

What is already known on this topic

Delay in presentation and assessment of patients with suspected stroke prevents the possible benefits from thrombolysis being achieved

Little is known about the presentation and early management of patients with acute stroke in the United Kingdom

What this study adds

Most patients with suspected stroke in the United Kingdom arrive at hospital within six hours of the onset of symptoms

Not all patients are evaluated by a senior doctor within three hours of arrival at hospital and most do not undergo computed tomography

The potential for thrombolysis in patients with acute stroke can be improved significantly by greater use of emergency services and expediting evaluation and investigations by doctors

(Sunderland Royal Hospital), M Power (Ulster Hospital, Dundonald), A K Sharma (University Hospital Aintree, Liverpool), K R Lees (Western Infirmary, Glasgow), and D G Smithard (William Harvey Hospital, Ashford, Kent).

Contributors: See bmj.com

Funding: This project was supported by an unrestricted grant from Boehringer Ingelheim.

Competing interests: LK and MMB have been reimbursed by Boehringer Ingelheim to attend conferences. AKS and KRL have been reimbursed by Boehringer Ingelheim to attend conferences and to give lectures. RIV is an employee of Boehringer Ingelheim. None of the authors stand to gain financially from publication.

- 1 American Heart Association. *Heart and stroke statistical update*. Dallas, TX: American Heart Association, 1999.
- 2 Hankey GJ, Warlow CP. Treatment and secondary prevention of stroke: evidence, costs and effects on individuals and populations. *Lancet* 1999;354:1457-63.

- 3 Grotta JC. Acute stroke therapy in the millennium: consummating the marriage between the laboratory and the bedside: the Feinberg lecture. *Stroke* 1999;30:1722-8.
- 4 Bath PM, Lees KR. ABC of arterial and venous disease: acute stroke. *BMJ* 2000;320:920-3.
- 5 Wardlaw JM, del Zoppo G, Yamaguchi T. Thrombolysis for acute ischaemic stroke. *Cochrane Library*. Issue 1. Oxford: Update software, 2000.
- 6 Lees KR. Thrombolysis. *Brit Med Bull* 2000;389-400.
- 7 Alberts MJ, Hademenos G, Latchaw RE, Jagoda A, Marler JR, Mayberg MR, et al. Recommendations for the establishment of primary stroke centers. *JAMA* 2000;283:3102-9.
- 8 Smith MA, Doliszny KM, Shahar E, McGovern PG, Arnett DK, Luepker RV. Delayed hospital arrival for acute stroke: the Minnesota stroke survey. *Ann Intern Med* 1998;129:190-6.
- 9 Katzan IL, Furlan AJ, Way LE, Farnk JJ, Harper DL, Hinchey JA, et al. A systematic audit of iv tPA in Cleveland area hospitals. *Stroke* 1999;30:266.
- 10 Evenson K, Rosamond W, Morris D. Prehospital and in-hospital delays in acute stroke care. *Neuroepidemiology* 2001;20:65-76.
- 11 Lacy C, Suh D, Bueno M, Kostis J, for the STROKE Collaborative Study Group. Delay in presentation and evaluation for acute stroke: Stroke Time Registry for Outcomes Knowledge and Epidemiology (STROKE). *Stroke* 2001;32:63-9.
- 12 Schroeder E, Rosamond W, Morris D, Evenson K, Hinn A. Determinants of emergency medical services use in a population with stroke symptoms: the Second Delay in Accessing Stroke Healthcare (DASH II) Study. *Stroke* 2000;31:2591-6.
- 13 Morris DL, Rosamond W, Madden K, Schultz C, Hamilton S. Prehospital and emergency department delays after acute stroke. The Genentech Stroke Presentation Survey. *Stroke* 2000;31:2585.
- 14 Kothari R, Jauch E, Broderick J, Brott T, Sauerbeck L, Khoury J, et al. Acute stroke: delays to presentation and emergency department evaluation. *Ann Emerg Med* 1999;33:3-8.
- 15 Rosamond W, Gorton R, Hinn A, Hohenhaus S, Morris D. Rapid response to stroke symptoms: the Delay in Accessing Stroke Healthcare (DASH) Study. *Acad Emerg Med* 1998;5:45-51.
- 16 Menon SC, Pandey DK, Morganstern LB. Critical factors in determining access to acute stroke care. *Neurology* 1998;51:427-32.
- 17 Wester P, Radberg J, Lundgren B, Peltonen M, for the Seek-Medical-Attention-in-Time Study Group. Factors associated with delay admission to hospital and in-hospital delays in acute stroke and TIA. *Stroke* 1999;30:40-8.
- 18 Morris D, Rosamond W, Hinn A, Gorton R. Time delays in accessing stroke care in the emergency department. *Acad Emerg Med* 1999;6:218-23.
- 19 Bratina P, Greenberg L, Pasteur W, Grotta J. Current emergency department management of stroke in Houston, Texas. *Stroke* 1995;26:409-14.
- 20 Intercollegiate Working Party on Stroke. *National clinical guidelines on stroke*. London: Royal College of Physicians, 2000.
- 21 *Coronary Heart Disease/Stroke Task Force report*. Edinburgh: Scottish Executive, 2001.
- 22 Barer D, Main A, Lodwick R. Practicability of early treatment of acute stroke. *Lancet* 1992;339:1540-1.
- 23 Harper GD, Haigh RA, Potter JF, Castleden CM. Factors delaying hospital admission after stroke in Leicestershire. *Stroke* 1992;23:835-8.
- 24 Hacke W. A late step in the right direction for stroke care. *Lancet* 2000;356:869-70.

