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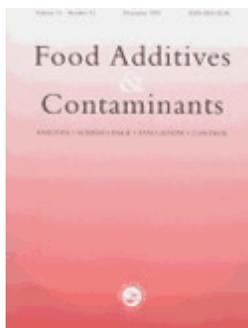
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A pilot survey of aflatoxin-albumin adducts in sera from Egypt

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1 **A pilot survey of aflatoxin-albumin adducts in sera from Egypt**

3 **Keywords:** aflatoxin, aflatoxin-albumin, biomarkers Egypt, serum

5 **Short title:** aflatoxin-albumin adducts in Egyptian sera

6 **Abbreviations:** aflatoxin B₁ (AFB₁), aflatoxin M₁ (AFM₁), aflatoxin-albumin (AF-alb),
7 hepatocellular carcinoma (HCC), hepatitis B virus (HBV), hepatitis C virus (HCV),

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2
3 **Abstract**
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5
6 Aflatoxins are potent liver carcinogens that frequently contaminate dietary cereals
7
8 within developing regions. Aflatoxin exposure has been predicted within Egypt but to
9
10 date no studies have measured the level of aflatoxin-albumin (AF-alb) adducts as a
11
12 validated biomarker to assess exposure. A limited number of sera were available from
13
14 an hepatocellular carcinoma (HCC) case control study within Egypt. In this pilot survey
15
16 AF-alb was detected in 24/24 samples from individuals without HCC diagnosis
17
18 (geometric mean 9.0pg/mg range 3.5-25.8pg/mg), whilst 7/22 samples from HCC cases
19
20 had detectable AF-alb (geometric mean 2.6pg/mg (range nd – 32.8pg/mg). These AF-
21
22 alb data do not represent a case control comparison due to inherent difficulties in
23
24 comparing markers of dietary intake between controls and patients with disease.
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26 Although these data are limited, the potential health consequences of aflatoxin exposure
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28 in this region merit further investigation.
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1 Introduction

2 Aflatoxins are metabolites of *Aspergillus flavus* and *parasiticus* which contaminate
3 common dietary staples during both cultivation and storage post-harvest (IARC 2002).
4 The most common and toxic of the naturally occurring aflatoxins is aflatoxin B₁
5 (AFB₁), and has been classified as a class 1A human liver carcinogen by the
6 International Agency of Research on Cancer (IARC 2002). The highest aflatoxin
7 exposures have been observed in parts of Africa, China and Southeast Asia, areas which
8 are also characterized by a high incidence of hepatocellular carcinoma (HCC) (IARC
9 2003). HCC is the fifth most common cancer in the world with around 500,000 new
10 cases annually, and HCC represents the third most common cause of cancer mortality in
11 the world (IARC 2003). The main risk factors for HCC in addition to aflatoxin are
12 hepatitis B virus (HBV) and hepatitis C viruses (HCV) (IARC 1994, 2002). Given the
13 burden of HCC in many regions of the world with mortality rates only slightly lagging
14 incidence rates, it is important to understand the contribution of all putative etiological
15 agents within a given region. In Egypt the prevalence of HCC is increasing (El-Zayadi
16 et al., 2005), and deaths due to HCC more than doubled in the previous two decades
17 increasing from 2.4 per 100,000 in 1987 to 5.2 per 100,000 in 2000 (El-Sawry et al.,
18 2001). Major etiological factors in this region are clearly HCV (Angelico et al., 1997;
19 Saeed et al., 1991; El-Zayadi et al. 2005, El-Kafrawy et al. 2005) and HBV (Attia,
20 1998), with a possible independent role for occupational pesticide exposures (Ezzat et
21 al. 2005). To date the potential role of aflatoxins in HCC development in Egypt has not
22 been fully explored. We recently reported that 8 of 41 liver samples from Egyptian
23 HCC cases contained a specific transversion mutation (AGG to AGT (arginine-to-
24 serine) at codon 249) within the TP53 tumour suppressor gene (TP53 Ser249) (El-
25 Kafrawy et al., 2005). This specific mutation is suggestive of aflatoxin being causative

