer le maïs en détruisant, modifiant ou absorbant les mycotoxines de façon à en réduire ou à en supprimer les effets toxiques.

Prevención y descontaminación de micotoxinas: estudio monográfico sobre el maíz

La prevención de las micotoxinas en el maíz comprende la prevención de la biosíntesis de toxinas y su metabolismo sobre el terreno o en almacén. La descontaminación de micotoxinas se refiere a los tratamientos poscosecha para eliminar o reducir los efectos tóxicos. El no evitar la formación de micotoxinas en el campo o en el almacén conducirá inevitablemente a un aumento del riesgo para la salud y a una pérdida económica. Sin embargo, un buen seguimiento impedirá que las micotoxinas se conviertan en causa importante de aumento del riesgo para la salud. La estrategia preferida para controlar la contaminación por micotoxinas es un enfoque polifacético integrado. La estrategia de precosecha o poscosecha más apropiada dependerá de las condiciones climáticas de ese determinado año. El conocer los factores medioambientales que fomentan la infección, el desarrollo y la producción de toxinas es el primer paso para un plan eficaz encaminado a reducir al mínimo las micotoxinas en los alimentos y los piensos. El *Fusarium moniliforme* es el patógeno más conocido del maíz. Dado que es un endofito asintomático transportado por la semilla, será difícil su eliminación. Las prácticas de labranza, la rotación de cultivos, el control de malezas, la pluviosidad en la temporada tardía, el viento y los vectores de plagas son factores que influyen en la cantidad y origen del inóculo fúngico que mantiene el ciclo de la enfermedad en el maíz. Son muchas las estrategias nuevas y prometedoras de precosecha para la prevención que se están explorando y que consisten en la producción de maíz resistente sobre la base de la ingeniería genética. Otra estrategia que puede resultar útil es la del control mediante el empleo de agentes no toxígenos y competitivos biológicamente. La prevención poscosecha de la producción de micotoxinas depende fundamentalmente de unas buenas prácticas de gestión antes de la cosecha y después de ella. Con las estrategias de descontaminación, que pueden ser físicas, químicas o microbiológicas, puede descontaminarse el maíz destruyendo, modificando o absorbiendo la micotoxina de suerte que se reduzcan o se eliminen sus efectos tóxicos. ◆

Quality assurance in mycotoxin analysis

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In recent years considerable attention has been directed towards improving and ensuring the quality of analytical data on contaminants in foods and animal feeds. Whether the data are used for assessing risk from exposure (food surveillance), for food control (regulatory monitoring) or for monitoring standards for trading purposes, it is critical that contaminants be identified correctly and that quantitative data be reliable. These requirements also apply to mycotoxins, which present unique analytical challenges in terms both of obtaining truly representative samples (Park, Njapau and Coker, 1998) and of undertaking analysis at the low regulatory limits of control (µg per kilogram and sub-µg per kilogram levels) required in many countries.

SAMPLING FOR MYCOTOXIN ANALYSIS

A number of papers (Park and Pohland, 1989; Gilbert, 1996; Park, Njapau and Coker, 1998) have identified the particular problems associated with the sampling of commodities for mycotoxin analysis and have reviewed the sampling schemes being used by various organizations. Unlike analytical methods, sampling schemes cannot be collaboratively tested; usually a particular sampling plan is proposed, based on statistical consideration of the measured toxin distribution, and thereafter adopted as an official procedure. It is important to understand that sampling plans have diverse objectives, and an acceptable sampling plan for quality control purposes may be very different from a plan intended for use in enforcement. In choosing to adopt a particular sampling plan, in addition to ensuring that it is based on sound statistical principles, practical considerations must be taken into account as there is little point in adopting a procedure that is so labour-intensive it becomes too costly to implement. General guidance is available from international organizations such as the Codex Alimentarius Commission (CAC, 1987) on the factors that should be taken into account when considering sampling schemes. In enforcement situations, there is some merit in specifying both the sampling scheme and the regulatory limit, so as to avoid dispute between parties on the level of mycotoxin contamination in a particular commodity when the individual samples have been taken in different ways.

The United States Food and Drug Administration (USDA) has well-defined sampling procedures for aflatoxins (Park and Pohland, 1989). These take account of the commodity type, whether samples are to be taken from retail or bulk commodities and, in the latter case, the lot size. For each circumstance the minimum number of subsamples to be taken is specified, as is the minimum unit size of each subsample. In addition, the equipment used for grinding and mixing of the bulk sample is specified, as is the subsample weight to be taken for analysis and the manner of its collection. In the United Kingdom, a study of aflatoxin contamination in a consignment of dried figs (Sharman *et al.*, 1994) led to a sampling plan based on the distribution of aflatoxin contamination as well as on practical considerations. Comparison of the United Kingdom, Netherlands and United States sampling plans (Whitaker *et al.*, 1995) gives an insight into sample sizes and the trade-off between consumer and producer risks.

VALIDATED ANALYTICAL METHODS

Validated analytical methods are those that have been subjected to collaborative trial assessment and for which performance characteristics such as recovery, repeatability (r) and reproducibility (R) have been determined. Such validation is intrinsically time-consuming as it takes several months to organize a trial and there are also lengthy procedural requirements, which have to be undertaken by official organizations (such as the European Standardization Organization, the European Committee for Standardization [CEN] and the Association of Official Analytical Chemists International [AOAC International]), that scrutinize the proposed methods. The *Official methods of analysis of AOAC International* have validated methods covering aflatoxins, deoxynivalenol, zearalenone, ochratoxin A, sterigmatocystin, patulin and fumonisins (AOAC International, 1995). A number of these methods date back to the 1970s and, although they can be reliable, when they are based on thin layer chromatography (TLC) they would not, today, be the favoured approach for many laboratories. In some instances, limits of detection are also inadequate to meet the increasingly stringent demands for measurement at low levels.

The collaborative testing of methodology requires considerable planning in terms of the design of the trial, the type of matrix or matrices to be analysed, the level of contamination of the mycotoxin of interest, and the numbers of samples that are to be included in the trial. Naturally contaminated materials are required for which homogeneity as well as stability of the mycotoxin during the period of the study have to be demonstrated. The requirement for blind duplicates, recovery experiments, supply of standards, minimum numbers of participants and the outline of the study protocol are set out in the International Organization for Standardization (ISO)/ International Union of Pure and Applied Chemistry (IUPAC)/AOAC harmonized protocol for collaborative studies (Horwitz, 1995).

After six to nine months' work in undertaking the trial and evaluating the data, assuming that the results are satisfactory in terms of acceptable r and R values, the report of the trial has to undergo extensive peer review before final adoption as an official method. The length and overall cost of this evaluation process, coupled with the fact that not all collaborative trials yield the desired results, help to explain the lag between methodological innovation and adoption as official methods.

PROFICIENCY TESTING

Proficiency testing is a means of continuous objective assessment of the ability of a laboratory to produce accurate and reliable results. In proficiency testing, laboratories receive samples for analysis at regular intervals, report the results to the scheme organizers, and are then given an assessment of their performance. The identities of the laboratories involved are kept confidential, although each laboratory receives a report with useful indications about the overall performance of all participants and information on performance related to the methods of analysis that have been employed.

Proficiency testing should be regarded as an integral part of accreditation and should be seen as providing valuable information for internal purposes, as well as being an indicator of laboratory performance for third parties. In proficiency testing (unlike collaborative trials) all participants use the methodologies to which they are accustomed and which are in everyday use in their laboratories. Ideally, both the matrix and the analyte should be routinely tested in the laboratory, and participants should be discouraged from undertaking proficiency testing with unfamiliar materials. Frequently, however, the desired matrix may not be available and the best approximation has to suffice.

The requirements for establishing and running proficiency testing schemes are stipulated in an ISO/IUPAC/AOAC International Harmonized Protocol (Thompson and Wood, 1993) and in ISO Guide No. 43. A number of national and international commercial schemes are run on a regular and systematic basis. For example, in the United Kingdom, a proficiency testing scheme called the Food Analysis Performance Assessment Scheme (FAPAS) has been operating since 1990, and has included mycotoxins among the analytes that it tests. FAPAS has expanded rapidly since its inception and, as of mid-1998, had some 600 participating laboratories in 50 countries worldwide (Key *et al.*, 1997). Proficiency testing has also been organized by the World Health Organization (WHO) under the Global Environmental Monitoring System (GEMS) programme, but sample distribution has been more sporadic under this than under commercial schemes (Weigert *et al.*, 1997).

Proficiency testing schemes require procurement or production of materials that closely resemble those experienced in practice. After blending or preparation of these materials into a suitable form for distribution, homogeneity testing needs to be carried out to ensure uniformity of samples. Test materials are distributed to participants, analysis is undertaken using the normal method of analysis and results are reported back to a Secretariat within one month. The results must be processed rapidly for maximum benefit to participants. In FAPAS, a report is issued within one month, giving all results for the round and individual performance scores (known as z-scores) for each analyte. The z-scores are calculated on the basis of the "true" value of the analyte and the standard deviation expected at that concentration (from collaborative trial data or the Horwitz curve). A z-score of + 2 is deemed satisfactory, a z-score between - 2 and - 3 or - 2 and + 3 is deemed questionable. Z-scores outside this range are unsatisfactory.

