- All letters must be typed with double spacing and signed by all authors.
- No letter should be more than 400 words.
- For letters on scientific subjects we normally reserve our correspondence columns for those relating to issues discussed recently (within six weeks) in the *BMJ*.
- We do not routinely acknowledge letters. Please send a stamped addressed envelope if you would like an acknowledgment.
- Because we receive many more letters than we can publish we may shorten those we do print, particularly when we receive several on the same subject.

Vaccinations and professional confusion

SIR,—One of the greatest impediments to high rates of vaccination uptake is the conflicting and incorrect advice given to parents by health professionals. This has received much publicity recently,¹ and action is being taken to rectify the problem. An issue that has received less attention is the conflicting advice given to the professionals.

The entries in the Association of the British Pharmaceutical Industry *Data Sheet Compendium* for 1990-1 that relate to the only available pertussis containing vaccines state²:

The administration of pertussis-containing vaccines is contraindicated in children with a personal or family history in parents or siblings of idiopathic epilepsy or other familial or hereditary diseases of the central nervous system. Administration of pertussis vaccine is also contraindicated in children with a history of seizures, convulsions, cerebral irritation in the neonatal period, developmental neurological defect or other disorder of the central nervous system.

In 1988 the Department of Health and Social Security advice was that in children with "problem histories"³ "The balance of risk and benefit should be assessed in each case."⁴ The groups listed were children with a documented history of cerebral damage in the neonatal period; children with a history of convulsions; and children whose parents or siblings have a history of idiopathic epilepsy. The document said that such children may be at risk of developing a similar condition irrespective of vaccine. This advice was reiterated in 1990.⁴

The advice in the *Data Sheet Compendium* is now out of date and much too conservative. The advice in the *Monthly Index of Medical Specialities (MIMS)* is even worse⁵: it states that a history of severe allergy is also a contraindication. Is it any wonder that some doctors are denying children protection against this potentially fatal disease?

It is not difficult to find other examples of such contradictions. The recommended interval for tetanus boosters is now 10 years,⁴ whereas the manufacturer recommends five to 15 years² and general practitioners will be remunerated if they give boosters every five years.⁶

Smallpox vaccination will attract a fee if given to a person travelling to a country requiring an international certificate of vaccination against smallpox.⁶ In the past decade no country has made such a requirement. In the same publication paratyphoid vaccine is listed, whereas it has not been recommended by the Department of Health for some years.

As is to be expected, advice in the *British National Formulary*⁷ is consistent with that of the Joint Committee on Vaccination and Immunisation.⁴ As many doctors use publications such as the *Data Sheet Compendium* and *MIMS* is there nothing that can be done to make the advice from such sources more compatible? It is only in this way that

consistent advice will be given to parents, so avoiding the present all too common confusion.

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Fetal and placental size and risk of hypertension in adult life

SIR,—Professor D J P Barker and colleagues found that low birth weight and high placental weight independently predicted increased risk of hypertension in adulthood and suggest that this is related to intrauterine malnutrition.¹ Though low birth weight may indicate intrauterine malnutrition, it may also be a consequence of genetic factors.^{2,3} Placental weight, however, is positively associated with both birth weight and enhanced intrauterine nutrition^{4,5} and thus almost certainly does not indicate intrauterine malnutrition.

An alternative explanation for the findings is that genetic predisposition to being overweight is protective against cardiovascular disease whereas being overweight from overeating increases the risk.^{6,7} Although studies on twins show that genetic factors influence weight between the ages of 12 months and 7 years, they have been less helpful with respect to birth weight because monozygotic twins commonly have unequal access to the placenta.⁸ In 20 000 singleton births, however, weight at 7 years was highly correlated with birth weight,⁹ indicating that genetic factors considerably influence birth weight in singleton pregnancies.

Abraham *et al* found that the incidence of hypertensive vascular disease was 75% in overweight men who had been underweight in childhood but only 20% in overweight men who had been overweight in childhood.¹⁰ Similarly, the incidence was 20% in underweight men who had been underweight in childhood but zero in underweight men who had been overweight in childhood. Thus the effect of adult body mass index on blood pressure varies according to the person's weight in infancy. This compounding effect is the basis of the artefactual association between placental weight and adult hypertension.