1 for the mutation (Bressec et al., 1991; Hsu et al., 1991; Kirk et al., 2000). In response,
2 we have undertaken a pilot biomarker survey to further assess the prevalence of
3 aflatoxin exposure within Egypt. The level of aflatoxin-albumin (AF-alb) adduct in
4 serum reflects the biologically effective aflatoxin dose, and serves as a useful aflatoxin
5 exposure biomarker in humans (Sabbioni et al., 1987, Chapot and Wild 1991; Wild and
6 Turner 2002). Moderate levels of aflatoxin exposure are predicted in Egyptian
7 populations based on measures of the parent aflatoxins (or phase 1 metabolites) in
8 biofluids (El-Nezami et al., 2000; Hatem et al., 2005; Hassan et al., 2006; Polychronaki
9 et al., 2006, 2007a, 2007b). However, to date there has not been an assessment of
10 aflatoxin exposure in Egypt using the more robust measure of the level of AF-alb
11 adducts in serum. The AF-alb adduct is particularly valuable in this respect as it
12 provides a good indicator of exposure over the previous two the three months
13 (Montesano et al., 1999; Wild and Turner 2002). This manuscript describes an
14 exploratory study in which the levels of AF-alb were measured for a subset of sera from
15 individuals within an Egyptian HCC case-control study, previously reported by Ezzat et
16 al., (2005). The prevalence and levels of exposure in this pilot study were compared to
17 exposure patterns reported elsewhere.

18 19 **Methods**

20 *Subject Recruitment*

21 A case-control study was conducted from 1999 - 2004 to study viral and environmental
22 risk factors associated with hepatocellular carcinoma (HCC) in Egypt. Detailed methods
23 of recruitment have been previously documented (Cowgill et al. 2004; Ezzat et al.
24 2005). In brief the study consisted of 343 confirmed cases of HCC and 524 non-cancer
25 controls matched by age, sex, and region of current residence. A subset of 46

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1 individuals, including 22 cases (aged 36-74; 18 males, 4 females) and 24 controls (aged
2 37-73; 20 males, 4 females), for whom blood samples were available, were tested for
3 the level of serum AF-alb adduct. All of these individuals were from the Cairo
4 metropolitan area or governorates within the Nile Delta, and all were HBsAg negative.
5 The subset of cases for this AF-albumin study were selected because they had TP53
6 gene mutation results available from a previous analysis (El-Kafrawy et al. 2005);
7 controls were randomly selected from the total pool of controls to match these cases on
8 age, gender and region distributions. However, due to difficulties in comparing
9 biomarkers related to dietary intake where one group are patients with disease, this
10 manuscript is not attempting to present case control data in relation to HCC causation.

12 *AF-albumin ELISA*

13 The levels of AFB₁-albumin adduct were determined by albumin extraction, digestion
14 and ELISA as previously described (Chapot and Wild 1991). The detection limit was
15 3pg AFB₁-lysine equivalents per mg of albumin (pg/mg). Three positive and one
16 negative control samples were analyzed with each batch of samples. Samples were
17 measured in quadruplicate on two separate days; CVs were less than 25%. AF-alb data
18 were natural log transformed to better approximate a normal distribution. Table 1,
19 reports the percentage of Egyptian samples with detectable AF-alb, and for clarity
20 adduct levels are back transformed and presented as geometric means.