CERTIFIED REFERENCE MATERIALS

Although they cannot substitute interlaboratory comparisons, certified reference materials do offer the possibility of demonstrating both the accuracy and the precision of a new method using naturally contaminated materials (Boenke, 1997; Gilbert, 1988). Two powdered-milk reference materials, which are available from the European Community Bureau of Reference Materials (BCR), have certified low level contents of aflatoxin M_1 (van Egmond and Wagstaffe, 1987). Peanut butters containing certified levels of individual aflatoxins are also available from BCR (Gilbert *et al.*, 1991), as are wheat and maize samples naturally contaminated with deoxynivalenol (Gilbert, 1995), animal feedstuffs containing certified levels of aflatoxins (van Egmond *et al.*, 1994) and wheat containing ochratoxin A. The production of pig kidneys containing certified levels of ochratoxin A has proved more difficult to prepare and certify (Wood *et al.*, 1997; Williams *et al.*, 1998). Projects are currently under way on the development of cereals containing certified contents of fumonisins (Visconti *et al.*, 1996) and zearalenone. This increasing range of certified mycotoxin reference materials should, in future, offer greater possibilities for rapid assessment of new methodology, for both different toxins and different matrices.

CONCLUSIONS

The analysis of mycotoxins in foods and feeds is now far less “hit and miss” than was once the case and there are now adequate quality assurance means in place, both to assist laboratories to get accurate and reliable results and to check and demonstrate consistent satisfactory performance. The adoption of best practices in sampling and the use of validated methods, together with accreditation and participation in proficiency testing, are recommended means of ensuring the recognition of mycotoxin results worldwide.

Assistance by international organizations such as FAO may be necessary, particularly in developing countries, to stimulate and implement the necessary infrastructure. ◆

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Summary/Résumé/Resumen

Quality assurance in mycotoxin analysis

To ensure that representative samples of foods and feeds are taken for analysis, it is important to follow the stipulations set out in sampling plans – many of these plans are now encompassed as part of the regulations for controlling mycotoxin contamination. Validated analytical methods are those for which performance characteristics have been established by interlaboratory collaborative trials and these are now widely accepted as being essential for monitoring and regulatory purposes. In addition to employing validated methods, internal quality control procedures need to be implemented in chemical laboratories – this normally implies accreditation, participation in proficiency testing and the proper use of control and reference materials. This paper presents an overview of all these important aspects of quality assurance for mycotoxin analysis.

Assurance de qualité dans l'analyse des mycotoxines

Pour s'assurer que les échantillons de produits alimentaires et fourragers représentatifs soient prélevés pour être analysés, il importe de suivre les stipulations des plans d'échantillonnage, dont beaucoup font à présent partie des réglementations de contrôle de la contamination par les mycotoxines. Les méthodes analytiques validées sont celles pour lesquelles des caractéristiques d'efficacité ont été établies lors d'essais interlaboratoires et il est à présent largement reconnu qu'elles sont essentielles aux fins de surveillance et de réglementation. Outre l'emploi de méthodes validées, des procédures de contrôle de qualité internes doivent être appliquées dans les laboratoires chimiques – ce qui implique habituellement leur accréditation, leur participation à des essais d'aptitude et l'utilisation appropriée du matériel de contrôle et de référence. Le présent document expose tous ces aspects importants de l'assurance de qualité pour l'analyse des mycotoxines.

Garantía de la calidad en el análisis de las micotoxinas

Para garantizar que se tomen muestras representativas de alimentos y piensos a fines de análisis, es importante seguir las normas establecidas en los planes de toma de muestras: muchos de ellos se hallan ahora incorporados como parte de la reglamentación para el control de la contaminación por micotoxinas. Por métodos de análisis validados se entienden aquellos cuyas características de eficacia se han determinado de acuerdo con ensayos colaborativos entre laboratorios y que ahora son generalmente aceptados como indispensables a efectos de control y reglamentación. Además de emplear métodos validados, en los laboratorios químicos es menester aplicar procedimientos internos de control de la calidad: esto supone normalmente la acreditación, la participación en ensayos de aptitud y el buen empleo de materiales de control y de referencia. En este artículo se ofrece una descripción general de todos esos aspectos, tan importantes para garantizar la calidad en el análisis de micotoxinas. ◆

Integrated mycotoxin management systems

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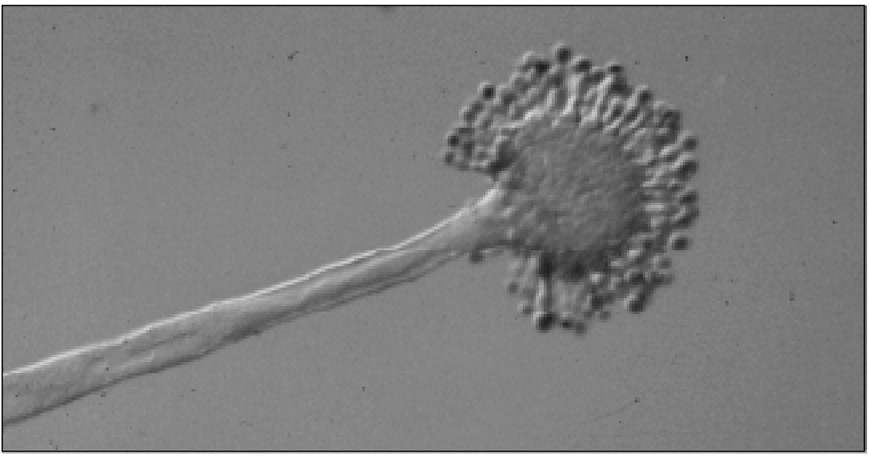
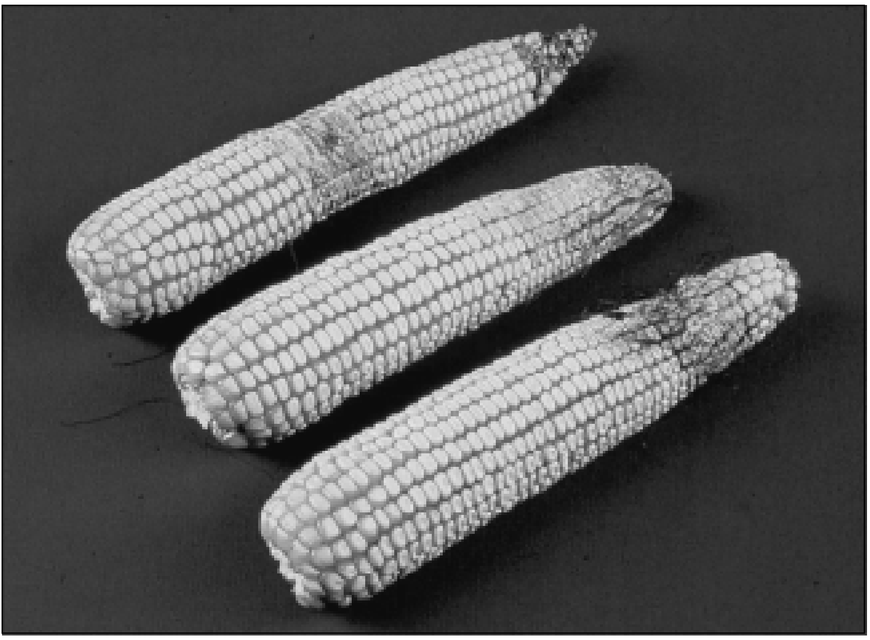
Mycotoxins are toxic secondary metabolites produced by certain fungi in agricultural products that are susceptible to mould infestation. Their production is unavoidable and depends on a variety of environmental factors in the field and / or during storage. Mycotoxin contamination is unavoidable and unpredictable, which makes it a unique challenge to food safety (Park and Stoloff, 1989; FAO, 1997). New mycotoxins and co-contamination of known mycotoxins are being discovered at high rates. Considerable evidence supports an association between mycotoxins and certain animal syndromes (CAST, 1989). Although definitive evidence on the cause and effect relationship of mycotoxins and human diseases is limited, this does not necessarily imply that dietary exposure does not represent a potential risk.

