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

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1 Barker DJP. The fetal origins of adult disease. *Fetal and Maternal Medicine Review* 1994;6:71-80.
2 Godfrey K, Robinson S, Barker DJP, Osmond C, Cox V. Maternal nutrition in early and late pregnancy in relation to placental and fetal growth. *BMJ* 1996;312:410-4. (17 February.)
3 Doyle W, Crawford MA, Wynn AHA, Wynn SW. The association between maternal diet and birth dimensions. *Journal of Nutritional Medicine* 1990;1:9-17.
4 Cosgrove M, Davies DP, Jenkins HR. Nucleotide supplementation and the growth of term small for gestational age infants. *Arch Dis Child* 1996;74:F122-5.

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.

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1 Leon DA, Koupilova I, Lithell HO, Berglund L, Mohsen R, Vågerö D, *et al.* Failure to realise growth potential in utero and adult obesity in relation to blood pressure in 50 year old Swedish men. *BMJ* 1996;312:401-6. (17 February.)
2 Hales CN, Barker DJP, Clark PMS, Cox LJ, Fall C, Osmond C, *et al.* Fetal and infant growth and impaired glucose tolerance at age 64. *BMJ* 1991;303:1019-22.
3 Barker DJP, Bull AR, Osmond C, Simmonds SJ. Fetal and placental size and risk of hypertension in adult life. *BMJ* 1990;301:259-62.
4 Martyn CN, Barker DJP, Jespersen S, Greenwald S, Osmond C, Berry C. Growth in utero, adult blood pressure, and arterial compliance. *Br Heart J* 1995;73:116-21.

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.

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1 Wald NJ, Major P, Murphy P, Parkes C, Frost C. One and two view mammography in breast cancer. *BMJ* 1996;312:509-10. (24 February.)
2 Fried C. *Medical experimentation and social policy*. Amsterdam: North Holland, 1974.
3 Baum M. The ethics of randomized controlled trials. *Eur J Surg Oncol* 1995;21:136-9.

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 amphiphylic compounds with a strong action on surface tension and properties similar to those of detergent. Onion (*Allium cepa*) saponins contain sitosterol, oleanolic acid, and a triterpene alcohol, β-amyrin.[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.

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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.)
2 Thompson LU. Phytic acid and other nutrients: are they partly responsible for health benefits of high fiber foods? In: Kritchevsky D, Bonfield C, eds. *Dietary fiber in health and disease*. St Paul, MN: Eagan, 1995:305-17.
3 Baker RA. Potential dietary benefits of citrus pectin and fiber. *Food Technology* 1994;48:133-9.
4 Velisek J. Saponins. In: Davidek J, ed. *Natural toxic compounds of foods: formation and change during processing and storage*. Boca Raton, FL: CRC, 1995:45-52.

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)					
	<3250	3250–	3750–	≥4250	All men	P value for trend
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