22 **Results and Discussion**

23 Aflatoxin is a potent hepatocarcinogen, and given that exposure can occur throughout
24 life it is important to understand the pattern of exposure in regions potentially at risk
25 from this toxin. AF-alb has been used as a specific biomarker of exposure in West

1 African adults (Wild et al., 2000; Turner et al., 2005a; Dash et al., 2007) and children
2 (Turner et al., 2000, 2003, 2005b, 2007; Gong et al., 2002, 2004), and exposure based
3 on this biomarker is frequent and at high levels. By comparison, there is less
4 information from Egypt on aflatoxin exposure using biomarkers but levels are predicted
5 to be lower than in West Africa (El-Nezami et al., 2000; Hatem et al., 2005). In this
6 pilot study of Egyptian samples, AF-alb adducts were detected in 31 of 46 (67.4%) of
7 the samples (geometric mean 5.0pg/mg (range non detectable to 32.8pg/mg), see Table
8 1. Of the 24 individuals without HCC, all were positive for AF-alb (n=24, geometric
9 mean 9.0pg/mg; range 3.5 – 25.8pg/mg. By contrast fewer individuals, 7 of 22 (31.8%),
10 with HCC had detectable adducts, and overall adduct levels were lower ($p < 0.001$) in
11 cases (geometric mean 2.6pg/mg; range non detectable to 32.8pg/mg). HCC is
12 frequently diagnosed late, and due to the advanced state of the disease it is known that
13 individuals diagnosed with HCC in Africa have modified or restricted diets, leading to
14 lower aflatoxin exposures (Kirk et al., 2005). Dietary surveys were not conducted
15 within this study to specifically address this issue. AF-alb adducts were not observed for
16 the eight HCC cases carrying the TP53 Ser249 mutation, which may again simply
17 reflect such changes in dietary intake for HCC cases. In addition, if aflatoxin exposure
18 were causative for the reported TP53 Ser249 mutations in these eight HCC cases, this
19 would be as a consequence of chronic exposure over years or decades, thus a measure of
20 recent exposure would not necessarily correlate with the mutation (Kirk et al., 2005).

21 For the non HCC cases, a non-significant trend ($p > 0.05$) towards higher adduct levels
22 was observed for those from rural areas (geometric mean 11.2pg/mg; 95%CI: 7.7,
23 16.2pg/mg, n= 9) compared to those in urban areas (geometric mean 7.9pg/mg; 95%CI:
24 5.8, 10.7, n=15), possibly reflecting less varied diets and reliance on basic dietary
25 staples in rural settings, as observed in The Gambia (Wild et al., 2000). A similar but

1 again non-significant trend was also observed within the cases (data not shown).
2 Numbers limit both the interpretation of this observation, and further analysis of the
3 data by age, sex, or seasonality.

4 A comparison of AF-alb adducts in this study and a number of other countries,
5 measured using the ELISA methodology, are made in Table 1. The frequency and level
6 of exposure in West African countries is clearly higher, and for many individuals in
7 West Africa the levels exceed 100pg/mg (Wild et al, 2000; Turner et al., 2007). A
8 similar high prevalence of AF-alb was reported for adults in Ghana (Dash et al., 2007),
9 however, differences in assay methodology restrict further comparison with their data.
10 Limited surveys in Western Europe revealed no positive samples for this adduct
11 (reviewed by Wild et al., 1993). The frequency and levels of exposure in these Egyptian
12 samples are therefore considered to be intermediate in comparison with the low risk and
13 high risk areas for exposure, and to be more in line with exposures recently observed by
14 Scussel et al., (2006) in Brazil, or previously reported from Thailand (reviewed by Wild
15 et al., 1993).

16
17 Urine samples and breast milk provide additional bio-fluids with which to monitor
18 aflatoxin exposure. AFM₁ is a major metabolite of AFB₁ and is the main aflatoxin that
19 is sequestered into breast milk following maternal exposure to AFB₁ (Zarba et al., 1992;
20 IARC 2002). The frequency of AF-alb in our present study are in line with recent
21 observations of aflatoxin M₁ in breast milk samples from Egyptian mothers
22 (Polychronaki et al., 2006) in which 138/388 (35.6%) were positive for this metabolite.
23 The difference in prevalence may reflect the longer half-life of the albumin adduct,
24 approximately 3 weeks (Chapot and Wild, 1991), compared to AFM₁.

