developed countries are needed to clarify the importance of suboptimum nutrient intakes as a cause of fetal growth retardation.

M COSGROVE
Lecturer
D P DAVIES
Professor

University of Wales College of Medicine,
University Department of Child Health,
Cardiff CF4 4XN

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Raised adult blood pressure linked to failure to achieve growth potential in utero

EDITOR,—In their study of men in Uppsala, David A Leon and colleagues found that the highest blood pressures were in men who had been small babies but grew to be tall adults.¹ They argue that these babies failed to achieve their growth potential in utero. We replicated their analysis in three studies of men born in England (in Hertfordshire (in 1920-30, n = 841), Preston (1935-43, n = 239), and Sheffield (1939-41, n = 170)). Their blood pressures were measured at ages 59-70, 46-54, and 50-53 respectively. Details of the methods have been published.²⁻⁴

Table 1 shows the results for the men living in Hertfordshire, with the groups as defined by Leon and colleagues. As in Uppsala, the inverse relation between blood pressure and birth weight was stronger in men who were taller than 176 cm (the median height in Uppsala) and the highest pressures were in men who had been small babies but were tall adults. In Preston and Sheffield, however, the relation between blood pressure and birth weight was not affected by adult height. The mean systolic pressure in men who were taller than 176 cm but had weighed less than 3250 g at birth was 154.2 mm Hg (n = 31), compared with an overall mean of 153.7 mm Hg, in Preston and 140.8 mm Hg (n = 15), compared with an overall mean of 153.7 mm Hg, in Sheffield. There was no trend in systolic or diastolic pressure across the range of birth weights in taller men in Preston or Sheffield.

We agree that raised blood pressure in adult life is linked to failure to achieve growth potential in utero. However, the combination of small size at birth with tall adult height indicates failure to achieve growth potential in utero only in a setting where postnatal nutrition is optimal. This may be why the men living in the relatively affluent area of Hertfordshire yield similar results to

those living in Uppsala while those living in the industrial areas of Preston and Sheffield do not.

CATHERINE M LAW
Epidemiologist
CAROLINE H D FALL
Epidemiologist
CHRISTOPHER N MARTYN
Clinical scientist
CLIVE OSMOND
Statistician

MRC Environmental Epidemiology Unit,
University of Southampton,
Southampton General Hospital,
Southampton SO16 6YD

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Not gaining patients' consent in trials is deceitful

EDITOR,—Nicholas J Wald and colleagues say that it is reasonable to enter patients into clinical trials without their consent if what the patients receive constitutes recommended practice.¹ But this view denies such patients the right to know all relevant details about the situation in which they find themselves.² It also denies them the opportunity to choose to act altruistically by giving their consent, as is urged by those conducting trials.³ It means, too, that patients' consent to the use of personal and clinical data about them for purposes other than their diagnosis and treatment is forgone.

Deceit, however inadvertent, has serious ethical detriments. It cannot further the cause of clinical research willingly entered into as a partnership between researchers and patients.

CHARLOTTE WILLIAMSON
Vice chair

York Health Services Trust,
York YO3 7BY

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Flavonoid intake and coronary mortality

Other antinutritional factors may also have a role

EDITOR,—Paul Knekt and colleagues report an inverse association between intake of flavonoids and incidence of coronary mortality.¹ Their data also show that the protective effect of flavonoids was associated with a diet high in intake of apples and onions.¹ I would like to draw attention to a

point that Knekt and colleagues mention in their discussion: "thus it cannot be excluded that the association in the present study between intake of flavonoids and coronary mortality may be due to other substances in fruits and vegetables—for example, fibre, carotenoids, and vitamin C—or due to differences in intake of fatty acids closely correlated with high flavonoid intake."

Fruits and vegetables contain antinutrients—for example, phytic acid, saponins, tannins, flavonoids, phyto-oestrogens, and protease inhibitors—that have been found to be associated with a cholesterol lowering effect and, therefore, with a reduction in the risk of heart disease.² Pectin, cellulose, and hemicellulose, with only trace amounts of lignin, are the main components of dietary fibre from most apples.³ Pectin added to a test meal significantly decreases the rate of uptake of glucose, with a concomitant reduction in the production of insulin. In addition, supplementation with pectin lowers low density lipoprotein cholesterol concentrations without reducing high density lipoprotein cholesterol concentrations. The proposed mechanisms for the hypocholesterolaemic effect of pectin are increased excretion of bile acids and stimulation of hepatic 3-hydroxy-3-methylglutaryl coenzyme A reductase activity.³