Unfortunately, information on toxicity, stability and



Peter J. Cotty/ United States Department of Agriculture

1
Aspergillus flavus, *primary mould responsible for aflatoxin contamination in numerous agricultural commodities, including maize, peanuts, tree nuts and cottonseed*



David M. Wilson/University of Georgia, Tifton

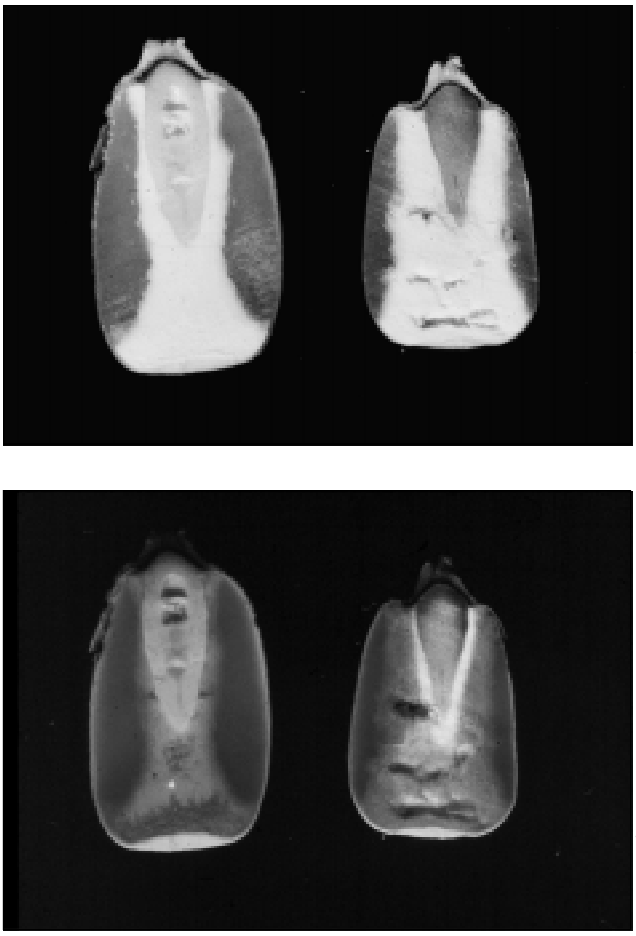
2
Aspergillus flavus-*contaminated maize showing the heterogenous nature of mould infestation*

extent of occurrence is limited for many of the mycotoxins that have been identified. The decision-making process for their control is, therefore, complicated (Park and Stoloff, 1989). In addition, there have been several reports on the co-contamination of various toxins, such as aflatoxin B_1 / fumonisin B_1, ochratoxin A / aflatoxin B_1, ochratoxin A / citrinin, ochratoxin A / deoxynivalenol, ochratoxin A / penicillic acid, ochratoxin A / T-2 toxin / aflatoxin / cyclopiazonic acid, aflatoxin / kojic acid, aflatoxin B_1 / deoxynivalenol, and aflatoxin B_1 / T-2 toxin (Lopez-Garcia and Park, 1998). The presence of multiple toxins in the same system is a new cause for concern, since toxicological information on the effects of simultaneous exposure is still very limited. However, in a diverse human diet, exposure will be to multiple toxins at low concentrations and intermittent rates over long periods of time. The ultimate effect of such constant exposure is still unknown. Although it is difficult to predict the effect of multiple toxins, certain *in vitro* studies can help to forecast the outcome. Recent studies have shown that simultaneous exposure to aflatoxin B_1 and fumonisin B_1 may elicit responses that are different to those arising from exposure to the toxins individually (Lopez-Garcia, 1998; Burgos-Hernandez, 1998). This effect could be caused by the combination of a multitude of factors which may include direct chemical interaction or enhancement / inhibition of different metabolic pathways. The overall response may be owing to equilibrium of several reactions. Direct chemical reaction, as well as involvement in mechanistic pathways, may participate in the interactive effects of these two toxins. Different responses were observed depending on different combination ratios. Therefore, different levels of contamination can pose different health hazards.

FOOD SAFETY PROGRAMMES

Mycotoxins cannot be considered a group of toxicants on the basis of their mechanism of action because they are very chemically diverse. For the same reason, it would be impossible to develop one single control method that would ensure the reduction of every mycotoxin present in every agricultural commodity. In addition, mycotoxin contamination is heterogeneous in nature, so sampling and analysis are complicated by the presence of “hot spots”. Considering all these factors, it can be concluded that the development of food safety programmes for mycotoxin control is not a simple issue (Park, 1993; Park and Liang, 1993).

One possible approach to management of the risks associated with mycotoxin contamination is the use of an integrated system. The proposed control programme for processed foods and feeds should be based on the Hazard Analysis and Critical Control Point (HACCP) approach and should involve strategies for prevention, control, good manufacturing practices and quality control at all stages of production, from the field to the final consumer. Prevention through pre-harvest management is the best method for controlling mycotoxin contamination but, when contamination does occur, the hazards associated with the toxin must be managed through post-harvest procedures, if the product is to be used as human food or animal feed. Ideally, the risks associated with mycotoxin hazards should be minimized at every phase of production. Control parameters for the processing of commodities that are susceptible to mycotoxin contamination would include time of harvesting, temperature, moisture during storage and transportation, selection of agricultural products prior to processing, processing / decontamination conditions, temperature, addition of chemicals, and final product storage and transportation.



Leonard Stoloff/United States Food and Drug Administration

Leonard Stoloff/United States Food and Drug Administration

3

Aflatoxin-free (upper) and contaminated (lower) maize in daylight and under ultraviolet light showing diffusion of aflatoxin to interior of kernel with no apparent mould damage

In integrated mycotoxin management, each phase of production should follow most of the steps outlined in

Box 1. The concept behind an integrated management system is similar to a "hurdle" effect, where at each phase of production, i.e. pre-harvest, harvest and post-harvest processing, the risks are minimized (Lopez-Garcia and Park, 1998).

PRE-HARVEST CONTROL

Prevention through pre-harvest control is the first step in ensuring a safe final product. While an association between mycotoxin contamination and inadequate storage conditions has long been recognized, studies have revealed that some seeds are contaminated with mycotoxins in the field. During the growing period, the seeds are exposed to environmental factors, such as weather, that are impossible to control. Once the crop becomes infected under field conditions, fungal growth will continue during post-harvest stages and storage. Thus, pre-harvest management is focused on controlling critical factors that have been shown to enhance mycotoxin production. Some of the most common strategies used for pre-harvest management are:

- *Management of insect infestation*. Although it has been reported that damage is not a prerequisite for aflatoxin formation, the incidence of *Aspergillus flavus* and *A. parasiticus* is usually higher in damaged kernels. Insect-damaged kernels are routes for infection and are likely to dry to moisture levels that are more favourable for the growth of *A. flavus* and aflatoxin production than of other fungi. Control of insect infestation may, therefore, help to prevent *A. flavus* and *A. parasiticus* proliferation and subsequent aflatoxin production.
- *Management of crop residues and crop rotation*. Inoculum potential is a prerequisite for *Aspergillus* infection and subsequent aflatoxin production. Soil type and condition, as well as availability of viable spores, have been considered important factors in aflatoxin production. When the crop is harvested, some residues remain on the field. These provide an environment that is conducive to the survival of fungal spores and the subsequent infection of the next crop. Proper management of crop residues would help avoid this problem.

  Crop rotation has also been recognized as an important factor in the spread of the inoculum. Adequate rotation may, therefore, aid the prevention of mycotoxin contamination. For example, field trials have reported that a maize-soybean rotation yielded a less extensive outbreak of *Fusarium* than did maize-maize planting operations.
- *Irrigation and soil condition*. Soil fertility and drought stress have been found to be contributing factors in pre-harvest aflatoxin contamination of maize. Moisture and temperature play the most important roles in the planning of any control strategy for fungal development. High moisture and high relative humidity are essential for spore germination and fungal proliferation. Therefore, adequate efforts should be made to avoid extreme conditions of either drought or excessive moisture. Some studies have shown that drought stress followed by high-moisture conditions is ideal for *Fusarium moniliforme* proliferation and fumonisin production. When this type of weather condition is present, it can be assumed that some degree of mycotoxin contamination will occur and other prevention / management strategies should be explored.

Development of resistant plant varieties

There has been extensive research on the development and promotion of plant varieties that are naturally resistant to fungal infection. Host resistance may present a promising

BOX 1
PHASES IN A FOOD SAFETY MANAGEMENT PROGRAMME

When developing a food safety management programme for naturally occurring toxicants, different phases such as the ones outlined below should be considered (Park and Stoloff, 1989; Park, 1993).

Setting of regulatory limits:
- commodity surveys to determine contamination levels;
- dietary intake surveys to determine consumption levels;
- evaluation of toxicological data:
- establishment of analytical capabilities;
- availability of food/feed supply based on different regulatory limits.

Establishment of a monitoring programme:
- establishment of a sampling plan:
  - sample collection;
  - preparation of test portion;
  - analysis of test portion;
- permitted uses of mycotoxin-contaminated products.

Control through good agricultural practices

Control through processing:
- good manufacturing practices;
- quality control.

Decontamination through specific treatments:[1]
- evaluation of the final product;
- designation of use of treated product.