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4 1 Depending on sex and geographic location within Egypt the HBV surface antigen
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6 2 (indicative of current infection) was detected in 3-11% of the total case-control study
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8 3 population (Ezzat et al., 2005), and HBV was estimated to contribute 5-10% to the
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10 4 burden of HCC in Egypt. In regions where co-exposure to aflatoxin and chronic carriage
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12 5 of HBV infection occur, a synergistic interaction in the development of HCC has been
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14 6 reported (Ross et al., 1992; Qian et al., 1994; Wang et al., 2001), with the relative risk
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16 7 of HCC increasing up to 60-fold with co-exposure. Given the level of chronic HBV
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18 8 carriage in Egypt, the significance of potential co-exposure to aflatoxin is of concern.
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20 9 HCV accounts for nearly 90% of the HCC burden in Egypt (Ezzat et al., 2005),
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22 10 however, to date no interaction between HCV infection and aflatoxin exposure are
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24 11 reported in the literature.
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32 13 The purpose of this survey was a pilot investigation of the prevalence of AF-alb
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34 14 adducts, as a biomarker of aflatoxin exposure, within Egypt. To our knowledge the
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36 15 measurement of this validated biomarker to assess exposure in this region has not
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38 16 previously been reported. Our data indicate moderate levels of aflatoxin exposure is
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40 17 occurring within this limited survey, though larger studies are needed to investigate both
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42 18 the sources and potential consequences of exposure to this potent toxin in Egypt.
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1 **Table 1:** Aflatoxin-albumin adducts in adults from selected countries.
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COUNTRY (n)	AF-Alb (pg/mg) Geometric Mean (range)	Prevalence of positive samples (%)	Reference
Egypt			
Total	5.0 (nd – 32.8)	31/46 (76)	This report
HCC cases	2.6 (nd – 32.8)	7/22 (31.8)	
Controls	9.0 (nd – 25.8)	24/24 (100)	
The Gambia			
Rural	61.8 (57.3 – 66.7)#	272/272 (100)	Wild et al., 2000
Peri-urban	39.1 (31.1 – 49.1)#	83/84 (98.8)	
Guinea##	18.4 (nd-66)	245/250 (98)	Turner et al., 2005b
The Gambia	40.4 (4.8-260.8)	119/119 (100)	Turner et al., 2007
Brazil*	10.7 (nd – 57.3)	31/59 (62)	Scussel et al., 2006
France/ Poland	0 (nd)	0/74 (0)	Wild et al., 1993

3 nd. non-detected

4 * Geometric means of positives only

5 # Geometric means and 95%CI

6 ## Data obtained for blood samples in Feb/Mar

7 \$ - Infants aged 4 months old.

References:

Angelico M, Renganathan E, Gandin C, Fathy M, Profili MC, Refai W, De Santis A, Nagi A, Amin G, Capcaccia L, Callea F, Rapicetta M, Badr G, Rocchi G, 1997. Chronic liver disease in the Alexandria governorate, Egypt: contribution of schistosomiasis and hepatitis virus infections. *Journal of Hepatology*. 26: 236-243.

Attia MA. 1998. Prevalence of hepatitis B and C in Egypt and Africa. *Antiviral Therapeutics* 3:1-9.

Bressac, B., Kew, M., Wands, J., and Ozturk, M. Selective G to T mutations of p53 gene in hepatocellular carcinoma from southern Africa. *Nature* 350:429-431, 1991.

Chapot B, and Wild CP. 1991. ELISA for quantification of aflatoxin-albumin adducts and their application to human exposure assessment., p. 135-155. *In* M. Warhol, D. van Velzen, and G. R. Bullock (ed.), *Techniques in Diagnostic Pathology*. Academic Press, San Diego

Cowgill KD, Loffredo CA, Eissa SA, Mokhtar N, Abdel-Hamid M, Fahmy A, Strickland GT. 2004 Case-control study of non-Hodgkin's lymphoma and hepatitis C virus infection in Egypt *International Journal of Epidemiology*.33(5):1034-9.