(Accepted 22 January 2002)

Dietary aflatoxin exposure and impaired growth in young children from Benin and Togo: cross sectional study

Y Y Gong, K Cardwell, A Hounsa, S Egal, P C Turner, A J Hall, C P Wild

Molecular Epidemiology Unit, Epidemiology and Health Services Research, School of Medicine, University of Leeds, Leeds LS2 9JT
Y Y Gong
research fellow
P C Turner
research fellow
C P Wild
professor

continued over

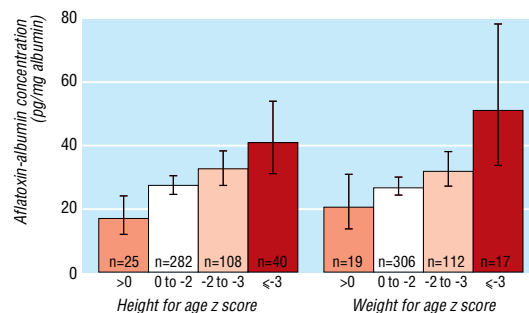
BMJ 2002;325:20-1

Fetal and early childhood environment, including the nutritional status of the pregnant mother and the infant, are considered critical for growth and risk of disease in later life.¹ Many people in developing countries are not only malnourished but also chronically exposed to high levels of toxic fungal metabolites (mycotoxins). One family of mycotoxins, the aflatoxins, are carcinogenic and immunotoxic and cause growth retardation in animals.² Aflatoxins contaminate staple foods in West Africa, particularly maize and groundnuts, as a result of hot, humid storage conditions that promote fungal growth. High exposure to aflatoxins occurs throughout childhood in the region,^{3,4} suggest-

ing that growth and development could be critically affected. We assessed exposure to aflatoxins in relation to anthropometric measures in children in Benin and Togo.

Methods and results

We studied 480 children (aged 9 months to 5 years) from 16 villages in four geographic zones (four in each zone): Sudan savannah, north Guinea savannah, south Guinea savannah, and coastal savannah. The Ministries for Health in Benin and Togo gave ethical approval, and parents gave informed consent. We determined



Concentrations of aflatoxin-albumin adduct categorised into four groups for height for age and weight for age z scores on the basis of the WHO classification of malnutrition (z score ≤ 2) and severe malnutrition (≤ 3). Geometric mean adduct concentrations are shown, with 95% confidence intervals, adjusted for weaning status, agro-ecological zone, and socioeconomic status. Height for age and weight for age z scores were significantly associated with aflatoxin-albumin concentration (trend test: $F=15.19$, $P=0.0001$, $r^2=0.3766$; and $F=8.48$, $P=0.0038$, $r^2=0.3680$).

weight for age, height for age, and weight for height z scores, according to the median value of a World Health Organization reference population. A z score ≤ 2 is classified as malnutrition, and ≤ 3 represents severe malnutrition. We also determined weaning status and the socioeconomic status of the mother and family. We assessed aflatoxin exposure over the previous two to three months by measuring aflatoxin bound to albumin in blood.³

We detected aflatoxin-albumin adducts in 475/479 (99%) samples (one sample missing), with a geometric mean concentration of 32.8 (range 5-1064) pg/mg albumin. Aflatoxin-albumin concentration increased with age up to 3 years, after which it reached a plateau. In the 302 children aged 3 years or under, the mean concentration was 2.5-fold higher in fully weaned children (45.6 pg/mg; 95% confidence interval 38.8 to 53.7) than in those still partially breast fed (18.0 pg/mg; 15.2 to 21.3). In a multivariable model adjusting for age, sex, socioeconomic status, and agro-ecological zone, weaning status was significantly associated with aflatoxin-albumin concentration ($P=0.0001$).