Consumer/producer education

[1] Chemical decontamination procedures are usually applied to animal feeds only.

strategy for the pre-harvest prevention of mycotoxin contamination. Until recently, the search for naturally resistant maize genotypes had not been successful. However, during extensive field testing, maize breeding populations with aflatoxin resistance have been identified. Genetic studies of these specific populations have yielded useful information for the development of resistant lines. Studies have identified the chromosome regions associated with aflatoxin resistance. This line of research is, therefore, a good option for future pre-harvest control and prevention of mycotoxin formation.

Genetic engineering has also been useful in the development of host resistance through the addition or enhancement of antifungal genes. Many endogenous compounds with low molecular weight and biomacromolecules in kernel tissues have been identified as antifungal compounds. Enhancing the production of these compounds may also enhance resistance to mycotoxin contamination. There may be toxicity implications associated with these antifungal compounds.

HARVEST CONTROL

During harvesting, it is important to control factors such as timeliness, clean-up and drying of the agricultural product. Such control is essential for preventing mycotoxin formation during storage. Studies have shown that the timing of harvesting greatly influences mycotoxin production. In some geographical regions, the planting date should be selected to take advantage of periods of higher rainfall.

Harvesting should take place as soon as the crop is fully grown and the crop cycle is completed. Studies have reported that crops left on the field for longer periods of time may present higher levels of toxin contamination. Adequate drying is also essential to prevent fungal proliferation during storage.

POST-HARVEST CONTROL AND DECONTAMINATION

Although prevention is the best control strategy, mycotoxin contamination will still sometimes occur. Post-harvest control and decontamination procedures represent, therefore, an important tool in avoiding consumer exposure. Several decontamination strategies have been reported for various mycotoxins, and specific information on each method is readily available in the literature. Some traditional processing methods are good either for physically separating toxins or for chemically inactivating them. However, the effectiveness of each processing method should be evaluated for the specific commodity and toxin present in the system.

BOX 2
CRITERIA FOR EVALUATING MYCOTOXIN REDUCTION OR DECONTAMINATION PROCEDURES

Procedures for the evaluation and acceptance of given mycotoxin reduction or decontamination should (Jemmali, 1979; Park *et al.*, 1988; Jemmali, 1989):

- inactivate, destroy or remove the toxin;
- not produce or leave toxic residues in the food or feed;
- retain nutritive value and food/feed acceptability of the product;
- not alter significantly the technological properties of the product;
- destroy fungal spores, if possible.

COMMON POST-HARVEST STRATEGIES

Physical methods of mycotoxin removal

Once a contaminated product has reached a processing facility, clean-up and segregation are the first control options. These procedures are usually non-invasive and, except for milling, will not alter the product significantly. In some cases, these are the best methods of reducing mycotoxin presence in final products. For example, when peanuts are processed, a significant amount of aflatoxins can be removed by electronic sorting and hand-picking (Table 1) (Dickens and Whitaker, 1975; Kirksey, Cole and Dorner, 1989). Separation of mould-damaged maize (Figure 4) and / or screening can significantly reduce fumonisin and aflatoxin concentrations (Bennett, Rottinghaus and Nelson, 1992; Murphy, Rice and Ross, 1993). In addition, the removal of rot from apples significantly reduces the patulin content in the final product (Lovett, Thompson and Boutin,1975). Although some contamination may persist, physical removal represents a good alternative for industry (Lopez-Garcia,

TABLE 1
Effectiveness of post-harvest aflatoxin management strategies at the processing level[1]

Technology	Aflatoxin level *(µg/kg)*	Reduction *(%)*	Cumulative reduction *(%)*
Farmer's stock	217.0	-	-
Belt separator	140.0	35	35.0
Shelling plant[2]	100.0	29	54.0
Colour sorting[2]	30.0	70	86.0
Gravity table[2]	25.0	16	88.0
Blanching/colour sorting	2.2	91	99.0
Colour re-sorting[2]	1.6	27	99.3

[1] Results from the processing of a 40 000 kg segregation I lot of contaminated peanuts.
[2] Data based on medium-category peanuts only.
Source: Park and Liang, 1993.

4
Mould-damaged maize in a ship's hold (typical hot spot); process of physical separation of damaged from intact kernels

Park and Gutierrez de Zubiarre, 1999; Lopez-Garcia and Park, 1998).

Milling is traditionally used for grain processing. This method will separate the grain into different fractions (Bennett and Anderson, 1978; Bennett *et al.*, 1976; Bennett and Richard, 1996; Bennett *et al.*, 1978; Seitz *et al.*, 1986; Schroeder, Boller and Hein, 1968). It is, therefore, important to identify the fractions that remain toxic so that they can be diverted to lower-risk uses or subjected to decontamination procedures (Scott, 1984; Wood, 1982).

Physical methods of decontamination

Some phases of industrial processes can reduce specific mycotoxins to a certain degree through thermal inactivation, but some mycotoxins are chemically stable and will not be completely destroyed at processing temperatures. Thus, thermal inactivation for a particular toxin should be evaluated for the temperatures of a specific process. Roasting is a good method for such commodities as peanuts and coffee. As mentioned before, if a traditional processing method is an effective decontamination procedure, it should be the first choice for management of a particular product (Lopez-Garcia and Park, 1998).

Irradiation may also be an option for mycotoxin control. A completely satisfactory way of destroying mycotoxins that have already been formed has not been identified. However, irradiation may be considered as a method to control mycotoxin-producing moulds in certain products (Lopez-Garcia and Park, 1998).

A novel approach to the prevention of aflatoxin intoxication in some animals is the dietary inclusion of aflatoxin-selective clays that tightly bind these poisons in the gastrointestinal (GI) tract, significantly decreasing their bio-availability and associated toxicities (Phillips, Clement and Park, 1994). These methods aim at preventing the deleterious effects of mycotoxins by sequestrating them to various sorbent materials in the GI tract, thereby altering their uptake and disposition to the blood and target organs. In pioneering studies, a phyllosilicate clay which was commonly used to reduce caking in animal feeds (NovaSil or hydrated sodium calcium aluminosilicate [HSCAS] clay) was reported to adsorb aflatoxin B_1 with high affinity and high capacity in aqueous solutions (including milk); reduce markedly the bio-availability of radio-labelled aflatoxins in poultry; diminish significantly the effects of aflatoxins in young animals such as rats, chicks, turkey poults, lambs and pigs; and decrease the level of aflatoxin M_1 in milk from lactating dairy cattle and goats. The effects of HSCAS clay in the diet did not alter the hyperoestrogenic effects of zearalenone (Grant, 1998; Grant and Phillips, 1998; Machen *et al.*, 1988; Lemeke, Grant and Phillips, 1998; Ramos and Hernandez, 1996).

A variety of other HSCAS binding agents are purported to adsorb aflatoxins, as well as other chemically diverse mycotoxins such as T-2 toxin, ochratoxin, deoxynivalenol, zearalenone and fumonisins. It is, therefore, possible that these agents may be non-selective in their action and pose significant hidden risks arising from their interaction with critical nutrients, etc. In addition, *in vitro* (test-tube) evidence indicated that some of these binders may provide little (if any) protection from aflatoxins or other mycotoxins.

Granulated activated carbon (GAC) has also been studied for its ability to bind aflatoxins, both *in vivo* and *in vitro*. Results from studies using GAC varied widely according to the type of activated carbon used. Activated carbon has also proved effective in reducing patulin in naturally contaminated fruit juices (Sands, McIntyre and Walton, 1976; Walton, Sands and McIntyre, 1976; Decker, 1980).

Clay and zeolitic minerals comprise a broad family of functionally diverse silico-aluminosilicates. Although, these agents have shown promising effects on the binding of mycotoxins, there may be significant risks associated with the inclusion of non-selective clays (or other adsorbents) in the diet. Aflatoxin adsorbents should be rigorously tested, with particular attention to their effectiveness and safety in aflatoxin-sensitive animals and their potential for interaction with nutrients.

Biological decontamination

Biological methods have been explored as options for mycotoxin decontamination. In the fermenting industry it has been found that aflatoxins are not degraded during fermentation; although the toxins are absent from the alcohol fraction after distillation. Aflatoxins are usually concentrated in the spent grains. When contaminated products are used for fermentation, it is therefore important to determine the end use of the contaminated by-products. It should be emphasized that biological methods demonstrating effective decontaminating properties usually depend on specific compounds produced by selected microorganisms. When a specific compound is found to be a good decontaminating agent, it is usually more efficient and economical to add the active agent directly. Studies suggest that certain fungi, including *A. parasiticus,* degrade aflatoxins, possibly through fungal peroxidases. Fermentation with yeasts has also been effective in destroying patulin and rubratoxin B (Lopez-Garcia and Park, 1998).