Dash B., Afrivie-Gyawn E., Hubner H.J., Porter W., Wang J.S., Jolly P.E., Phillips T.D. (2007). Determinants of the variability of aflatoxin-albumin adduct levels in Ghanaians. *J. Toxicol. Environ. Health A*. 70(1):58-66

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57
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59
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1 El-Kafrawy SA, Abdel-Hamid M, El-Daly M, Nada O, Ismail A, Ezzat S, Abdel-Latif
2 S, Abdel-Hamid A, Shields PG, Loffredo C. 2005 p53 mutations in hepatocellular
3 carcinoma patients in Egypt. International Journal of Hygiene and Environmental
4 Health 208: 263-70.

5
6 El-Nezami H, Mykkänen H, Kankaanpää P, Suomalainen T, Salminen S, Ahokas J.
7 2000. Ability of a mixture of *lactobacillus* and *propionibacterium* to influence the
8 faecal aflatoxin content in healthy Egyptian volunteers: a pilot clinical study. Bioscience
9 Microflora 19:41-45.

10
11 El-Sawy MT, Mohamed MK, Boutros SG, El Hosaini M, Ibraheim T, Boutros S,
12 Ahmed SS. The burden of disease and injury in Egypt. Ministry of Health
13 and Population: Cairo, Egypt, 2004.

14
15 El-Zayadi AR, Badran HM, Barakat EM, Attia Mel D, Shawky S, Mohamed MK, Selim
16 O, Saeid A. 2005. Hepatocellular carcinoma in Egypt: a single center study over a
17 decade. World Journal of Gastroenterology 11: 5193-5198.

18
19 Ezzat S, Abdel-Hamid M, Abdel-Latif E, Mokhtar N, Labib NA, El-Ghorory L, Mikhail
20 NN, Abdel-Hamid A, Hifnawy T, Stickland GT, Loffredo CA. 2005. Associations of
21 pesticides, HCV, HBV, and hepatocellular carcinoma in Egypt. International Journal of
22 Hygiene and Environmental Health 208: 329-339.

23

- 1
2
3
4 1 Gong Y, Cardwell K, Hounsa A, Egal S, Turner PC, Hall AJ, Wild CP. 2002. Dietary
5
6 2 aflatoxin exposure and impaired growth in young children from Benin and Togo: cross
7
8 3 sectional study. *British Medical Journal* 325: 20-21.
9
10
11 4
12
13 5 Gong Y.Y., Hounsa A., Egal S., Turner P.C., Sutcliffe A.E., Hall A.J., Cardwell K.
14
15 6 Wild C.P. (2004) Post-weaning exposure to aflatoxin results in impaired child growth: a
16
17 7 longitudinal study in Benin, West Africa. *Environmental Health Perspectives*. 112(13)
18
19 8 1334-8.
20
21
22 9
23
24
25 10 Hassan AM, Sheashaa HA, Abdel Fatah MF, Ibrahim AZ, Gaber OA. 2006 Does
26
27 11 aflatoxin as an environmental mycotoxin adversely affect the renal and hepatic
28
29 12 functions of Egyptian lactating mothers and their infants? A preliminary report.
30
31 13 *International urology and nephrology*. 38(2): 339-42.
32
33
34 14
35
36 15 Hatem NL, Hassab HM, Abd Al-Rahman EM, El-Deeb SA, El-Sayed Ahmed RL. 2005.
37
38 16 Prevalence of aflatoxins in blood and urine of Egyptian infants with protein-energy
39
40 17 malnutrition. *Food and Nutrition Bulletin* 26: 49-56.
41
42
43 18
44
45
46 19 Hsu, I.C., Metcalf, R.A., Sun, T., Welsh, J.A., Wang, N.J., and Harris, C.C. Mutational
47
48 20 hotspot in the p53 gene in human hepatocellular carcinomas. *Nature* 350:427-428, 1991.
49
50
51 21
52
53
54 22 International Agency for Research on cancer (IARC) 1994, Hepatitis viruses,
55
56 23 monographs on the evaluation of carcinogenic risks to humans. *IARC Sci. Publ.* **59**
57
58 24 Lyon, France.
59
60

1
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5
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47
48
49
50
51
52
53
54
55
56
57
58
59
60

1 International Agency for Research on cancer (IARC). 2002. Some traditional herbal
2 medicines, some mycotoxins, naphthalene and styrene. Lyon, France: World Health
3 Organization, IARC. Report nr 82. 1-556 p.