Other important factors present in vegetables are saponins, which are amphiphilic compounds with a strong action on surface tension and properties similar to those of detergent. Onion (*Allium cepa*) saponins contain sitosterol, oleonic acid, and a triterpene alcohol, β -amyirin.⁴ These compounds become active in the prevention of cardiovascular diseases by interacting with bile acids (forming micelle-like aggregates) and with cell membranes or membrane constituents such as cholesterol, thus interfering with their absorption.⁴

I agree with Knekt and colleagues that further studies are needed to confirm the importance of flavonoids in the prevention of coronary heart disease.¹ A possible role for the above mentioned antinutritional factors may not, however, be completely ruled out as they may exert a complementary protective effect by means of distinct mechanisms.

GEMA FRÜHBECK
Research fellow

Department of Physiology and Nutrition,
University of Navarra,
31080 Pamplona,
Spain

1 Knekt P, Järvinen R, Reunanen A, Maatela J. Flavonoid intake and coronary mortality in Finland: a cohort study. *BMJ* 1996;312:478-81. (24 February.)
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Objective data trials are needed

EDITOR,—Paul Knekt and colleagues' study showing an apparent protective effect of consumption of flavonoids on the risk of coronary death illustrates the pitfalls of such investigations.¹ Intake of flavonoids shows the same association with both non-coronary and coronary mortality. It either reduces biological susceptibility to many diseases or it serves as a marker for a complex of sociobehavioural factors associated with the risk of death.

Observational studies of diet and health have two main problems. Firstly, dietary intakes are socially and culturally determined and are confounded with other exposures influencing risk of death. In a recent study showing an apparent protective effect of dietary fibre against

Table 1—Mean systolic and diastolic blood pressure (mm Hg) at age 59-70 by birth weight and height at examination among men resident in Hertfordshire

	Birth weight (g)				All men	P value for trend
	<3250	3250–	3750–	≥4250		
Height ≤176 cm	(n = 202)	(n = 245)	(n = 138)	(n = 61)	(n = 646)	
Systolic	165.5	164.2	162.2	163.3	164.1	0.12
Diastolic	90.4	90.1	88.3	89.4	89.7	0.07
Height >176 cm	(n = 32)	(n = 70)	(n = 62)	(n = 31)	(n = 195)	
Systolic	174.0	164.4	161.5	161.3	164.6	0.03
Diastolic	95.8	90.6	89.7	90.1	91.1	0.07

coronary disease there was a greater than fivefold difference in smoking across quintiles of fibre intake.² With strongly correlated exposures, each measured with some error, it is difficult to separate confounding from real associations reliably. Secondly, characteristics of the participants are associated with biased reporting of dietary intake. People seeking social approval are more likely to report dietary fat intakes that are in keeping with current guidelines, independent of their actual intake,³ and have different risks of death. Such biases may, for example, have given rise to the finding that consumption of trans fatty acids is associated with increased coronary risk in studies that use potentially biased dietary, questionnaire methods but not in studies that assess intake objectively.⁴

The situation has been well illustrated with respect to intake of β carotene. As in Knekt and colleagues' study, many observational studies have shown that consumption of β carotene seems to offer protection against coronary heart disease and death from cancer. Two recent randomised trials of supplementation with β carotene, however, show increased rather than decreased mortality.^{5,6} Yet, in both studies, subjects in the control arm with a high baseline intake of β carotene had lower rates of cancer and heart disease.^{5,6} These opposing findings from experimental and observational analyses in the same studies powerfully show the limitations of observational data.

We live in an associational world, and it is more remarkable when dietary factors ascertained by questionnaire do not, rather than do, relate to risk of disease. In these circumstances, data from randomised trials are worth more than even a large bulk of observational findings. Collecting imprecise and potentially biased measurements in large numbers of individuals is not the optimal epidemiological strategy. Greater effort should be made to obtain objective data with repeat measurements and to examine populations in which confounding between key exposures is minimal.

GEORGE DAVEY SMITH

Professor of clinical epidemiology

YOAV BEN-SHLOMO

Senior lecturer in epidemiology

Department of Social Medicine,
University of Bristol,
Bristol BS8 2PR

1 Knekt P, Järvinen R, Reunanen A, Maatela J. Flavonoid intake and coronary mortality in Finland: a cohort study. *BMJ* 1996;312:478-81. (24 February.)