Chemical inactivation

Numerous studies have evaluated the use of chemicals for the inactivation and hazard reduction of selected mycotoxins. Most studies have, however, focused on aflatoxins and application to animal feeds. Ammoniation is the chemical method that has received the most research attention. Extensive evaluation of this procedure has demonstrated that it is an efficacious and safe way of decontaminating aflatoxin-contaminated feeds. More than 99 percent effective, this process has been used selectively with success in the United States, France, Senegal, the Sudan, Brazil, Mexico and South Africa, in some cases for almost 20 years. The two ammoniation processes primarily used for aflatoxin contamination in maize, peanuts, cottonseed and meals are: high pressure / high temperature(HP / HT); and atmospheric pressure / ambient temperature (AP / AT) where the HP / HT process is used for feedmill operations (Figures 5 and 6) and AP / AT is primarily for on-farm use (Figure 7). The AP / AT process is limited to dealing with aflatoxins in whole-kernel seeds / nuts. Ammoniation has been shown to be less effective against fumonisin decontamination. For aflatoxin control, however, practical applications together with research results strongly support the use of ammonia treatment. Other chemical-based procedures utilizing, for instance, monomethylamine, lime or urea / urease have been reported. In-depth reviews and articles have been published and these can be used as a basis for policy-making decisions (Lopez-Garcia, Park and Gutierrez de Zubiarre, 1999; Lopez-Garcia and Park, 1998; Park *et al.*, 1988; Park and Stoloff, 1989; Phillips, Clement and Park, 1994; Piva *et al.*, 1995).

Nixtamalization, the traditional alkaline treatment of maize used to manufacture tortillas in Latin America, partially degrades aflatoxins and fumonisin, but the residual molecules can either be regenerated by digestive processes or become more toxic (Price and Jorgensen, 1985). The addition of oxidizing agents, such as hydrogen peroxide, has been shown to be an effective aid in nixtamalization. These chemicals degrade aflatoxins and fumonisin, thereby reducing toxicity (Lopez-Garcia, 1998; Burgos-Hernandez, 1998). Some recent studies have shown that hydrogen peroxide and sodium bicarbonate are effective for simultaneous degradation / detoxification of aflatoxins and fumonisin.

Other chemical processes that have shown promise in controlling aflatoxins are the use of sodium chloride during thermal processing, sodium bisulphite at various temperatures and ozonation. Wet and dry milling processes, which are widely used for maize and cereal

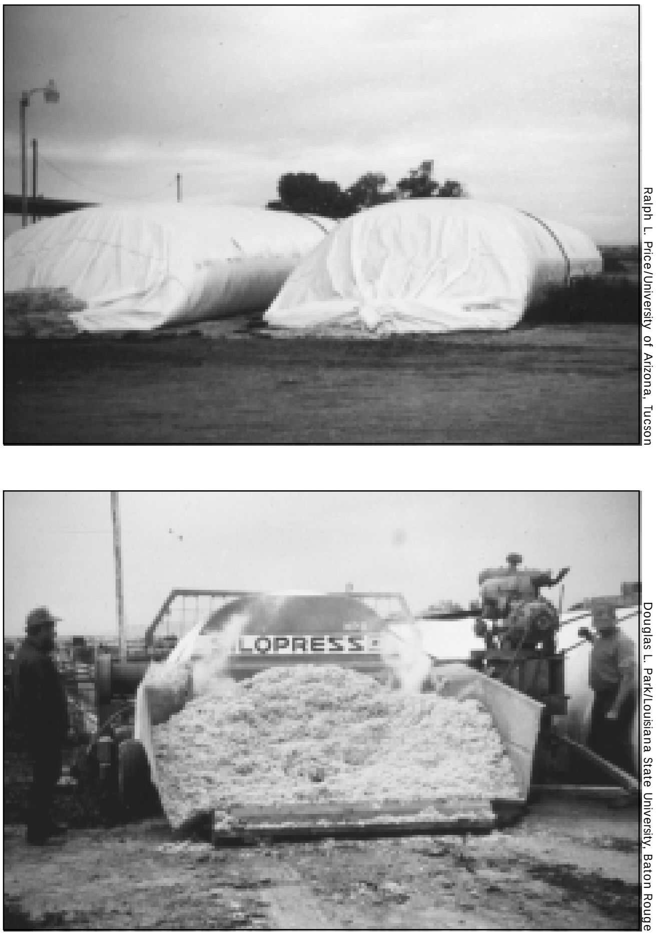
5

Ammonia mycotoxin decontamination plant (Walker Cottonseed, Stanfield, Arizona) using the high temperature/high pressure process

R.D. Walker/Walker Cottonseed

R.D. Walker/Walker Cottonseed

6
Mobile ammonia mycotoxin decontamination unit capable of on-site processing using the high temperature/high pressure process



Ralph L. Price/University of Arizona, Tucson

Douglas L. Park/Louisiana State University, Baton Rouge

7
Ambient temperature/ atmospheric pressure mycotoxin decontamination process showing addition of aqueous ammonia and bagging operations

grains, have been shown to result in reduced mycotoxin levels (zearalenone, fumonisins, aflatoxins, trichothecenes and ochratoxin A) in several fractions such as milling solubles, gluten, fibre, starch and germ (Lopez-Garcia and Park, 1998).

Processing alters food matrices into different complex systems. It also adds new ingredients and conditions. These new factors change the environment, and innumerable new interactions may take place. Exploring the application of known food additives to the control of mycotoxins during processing may provide new opportunities for risk management by chemical methods.

CONCLUSIONS

Mycotoxins are a chemically diverse group of fungal metabolites that have a wide variety of toxic effects. In a normal varied human diet, constant exposure to low levels of several toxins is possible. Information on the potential interactions among all these compounds is still very limited. Furthermore, some mycotoxins, such as aflatoxin B_1, are known to be associated with animal and human disease. The development of practical control and management strategies is, therefore, essential to ensure consumer safety. Because of the unpredictable, heterogeneous nature of mycotoxin contamination, 100 percent destruction of all mycotoxins in all food systems is not considered a practical option. However, a practical approach would be the use of a HACCP-based “hurdle” system, in which contamination is controlled throughout production and post-production operations. An example of this is presented in Table 1 (p. 41) – the procedures referred to are used by the peanut industry in the United States in processing peanut butter for human consumption.

Integrated mycotoxin management systems should consider control points from the field to the consumer. This type of management system considers the communication between experts in pre-harvest, harvest and post-harvest control. With this approach, every phase of production would help reduce the risk, so by the time the

TABLE 2
Purpose, status and application of pre-harvest, harvest and post-harvest procedures for removing mycotoxins from human foods and animal feeds

Procedure	Mycotoxins	Commodities	Purpose/status/application
Pre-harvest			
Reduction of insect infestation	Aflatoxins, fumonisins	Maize, cottonseed	Avoid insect infestation which can serve as a vector for mould invasion to agricultural commodities; use integrated pest management control programmes
Crop rotation	*Aspergillus*, *Fusarium* toxins	Maize, soybean	Limit mould inoculum in the field
Irrigation	*Aspergillus*, *Fusarium* toxins	Maize, cottonseed, peanuts, tree nuts	Avoid drought stress during crop growth
Planting of resistant varieties	Aflatoxins	Maize	Strong potential for control of mycotoxin formation during crop growth
Harvesting operations			
Timeliness of clean-up and drying of commodities	Aflatoxins	Maize	Reduce exposure to toxigenic moulds and and moisture levels in commodities
Post-harvest procedures Physical separation of damaged, immature and mould-infested kernels, nuts, seeds, etc.	Aflatoxins, fumonisins	Maize, peanuts	Effective in reducing mycotoxin levels in final product; mycotoxins can diffuse into apparently good commodities
Thermal processing	*Aspergillus*, *Fusarium* toxins	Maize, cereal grains, coffee	However, many mycotoxins are thermally stable
Dietary mycotoxin-selective clays	Aflatoxins, *Fusarium* toxins, ochratoxin A	Maize	Strong potential and application for clays shown safe and effective; some non-selective clays may pose significant risk by binding critical nutrients, etc.
Chemical inactivation by ammoniation	Aflatoxins, fumonisins	Maize, peanuts, cottonseed and meals	Feed mill and farm applications
Chemical inactivation by ozonation	Aflatoxins	Maize	Strong potential; more research needed
Nixtamalization with addition of hydrogen peroxide and sodium bicarbonate	Aflatoxins, fumonisins	Maize	Minor modification of an industrial process; good potential practical application

final food or feed reaches the consumer the hazards associated with mycotoxin contamination have been minimized. These concepts are summarized in Table 2.