4
5 International Agency for Research on cancer (IARC) (2003). Cancer in Africa:
6 epidemiology and prevention. Lyon (France): IARC Scientific Publication 153

7
8 Kirk GD, Camus-Randon AM, Mendy M, Goedert JJ, Merle P, Trepo C, Brechot C,
9 Hainaut P, Montesano R. 2000. Ser-249 p53 mutations in plasma DNA of patients with
10 hepatocellular carcinoma from The Gambia. Journal of the National Cancer Institute 92:
11 148-153.

12
13 Kirk GD, Lesi OA, Mendy M., Szymanska K., Whittle H., Goedert J.J., Hainaut P.,
14 Montesano R. (2005) 249(ser) TP53 mutation in plasma DNA, hepatitis B viral
15 infection, and risk of hepatocellular carcinoma. Oncogene24(38):5858-67.

16
17 Kirk GD, Camus-Randon AM, Mendy M, Goedert JJ, Merle P, Trepo C, Brechot C,
18 Hainaut P, Montesano R. 2000.. 249(ser) TP53 mutation in plasma DNA, hepatitis B
19 viral infection, and risk of hepatocellular carcinoma. Oncogene. ;24(38):5858-67.

20
21 Montesano R, Hainaut P, Wild CP. 1997 Hepatocellular Carcinoma: From gene to
22 public health Journal of the National Cancer Institute **89** 1844-1851

23

- 1 Polychronaki N, Turner PC, Mykkanen H, Gong Y, Amra H, Abdel-Wahhab M, El-
2 Nezami H. 2006. Determinants of aflatoxin M₁ in breast milk in a selected group of
3 Egyptian mothers. *Food Additives and Contaminants* 23:700-708.
- 4
- 5 Polychronaki N, West RM, Turner PC, Amra H, Abdel-Wahhab M, Mykkanen H, El-
6 Nezami H. 2007a. A longitudinal assessment of aflatoxin M₁ excretion in breast milk of
7 selected Egyptian mothers. *Food and Chemical Toxicology*. 45: 1210-1215 .
- 8
- 9 Polychronaki N, Wild CP, Mykkänen H, Amra H, Abdel-Wahhab M, Sylla A, Diallo
10 M, El-Nezami H, Turner PC. (2007b) Urinary biomarkers of aflatoxin exposure in
11 young children from Egypt and Guinea. *Food and Chemical Toxicology (in press)*.
- 12
- 13 Qian GS, Ross RK, Yu MC, Yuan JM, Gao YT, Henderson BE, Wogan GN, Groopman
14 JD. 1994. A follow-up study of urinary markers of aflatoxin exposure and liver cancer
15 risk in Shanghai, People's Republic of China. *Cancer Epidemiology Biomarkers and*
16 *Prevention* 3:3-10.
- 17
- 18 Ross RK, Yuan JM, Yu MC, Wogan GN, Qian GS, Tu JT, Groopman JD, Gao YT,
19 Henderson BE. 1992 Urinary aflatoxin biomarkers and risk of hepatocellular carcinoma.
20 *Lancet*, 339: 943–946.
- 21
- 22 Sabbioni G., Ambs S., Wogan G.N., Groopman J.D. (1990) The aflatoxin-lysine adduct
23 quantified by high-performance liquid chromatography from human serum albumin
24 samples. *Carcinogenesis* 11(11):2063-6.
- 25