Prevalence of malnutrition was 33% for stunting (height for age z score ≤ 2), 29% for being underweight (weight for age z score ≤ 2), and 6% for wasting (weight for height z score ≤ 2). Children with stunting or who were underweight had 30-40% higher mean aflatoxin-albumin concentrations. After adjustment as above, the negative correlation between individual aflatoxin-albumin concentration and each of the three growth parameters was highly significant ($P=0.001$ for height for age, $P=0.005$ for weight for age, and $P=0.047$ for weight for height). In a categorical analysis, the association with aflatoxin-albumin concentration was again significant, with clear dose-response relations with height for age and weight for age z scores (figure).

Comment

This study reveals a striking association between exposure to aflatoxin in children and both stunting

(a reflection of chronic malnutrition) and being underweight (an indicator of acute malnutrition). In West Africa, people are chronically exposed to high levels of aflatoxins starting in utero and continuing throughout life.⁴ In this study, children still partially breast fed had lower exposure, almost certainly reflecting lower toxin levels in milk than in weaning and family foods. Thus growth faltering occurs at a time of change to solid foods, when there is co-exposure to aflatoxin and a plethora of infectious hazards (for example, malaria, diarrhoea, respiratory infections). Whether the association between aflatoxin exposure and impaired growth is a direct result of aflatoxin toxicity or reflects consumption of fungus affected food of poor nutritional quality cannot be confirmed from the cross sectional design. However, these observations emphasise the need to investigate this question and to develop strategies to reduce exposure to aflatoxin, possibly involving interventions targeted at the post-weaning period in African children.⁵

We thank C. Aquereburu for participating in the planning process; M. Koube, Anik Gandjeto, Zenato Assani, Marius Adjabga, and G. Ayeni from IITA Benin, who participated in the field work; and the people of Benin and Togo who agreed to be part of this research.

Contributors: YYG, KC, AH, PCT, AJH, and CPW were all responsible for the design of the study. KC, AH, SE, and AJH took part in the fieldwork. YYG, PCT, and CPW were responsible for the laboratory analysis. YYG and SE computed the data and conducted the statistical analysis. All authors contributed to writing the manuscript. CPW is guarantor for the paper.

Funding: This study was funded by a grant from GTZ (project no 98.7860.4-001.00) and support to CPW and PCT from a grant from the NIEHS, USA (no ES06052).

Competing interests: None declared.

- 1 Terry MB, Susser E. The impact of fetal and infant exposures along the life course. *Int J Epidemiol* 2001;30:95-6.
- 2 Hall AJ, Wild CP. Epidemiology of aflatoxin-related disease. In: Eaton DA, Groopman JD, eds. *Human health, veterinary and agricultural significance*. San Diego, CA: Academic Press, 1994:233-58.
- 3 Turner PC, Mendy M, Whittle H, Fortuin M, Hall AJ, Wild CP. Hepatitis B infection and aflatoxin biomarker levels in Gambian children. *Trop Med Int Health* 2000;5:837-41.
- 4 Montesano R, Hainaut P, Wild CP. Hepatocellular carcinoma: from gene to public health. *J Natl Cancer Inst* 1997;89:1844-51.
- 5 Wild CP, Hall AJ. Primary prevention of hepatocellular carcinoma in developing countries. *Mutat Res* 2000;462:381-93.

(Accepted 20 February 2002)

What is a good doctor and how can we make one?

We want your views on this for a future theme issue of the *BMJ*.

Governmental and professional regulation now operates in most aspects of doctors' lives yet doctors themselves have had little opportunity to air their views on what they think makes a good doctor or how good doctors should be made.

Contribute to this debate now by visiting our home page (bmj.com) or going direct to the debate at www.bmj.com/gooddoctor

All submissions will be published on the website and a selection of the best letters will be published in the theme issue that will be devoted to this topic in September 2002.

International
Institute of Tropical
Agriculture,
Cotonou, Benin,
West Africa
K Cardwell
research plant
pathologist
A Hounsa
public health doctor
S Egal
junior professional
officer

London School of
Hygiene and
Tropical Medicine,
London
WC1E 7HT
A J Hall
professor

Correspondence to:
C P Wild
cp.wild@leeds.ac.uk