Continued research is required in these areas to provide more effective management of the risks posed by mycotoxin contamination. In the meantime, procedures that have proved effective for specific mycotoxins and / or commodities should be evaluated for other applications. ◆

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Integrated mycotoxin management systems

Naturally occurring toxicants pose a unique challenge to food safety. They are unavoidable and their occurrence is unpredictable. The destruction of contaminated products or their diversion to non-human uses is not always practical and could seriously compromise the food supply. Procedures for the prevention of mycotoxin formation in the field as well as during storage have been developed but, in spite of these efforts, contamination continues to occur. The hazards associated with toxins must, therefore, be managed through appropriate post-harvest procedures if the safety of food and feed is to be assured. One approach to the management of the risks associated with mycotoxin contamination is the use of an integrated system. The proposed control programme would entail strategies for the prevention of mycotoxin formation, the establishment of regulatory limits and monitoring programmes, and the use of processing and decontamination operations to remove, destroy or inactivate the toxins while, at the same time, preserving an adequate, safe and wholesome food supply.

Systèmes de gestion intégrée des mycotoxines

La présence naturelle de toxiques est inévitable et imprévisible, et pose un problème spécifique en matière d'innocuité des aliments. La destruction des produits contaminés ou leur affectation à des usages non humains n'est pas toujours pratique, et peut compromettre gravement les approvisionnements alimentaires. Des procédures destinées à éviter la formation de mycotoxines sur le terrain comme pendant l'entreposage ont été mises au point; toutefois, malgré tous ces efforts, la contamination continue de se produire. Il faut donc gérer les dangers liés aux toxines au moyen de mesures après récolte appropriées si l'on veut s'assurer que le produit destiné à la consommation humaine ou animale soit réellement sain. L'utilisation d'un système intégré est une approche possible de la gestion des risques associés à la contamination des mycotoxines. Le programme de lutte proposé comporte des stratégies pour la prévention de la formation des mycotoxines, l'établissement de limites réglementaires et de programmes de suivi, et le recours à des opérations de transformation et de décontamination pour retirer, détruire ou désactiver les toxines tout en préservant la qualité et l'innocuité des approvisionnements en denrées alimentaires.

Sistema integrado de gestión de micotoxinas

Las sustancias tóxicas de origen natural son inevitables y su presencia es imprevisible, y por lo tanto plantean un problema especial para la inocuidad de los alimentos. La destrucción de los productos contaminados o su utilización con fines distintos del consumo humano no siempre es posible y puede poner en grave peligro el suministro alimentario. Se han elaborado procedimientos para prevenir la formación de micotoxinas tanto en el campo como durante el almacenamiento, pero a pesar de estos esfuerzos se siguen produciendo casos de contaminación. Por consiguiente, para asegurar la inocuidad de alimentos y piensos, el peligro asociado con las toxinas debe afrontarse también mediante procedimientos aplicados después de la cosecha. Un modo para afrontar los riesgos asociados con la contaminación por micotoxinas consiste en utilizar un sistema integrado. El programa de control propuesto entrañaría estrategias para impedir la formación de micotoxinas, el establecimiento de límites reglamentarios y programas de vigilancia y la utilización de operaciones de elaboración y descontaminación para eliminar o inactivar las toxinas conservando al mismo tiempo un suministro suficiente de alimentos inocuos y sanos. ◆

Minimizing risks posed by mycotoxins utilizing the HACCP concept

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Unavoidable, naturally occurring toxicants pose a unique challenge to food safety. According to FAO, at least 25 percent of the world's food crops are contaminated with mycotoxins, at a time when the production of agricultural commodities is barely sustaining the increasing population (Boutrif and Canet, 1998). The global volume of such agricultural products as maize, groundnuts, copra, palm nuts and oilseed cake, which are high-risk commodities, is about 100 million tonnes – 20 million tonnes of which come from the developing countries (FAO, 1996). The destruction of contaminated products or their diversion to non-human uses is not always practical and could seriously compromise the world food supply. Efforts to limit mycotoxins in human foods and animal feedstuffs are based on two major concerns: the adverse effects of mycotoxin-contaminated crops or feeds on human or animal health and productivity; and potential residues of mycotoxin or toxic metabolites in edible animal food products.

Hazard Analysis and Critical Control Point (HACCP) is a system of food safety control based on the systematic identification and assessment of hazards in foods and the definition of means to control them. It is a preventive, rather than a reactive, tool that places the protection of the food supply from microbial, chemical and physical hazards into the hands of food management systems. The HACCP system is designed to minimize the risk of food safety hazards by identifying the hazards, establishing controls and monitoring these controls (FAO, 1995; Gamboa, 1998). When the HACCP concept is applied to the management of likely adverse health effects resulting from exposure to mycotoxins, an adequate, wholesome and safe food supply can be maintained. In order to design and develop effective HACCP-based integrated mycotoxin management programmes, a given country has to consider such factors as the climate, farming systems, pre- and post-harvest technologies, public health significance of the contaminant, producer and processor compliance, availability of analytical resources and, last but not least, the economy (FAO, 1979).

Prevention through pre-harvest management is the best method for controlling mycotoxin contamination; however, should contamination occur, the hazards associated with the toxins must be managed through post-harvest procedures, if the product is to be used for food and feed purposes. In an ideal integrated management system, mycotoxin hazards would be minimized in every phase of production, harvesting, processing and distribution (Lopez-Garcia and Park, 1998; FAO, 1979).

HACCP PROGRAMME FOR MYCOTOXIN CONTAMINATION

In the terminology of HACCP systems, "hazard" refers to conditions or contaminants in foods that can cause illness or injury. It does not refer to certain other undesirable conditions or contaminants such as insects, hair, filth and spoilage, which would be considered in the context of a broader quality assurance system. The HACCP concept is built on seven principles and actions:

- conduct hazard analysis and identify preventive measures;
- identify critical control points (CCPs);
- establish critical limits;
- monitor each CCP;
- establish corrective action in the event of a deviation from a critical limit;
- establish record keeping;
- establish verification procedures.

The development and application of HACCP programmes are complex matters, and not all countries have the required technical expertise and experience to establish effective integrated mycotoxin management systems that are based on the HACCP approach. Given the importance of HACCP in food safety programmes, FAO has given high priority to the provision of training to professionals in developing countries on the HACCP approach and its application (FAO, 1995).

Integrated mycotoxin management systems based on the HACCP approach must, of course, consider hazards at all stages of production, handling and processing. Furthermore, a prerequisite for the development of HACCP programmes is observance of good agricultural practice (GAP) and good manufacturing practice (GMP) (Sperber *et al.*, 1998). In the field, mycotoxin contamination is primarily the result of environmental conditions such as ambient temperature, precipitation, relative humidity, moisture of the product and its susceptibility, and the mould inocula that occur naturally throughout the world (*Aspergillus, Penicillium, Fusarium*, etc.). It has now been universally acknowledged that mycotoxin formation may also occur at various stages of processing. Based on findings in the literature regarding mycotoxins, control can be effected during pre-harvest, harvest and post-harvest phases which, for the purposes of this article, will include storage and all forms of processing. It is important that these points in the food handling systems are identified, understood and well managed. In integrated mycotoxin management incorporating the HACCP concept, each identified and appropriately managed phase will help prevent the risk of exposure to the toxins.

The prevention and control of mycotoxin contamination to reduce qualitative and quantitative losses in food and agricultural products were integrated into many of FAO's Prevention of Food Losses projects. Of about 200 projects within this programme, over 50 included components for mycotoxin control (Boutrif and Canet, 1998).

Pre-harvest procedures

Significant levels of mycotoxins can occur in food crops in the field. Drought, insect infestation, primary inoculum and delayed harvesting are important external factors that contribute to this. Some of these factors are environmental and humans have minimal control over them. However, good crop husbandry practices, such as crop rotation, irrigation, timed planting and harvesting, and the use of pesticides are preventive actions that reduce mycotoxin contamination of field crops. Numerous studies have shown that insect infestation can serve as a vector for mould infection in commodities that are susceptible to mycotoxin formation. Reduction of insect infestation is, therefore, critical for pre-harvest mycotoxin control. The main objective is to prevent mycotoxin formation at this phase of food production.

Harvesting procedures

Harvesting may inflict mechanical damage on commodities. When damage is kept to a minimum during this phase, subsequent contamination is significantly reduced. Field crops should be harvested in a timely manner to reduce the moisture or water activity (Aw) levels to a point where mycotoxin formation will not occur.

Post-harvest procedures

Prevention through pre-harvest management is the best method for controlling mycotoxin contamination; however, should the contamination occur or persist after this phase, the hazards associated with the toxins must be managed through post-harvest procedures if the product is to be used for food and feed purposes. In the post-harvest phase, storage and processing are the major areas where contamination can be prevented. Processing can involve the removal of parts of the commodity, and this may make it more susceptible to mould infestation. The toxin may also be eliminated through the physical separation or chemical inactivation that occurs during specific processing procedures. In this regard, the activity will prevent exposure of consumers to the hazard.