- 1
2
3
4 1 Saeed AA, Al-Admawi AM, Al-Rasheed A, Fairclough D, Bacchus R, Ring C, Garson
5
6 2 J. 1991. Hepatitis C virus infection in Egyptian volunteer blood donors in Riyadh.
7
8 3 Lancet 338: 459-460.
9
10 4
11
12 5 Scussel VM, Haas P, Gong YY, Turner PC, Wild CP. 2006 Study of aflatoxin exposure
13
14 6 in a Brazilian population using an aflatoxin-albumin biomarker. In Mycotoxins and
15
16 7 phycotoxins: Advances in determination, toxicology and exposure management. Ed H.
17
18 8 Njapau, S. Trujillo, H.P van Egmond, D.L.park pp197-202
19
20 9
21
22 10 Turner PC, Collinson AC, Cheung YB, Gong YY, Hall AJ, Prentice AM, Wild CP.
23
24 11 2007 Aflatoxin exposure *in utero* causes growth faltering in Gambian infants.
25
26 12 International Journal of. Epidemiology. [Epub ahead of print]
27
28 13
29
30 14 Turner PC, Mendy M, Whittle H, Fortuin M, Hall AJ, Wild CP. 2000. Hepatitis B
31
32 15 infection and aflatoxin biomarker levels in Gambian children. Tropical Medicine and
33
34 16 International Health 5: 837-841.
35
36 17
37
38 18 Turner PC, Moore SE, Hall AJ, Prentice AM, Wild CP. 2003. Modification of immune
39
40 19 function through exposure to dietary aflatoxin in Gambian children. Environmental
41
42 20 Health Perspectives 111: 217-220.
43
44 21
45
46 22 Turner PC, Sylla A, Gong YY, Diallo MS, Sutcliffe AE, Hall AJ, Wild CP. 2005a.
47
48 23 Reduction in exposure to carcinogenic aflatoxins by postharvest intervention measures
49
50 24 in west Africa: a community-based intervention study. Lancet 365: 1950-1956.
51
52 25
53
54
55
56
57
58
59
60

- 1
2
3
4 1 Turner PC, Sylla A, Kuang SY, Marchant CL, Diallo MS, Hall AJ, Groopman JD, Wild
5
6 2 CP. 2005b. Absence of TP53 codon 249 mutations in young Guinean children with high
7
8 3 afltoxin exposure. *Cancer Epidemiology Biomarkers and Prevention* 14: 2053-2055.
9
10 4
11
12 5 Wang JS., Huang T, Su J, Liang F, Wei Z, Liang Y, Luo H, Kuang SY, Qian GS, Sun
13
14 6 G. He X, Kensler TW, Groopman JD.. 2001. Hepatocellular carcinoma and aflatoxin
15
16 7 exposure in Zhuqing Village, Fusui County, People's Republic of China. *Cancer*
17
18 8 *Epidemiology Biomarkers and Prevention* 10: 143-146.
19
20 9
21
22 10 Wild CP and Turner PC. 2002. The toxicology of aflatoxins as a basis for public health
23
24 11 decisions. *Mutagenesis* 17: 471-481.
25
26 12
27
28 13 Wild CP, Jansen LA, Cova L, Montesano R. 1993. Molecular dosimetry of aflatoxin
29
30 14 exposure: contribution to understanding the multifactorial etiopathogenesis of primary
31
32 15 hepatocellular carcinoma with particular reference to hepatitis B virus. *Environmental*
33
34 16 *Health Perspectives* 99: 115-122.
35
36 17
37
38 18 Wild CP, Yin F, Turner PC, Chemin I, Chapot B, Mendy M, Whittle H, Kirk GD, Hall
39
40 19 AJ. 2000. Environmental and genetic determinants of aflatoxin-albumin adducts in the
41
42 20 Gambia. *International Journal of Cancer* 86: 1-7.
43
44 21
45
46 22 Zarba A, Wild CP, Hall AJ, Montesano R, Hudson GJ, Groopman JD. 1992. Aflatoxin
47
48 23 M1 in human breast milk from The Gambia, west Africa, quantified by combined
49
50 24 monoclonal antibody immunoaffinity chromatography and HPLC. *Carcinogenesis* 13:
51
52 25 891-894.
53
54
55
56
57
58
59
60