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Authors' reply

EDITOR,—Controlling for confounding factors is a major problem of dietary and other observational epidemiological studies. It is always difficult to conclude whether an association is merely a correlation or a causal connection.¹ As Gema Frühbeck emphasises, we cannot completely rule out the possibility that other compounds in vegetables may also have a role in the associations that we observed. It is well known that when the association between the suggested protective factor and the disease is

weak, adjustment for potential confounding factors with low reliability may be unsatisfactory.

We believe, however, that to rely only on intervention trials, as George Davey Smith and Yoav Ben-Shlomo suggest, is not the solution. Although the issue of confounding is eliminated by randomisation in such studies, several methodological problems still remain. These are related to the duration of supplementation and follow up, the combinations and doses of supplements, and the selection of the study population.² Accordingly, inconsistent findings have been reported from two large scale intervention trials. For instance, a study of chemoprevention of cancer in Linxian found a reduction in the risk of stomach cancer among people receiving a combination of vitamin E, β carotene, and selenium,³ whereas a study of α tocopherol and β carotene in Finland showed a non-significant increased risk among smoking men receiving supplements of vitamin E or β carotene.⁴

We suggest that conclusions about a possible beneficial effect of a substance alone or in combination with other substances cannot be made on the basis of any single study or any single study design. Conclusions should be based on the complementary information from basic research, experimental models, observational epidemiological studies, and intervention trials. Thus comprehensive observational studies in different populations with different patterns of risk factors and of factors that modify the effect should still be carried out. In addition, combined data from existing observational studies should be analysed, so that small subgroups of populations and diseases of low incidence can be investigated.

On the basis of information from such studies it will perhaps then be possible to design intervention trials to provide more definitive answers about causality between dietary factors and chronic disease.

PAUL KNEKT

Head of laboratory

ANTTI REUNANEN

Head of laboratory

National Public Health Institute,
00300 Helsinki,
Finland

RITVA JÄRVINEN

Lecturer

Department of Clinical Nutrition,
University of Kuopio,
Kuopio,
Finland

JOUNI MAATELA

Chief physician

Research and Development Centre,
Social Insurance Institution,
Helsinki and Turku,
Finland

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GPs' management of acute back pain

Is evidence based

EDITOR,—Paul Little and colleagues have examined the nature of the evidence underpinning clinical guidelines on the management of acute back pain in general practice and general prac-

tioners' compliance with such guidelines.¹ I take issue with both the authors' interpretation of the published evidence and the findings of their survey.

The authors are rather nihilistic about the generalisability to general practice of several of the good quality epidemiological studies. Generalisability is always a matter of judgment, but, as a practising general practitioner and clinical epidemiologist, I prefer to adopt the approach advocated by Glasziou and Irwig.² They emphasise that generalisation that is too restrictive needs to be avoided and the question that should be asked is, "Are the patients in this study so different from my patients that I could not apply the study results?" Having used this question to examine the studies on back pain, I consider that the precise setting is, in many situations, irrelevant.

Recently, I reviewed the epidemiological evidence on the management of acute back pain in general practice. Before 1992 the Agency for Health Care Policy and Research commissioned a thorough search of English language publications; I used this as the baseline to assimilate the evidence.³ The agency's panel graded the available evidence into four categories (A (strong), B (moderate), C (limited), or D), and these categories were modified in accordance with the more recent evidence. In parallel, I also conducted a questionnaire survey among all 104 general practitioners on the Huddersfield medical list, using a well validated survey instrument. To assess the general practitioners' management of acute low back pain, I asked them to state their most likely responses when confronted with a patient presenting with acute low back pain of less than two weeks' duration, no hard neurological signs, no history of trauma, and no evidence of systematic illness. The response rate was 70%. Table 1 lists the replies in conjunction with the appropriate evidence rating.

Table 1—Number of general practitioners who said that they were likely or very likely to choose each type of management for acute low back pain, and rating of available evidence in support of choice

Management	No of practitioners	Rating of evidence
Advice on risk factors (n = 70)	67	B
Gentle activity (n = 69)	61	B
Oral non-steroidal anti-inflammatory drugs (n = 71)	58	B
Short bed rest followed by mobilisation (n = 71)	57	B
Referral for physiotherapy (n = 70)	31	C/D
Active exercises (n = 69)	26	D
Antispasmodic drugs (n = 70)	12	D

On the basis of my findings that most practice is supported by fairly strong evidence, I would conclude that the management of acute back pain in general practice is evidence based.

NICHOLAS SUMMERTON

Senior registrar in public health

Clinical Development Directorate,
Huddersfield NHS Trust,
Huddersfield Royal Infirmary,
Huddersfield HD3 3EA

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