Storage

Storage, whether on the farm, at the manufacturing premises or in the grocery store, is the most critical post-harvest phase in food handling. An inappropriate storage facility, improper packaging and / or the state of the food product can cause mycotoxin contamination during storage. An accumulation of moisture and heat and / or physical damage to the product enhance fungal invasion, leading to the occurrence of mycotoxins. Stored products should not be exposed to environmental conditions, such as moisture, that promote mould growth. Neither should storage pests be allowed to be present in large enough numbers to cause significant physical damage to the product. Appropriate packaging is often a successful way of excluding insect pests and, where deficits in packaging are likely, general hygiene and the use of pesticides could help minimize contamination. When operating limits are violated, operators of storage facilities need to adjust the processes followed. Under such a scheme mycotoxin contamination is detected before it becomes unmanageable, and the situation is rectified.

Processing

After the pre-harvest and harvesting phases, a commodity may undergo various changes during processing. This is another stage at which mycotoxins could be intentionally eliminated or their formation unintentionally enhanced. The nature of the processing procedure may increase the likelihood of clean commodities becoming colonized by moulds and the subsequent production of toxins. Processors must always be aware of this possibility. Decreasing contamination at this phase ensures that the product reaching the consumer will have minimal likelihood of suffering the hazards associated with mycotoxin contamination of food. Among control procedures that could be employed during the processing phase are clean-up and separation, and thermal and chemical inactivation.

Once a contaminated product has been identified at a processing facility, clean-up and separation are the first alternatives of control. For example, electronic sorting and hand-picking to remove damaged, immature or mould-infested kernels, grains or nuts can remove a significant proportion of the aflatoxins in shelled peanuts. These procedures are usually non-invasive and will not significantly alter the product. The separation of grain into fractions by milling, followed by the elimination of the toxic portions is another decontamination strategy. Complete separation of all contaminated particles may not, however, be achieved since the toxin can diffuse into the interior of the kernel. Other procedures must, therefore, be used to manage contamination in the final product.

Thermal inactivation is a good alternative for products that are usually heat-processed. Fumonisin and ochratoxin levels have been shown to be lower in thermally processed maize and wheat products. On the other hand, aflatoxins and deoxynivalenol are resistant to thermal inactivation and are not destroyed completely by boiling water, autoclaving or a variety of food and feed processing procedures. Thermal inactivation for use at a CCP during processing should be evaluated for the conditions of the particular process and the subsequent fraction(s) containing mycotoxin residues identified.

Other potential control processes

Exploring the application of other processes to control mycotoxins could widen the opportunities for risk management. Where physical separation and thermal inactivation are inappropriate, other techniques may be employed, as long as the end product is acceptable to the consumer. For instance, ammoniation has been successfully employed to reduce aflatoxin contamination in maize, peanuts, cottonseed and meals. Extensive evaluation of this procedure has demonstrated the efficacy and safety of ammoniation in decontaminating animal feeds (Park *et al.*, 1988) and it has been successfully used for many years in the United States, France, Senegal, the Sudan, Brazil, Mexico and South Africa. By including hydrogen peroxide and sodium bicarbonate in the nixtamalization procedure (a traditional alkaline heat treatment of maize used in the manufacture of tortillas), its efficacy against fumonisin and aflatoxin toxicity is increased.

In such industries as oil refining, the use of adsorbent materials is part of normal processing operations. A variety of adsorbent materials, i.e. activated carbon and clays, have been shown to bind aflatoxins in aqueous solutions, and certain aluminosilicates have been reported to bind aflatoxins in peanut oil and animal feeds. Phyllosilicate clay has been shown to prevent acute aflatoxicosis in farm animals and decrease the levels of aflatoxin M1 residues in milk. Activated charcoal has also proved to be effective in reducing patulin in naturally contaminated fruit juices. However, since some adsorbent materials may pose a greater risk than benefit, care must be taken when choosing these products.

ASSOCIATED PROGRAMMES IN MYCOTOXIN CONTROL

Effective integrated mycotoxin management programmes not only cover prevention of mycotoxin formation in agricultural products or their detoxification/ decontamination, but also involve: routine surveillance; regulatory measures to control the flow of mycotoxin-contaminated material in national and international trade; and information, education and communication activities.

FAO has been widely involved in reviewing national food control systems in its developing member countries, in many instances focusing on problems of mycotoxin control. Such reviews involve the identification of weaknesses in the food control infrastructure – i.e. the food control administration, inspection and analytical capacity, regulatory issues, etc. After the review process, FAO is frequently involved in the implementation of technical assistance projects to address existing problems.

FAO has played an important role in the dissemination of technical literature to its member countries in support of their efforts in the area of mycotoxin control. Several publications and training aids on various aspects of mycotoxin control have been prepared and distributed. The publications cover a variety of topics, such as methods of sampling and analysis; a training syllabus for use in short-term courses on aflatoxin analysis; a compilation of mycotoxin regulations; and directories of mycotoxin prevention and control institutions in selected regions. The latter are examples of FAO's efforts to facilitate regional networking so as to optimize the use of scarce financial, human and technical resources in the implementation and upgrading of mycotoxin management programmes. Such networking is also promoted through FAO's regional mycotoxin projects and programmes.

Establishment of regulatory limits

Hazard analysis and CCP systems must be built on existing or simultaneously established food safety programmes in each country. Implementation of HACCP cannot be expected to succeed in the absence of regulatory activities. Regulatory limits or standards provide a benchmark against which the effectiveness of food safety programmes can be tested. Regulatory limits are law, violation of which has legal consequences.

FAO has supported the compilation of information, at regional and global levels, on maximum tolerable levels for mycotoxins in food and feed. The last global compilation dates from 1995 and contains data from 90 countries on mycotoxin regulations, tolerance levels and methods of sampling and analysis. It has been published and widely distributed (FAO, 1997).

The importance of the development of internationally harmonized regulatory mycotoxin control measures that protect public health and promote fair trade at the international level cannot be overemphasized. It is of particular importance in view of the World Trade Organization (WTO) Agreements on Sanitary and Phytosanitary Measures (SPS) and Technical Barriers to Trade (TBT). These agreements call for greater harmonization and transparency in the establishment of food regulations that are meant to facilitate trade without compromising consumer protection. The SPS Agreement states that measures conforming to international Codex standards, guidelines or other recommendations are deemed to be appropriate, necessary and non-discriminatory. WTO's recognition of Codex standards, guidelines and other recommendations as benchmarks for food safety is undoubtedly related to the role of science in the Codex process. The Joint FAO / WHO Expert Committee on Food Additives (JECFA) plays an important role in the elaboration of Codex standards and guidelines related to mycotoxin contamination by providing evaluations based on sound scientific and risk assessment principles.

Considerations that enter into regulatory decisions for controlling mycotoxin levels in human foods and animal feeds include:

- control of human exposure to mycotoxins;
- the source of the mycotoxin contamination;
- toxicological characteristics of mycotoxin residues and their metabolites;
- the capability of current analytical methods to measure and confirm the identity of such residues;
- relationships between mycotoxin levels in feeds and their residues in animal products;
- the effects of particular control levels on the availability of the food or feed;
- the effects of the mycotoxins on human and animal health and productivity;
- the practicability and effectiveness of various possible regulatory enforcement strategies.

Consideration of all of these factors is required in the design and implementation of a mycotoxin control programme.

Implementation of surveillance and monitoring programmes

Surveillance and monitoring activities fall within HACCP principles 4 to 7. In the absence of regulation and surveillance, voluntary compliance with any system may not be wholly achieved. Announcing the seafood HACCP regulation in 1995, David Kessler, the US Food and Drug Administration Commissioner at the time, stated "Our safety inspections should focus on preventing problems rather than chasing the horses after they are out of the barn". Safety inspections are the responsibility of government regulatory agencies that ensure the adequacy of industry food safety programmes. Inspections to uncover violations are based on set limits and standards. In order to set up a monitoring and management programme, the following data and policy decisions must be acquired and made:

- identify the mycotoxin(s) and the products or commodities that are to be included in the programme;
- set up a system of inspection and sample collection;
- set up a sampling plan;
- establish a policy guide for end use of the products, for example:
  - proceed into market channels "as is";
  - use as designated animal feed, e.g. dairy, feed lot, finishing, starter;
  - divert to decontamination procedures or lower-risk uses.

Once a regulatory limit has been set, monitoring programmes play an important role in determining compliance. For mycotoxin contamination, it is important to consider adequate random sampling techniques that consider the existence of "hot spots" or highly contaminated portions of the product. A well-designed sampling plan and validated methodology will provide, within limitations, the concentrations of specific analyte for a specified lot of material. The greatest likelihood of obtaining a representative sample occurs when several small portions of a lot are taken and combined. For instance, when collecting the analytical sample for cottonseed or maize, ten randomly selected samples of about 0.5 to 1.5 kg each are required (FAO, 1993). It is important that the analyst is competent to conduct the method. The analytical result is of no value if the sample collected and prepared for analysis does not represent the lot and conceals or overexpresses violations of critical limits. Care must therefore be taken to assure that proper procedures are followed.

A good example of management through a monitoring programme is the aflatoxin control programme established by the State of Arizona in the United States. In 1978, almost 910 000 pounds of milk were discarded because of high aflatoxin M_1 levels. As a result of this huge commercial loss, the state instituted a programme to monitor aflatoxin levels in whole cottonseed and cottonseed products at processing points. All cottonseed produced in the state is tested for aflatoxin content. The maximum size of the lots tested is 100 tonnes, and the testing is conducted in state-certified laboratories. The end use of the product is dictated by the aflatoxin levels that are found. Cottonseed lots testing over 20 µg of aflatoxin per kilogram are usually treated with ammonia to reduce these levels, and then re-tested (Park and Pohland, 1986). The use of this programme has kept Arizona's milk supply safe from aflatoxin. The same concept can also be applied to other commodities.

The establishment of monitoring and surveillance programmes for mycotoxins requires suitably equipped laboratories, well-trained staff for both analytical and inspection activities, reliable analysis and sampling methods, and application of analytical quality assurance programmes. Specific FAO projects in a number of countries have addressed these issues in providing technical assistance in the area of surveillance of mycotoxin contamination. Although aflatoxin was the first priority in most of the projects, they all also gave some attention to the surveillance of other mycotoxins. Existing systems for monitoring food contaminants, including various mycotoxins, have been studied and strengthened in Asian countries such as Bhutan, China, India, Indonesia, Nepal, Pakistan, the Philippines, Sri Lanka, Thailand and Vanuatu; Latin American countries such as Chile, Cuba, Guatemala and Uruguay; and in African countries such as Malawi, Rwanda, the United Republic of Tanzania and several West African States (Boutrif and Canet, 1998).

Analytical quality assurance studies were carried out at regional level in Latin America and Asia. Results highlighted the need for continuing such exercises and increasing the number of participating laboratories.

As a means of building sustainable national capacity, training has been a major component of FAO's assistance to developing countries in improving mycotoxin control. A long-term, international training programme was carried out during the 1980s in collaboration with the United Nations Environment Programme (UNEP) and what was then the Union of Socialist Soviet Republics (USSR). Other activities included local and regional courses for laboratory staff and practical demonstrations on field detection, identification and analysis of various mycotoxins. In Asia, a training network was implemented to provide training in methods of analysis and sampling of various mycotoxins, including guidance on policy issues. Regional workshops on mycotoxin analysis were held in Senegal, Botswana and various Latin American countries.

CONCLUSIONS

Much has been accomplished at national, regional and international levels regarding mycotoxin prevention and

Possible stages in application of the HACCP principle to agricultural commodities, food products and animal feedstuffs

Stage	Commodity	Hazard	Corrective action
Pre-harvest	Cereal grains, oilseeds, nuts, fruits	Mould infestation with subsequent mycotoxin formation	Utilize crop resistant varieties Enforce effective insect control programmes Maintain adequate irrigation schedules Perform good tillage, crop rotation, weed control practices, etc.
Harvesting	Cereal grains, oilseeds, nuts, fruits	Increase in mycotoxin formation	Harvest at appropriate time Maintain at lower temperature, if possible Remove extraneous material Dry rapidly to below 10% moisture
Post-harvest and storage	Cereal grains, oilseeds, nuts, fruits	Increase and/or occurrence of mycotoxin	Protect stored product from moisture, insects, environmental factors, etc. Store product on dry clean surface
Post-harvest, processing and manufacturing	Cereal grains, oilseeds, nuts, fruits	Mycotoxin carryover or contamination	Test all ingredients added Monitor processing/manufacturing operation to maintain high-quality product Follow good manufacturing practices
Animal feeding	Dairy, meat and poultry products	Transfer of mycotoxin to dairy products, meat and poultry products	Monitor mycotoxin levels in feed ingredients Test products for mycotoxin residues

control, but much still remains to be done. It is now widely recognized that food safety programmes should be based on the strict observance of good agricultural, processing and handling practices, including the application of HACCP concepts; governments should therefore upgrade their mycotoxin management programmes to include the HACCP principles. HACCP-based mycotoxin management programmes must involve control and surveillance at all stages of production and post-production, as there are several factors at pre-harvest, harvest and post-harvest stages that are implicated in mycotoxin contamination of crops. FAO has been active in providing assistance to its member countries in various aspects of mycotoxin management including mycotoxin prevention and control, routine surveillance and regulatory matters. Minimizing the risks posed by mycotoxins through applying good agricultural, processing and handling practices and utilizing the HACCP concept continues to be priority for FAO. ◆

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Minimizing risks posed by mycotoxins utilizing the HACCP concept

Mycotoxin contamination of susceptible commodities occurs as a result of environmental conditions in the field and improper harvesting, storage and processing operations. Hazard Analysis Critical Control Point (HACCP) programmes have been useful in managing the risks associated with potential contamination of food products with pathogenic micro-organisms and chemical toxicants. Food safety programmes routinely use information about the factors leading to contamination to establish preventive and control procedures, thus providing the consumer with a safe, wholesome food supply. When an effective HACCP programme for mycotoxins is being established, key elements are identified that can be used or modified to reduce mycotoxin formation in field and storage environments. Such elements include limiting insect infestation and moisture levels in the commodities. Specific processing and decontamination procedures can play a role in reducing mycotoxin levels through the physical separation of damaged, immature and mould-infested kernels, grains or nuts, and the physical and chemical inactivation and/or removal of the toxin. The development and application of HACCP-based food safety programmes require expertise in a range of fields. FAO has been active in providing technical assistance to its member countries, helping to build national capacity to implement and maintain effective HACCP-based mycotoxin management programmes.

Minimiser les risques associés aux mycotoxines, à l'aide du concept HACCP

La contamination des produits sensibles par les mycotoxines est une conséquence de certaines conditions écologiques sur le terrain et d'opérations de récolte, d'entreposage et de transformation inappropriées. Les programmes du Système d'analyse des risques – points critiques pour leur maîtrise (HACCP) ont permis de limiter les risques associés à la contamination potentielle des produits alimentaires par des micro-organismes pathogènes et des produits chimiques toxiques. Les programmes visant à garantir l'innocuité des aliments utilisent régulièrement des informations sur les facteurs favorisant la contamination pour établir des procédures de prévention et de contrôle et garantir aux consommateurs l'accès à des aliments sains et salubres. Lors de la mise en place d'un programme HACCP efficace, des éléments clés sont identifiés pouvant être utilisés ou modifiés pour réduire la formation de mycotoxines dans les champs et dans les lieux d'entreposage. De tels éléments comprennent la limitation des infestations d'insectes et la teneur en humidité des produits alimentaires. Des procédures de transformation et de décontamination spécifiques peuvent contribuer à réduire les concentrations de mycotoxines, par la séparation physique des amandes, des semences ou des coques abîmées, non mûres et moisies, et par l'inactivation physique et chimique et/ou l'élimination de la toxine. L'élaboration et l'application de programmes destinés à assurer l'innocuité des aliments fondés sur le HACCP nécessite des compétences dans divers domaines. La FAO a fourni une assistance technique à ses pays membres en les aidant à renforcer leurs capacités nationales afin qu'ils soient mieux à même de mettre en œuvre et de maintenir des programmes efficaces de gestion des mycotoxines, basés sur le HACCP.

Reducción al mínimo de los riesgos que plantean las micotoxinas mediante la utilización del concepto de HACCP

La contaminación por micotoxinas de productos expuestos se produce como resultado de las condiciones ambientales en el campo o de operaciones inadecuadas de recolección, almacenamiento y elaboración. Los programas de análisis de peligros y puntos críticos de control (HACCP) han sido útiles para hacer frente a los riesgos asociados con la posible contaminación de productos alimenticios y sustancias químicas tóxicas. Los programas de inocuidad de los alimentos suelen utilizar información sobre los factores que propician la contaminación para establecer medidas preventivas y de control y ofrecer de ese modo al consumidor un suministro de alimentos inocuos y sanos. Al introducir un programa eficaz de HACCP para las micotoxinas, se determinan los principales elementos que pueden utilizarse o modificarse para reducir la formación de micotoxinas en el campo y en el lugar de almacenamiento, por ejemplo la limitación de la infestación por insectos y del nivel de humedad en los productos. Determinados procedimientos de elaboración y descontaminación pueden contribuir a reducir el nivel de las micotoxinas mediante la separación física de las almendras, granos o nueces dañados, inmaduros e infestados por mohos, y la inactivación física y química o la eliminación de la toxina. La elaboración y aplicación de programas de inocuidad de los alimentos basados en el sistema de HACCP exigen conocimientos técnicos en diversos ámbitos. La FAO se ha esforzado por proporcionar asistencia técnica a sus Estados Miembros con el fin de fortalecer la capacidad nacional para introducir y mantener programas eficaces de gestión de micotoxinas según el sistema de HACCP. ♦

CORRIGENDUM

In *Food, Nutrition and Agriculture* 22, 1998, the photo caption on p. 9 should read “A small garden in Dar-es-Salaam, United Republic of Tanzania”.