The real importance of placental weight is that it is a marker for maternal weight.^{6,11} Babies born with large placentas are likely to have fat mothers. Maternal weight in turn influences subsequent changes in children's weight: in a Western society lean children of fat mothers tended to grow up fatter and fat children of lean mothers tended to grow up leaner.¹²

Acquired obesity and its consequences, diabetes and cardiovascular disease, are increasing in developing countries. I believe that the apparent protective effect of heaviness in infancy is genetically based and is specific to certain European populations. Any attempt to emulate this by the injudicious overfeeding of lighter infants in developing countries would increase not decrease the incidence of cardiovascular disease.

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AUTHORS' REPLY.—In stating that placental weight is simply a marker for maternal fatness Dr Bradley overlooks the strong relation between placental weight and maternal anaemia.¹ We think that discordance between placental and fetal weight reflects poor maternal nutrition. We do not agree that the lower rates of cardiovascular disease associated with greater fetal and infant growth are best explained by a hypothetical gene.² Evidence is rapidly accumulating that they are part of the long term benefits of a favourable environment in early life.³

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SIR,—Professor D J P Barker and colleagues suggest that the prevention of hypertension may depend on improving maternal nutrition.¹ Food rationing introduced in Britain during 1940-1 resulted in a more equitable distribution of food, and expectant mothers received free supplements of milk, eggs, and vitamins.² These changes were accompanied by an abrupt decline in perinatal mortality, particularly in the rate of stillbirths.³ We investigated whether the blood pressure adjusted for age of British adults born during food rationing differed from that of those born before rationing was introduced.

During 1984-5 as part of the health and lifestyle survey the blood pressure of a random sample of British adults was measured at home by automated sphygmomanometry.⁴ We analysed data on 5383 people born during 1927-66 (figure). Each year's data are based on at least 90 people. We found no discernible step around 1941-5 for either systolic or diastolic pressure.

Trends in mean unadjusted blood pressure (mm Hg) and perinatal mortality in England and Wales (per 1000 births)

Each person's blood pressure was modelled by multiple regression as a function of age (linear and quadratic terms) and the perinatal mortality rate in the year of birth. After adjustment for curvilinear effects related to age a decline in perinatal mortality rate of 10 per 1000 was associated with the following changes in blood pressure: systolic -0.3 (95% confidence interval -1.4 to 0.8) mm Hg, diastolic -0.6 (-1.4 to 0.2) mm Hg.

Whether or not the reduction in perinatal mortality during the 1940s was a direct result of wartime nutritional policy, it suggests more favourable intrauterine circumstances for babies born during the war. We found no evidence that this improvement had substantially influenced the blood pressures of today's middle aged adults.

Our analyses relate only to maternal nutrition during pregnancy and cannot assess the indirect effects of nutrition during the mother's own childhood. Nevertheless, we would be interested to know if Professor Barker and colleagues find any evidence in their data of a change in the distribution of birth weight, placental weight, or the ratio of the two among births from 1941 onwards.

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Lowering cholesterol concentrations and mortality

SIR,—Dr Matthew F Muldoon and colleagues suggest that low serum cholesterol concentration may lead to behaviour that increases the risk of violent death.¹ We examined whether plasma cholesterol concentration was related to death from violent causes in a large cohort study.

In the Whitehall study of London civil servants plasma cholesterol concentrations were measured in 17718 men aged 40-64 during 1967-9.² Follow up to 31 January 1987 showed that 90 had died because of accidents, violence, or suicide (ICD codes E800-E999, 8th revision), of whom 36 had committed suicide (ICD codes E950-E959). Including the 10 violent deaths for which no responsibility could be attributed (ICD E980-E989) in the suicide group did not appreciably alter the results.

We found no significant association between plasma cholesterol concentration and all violent deaths or death by suicide (table). Proportional hazards analyses were performed with age and plasma cholesterol concentration as continuous variables. For all the violent deaths the relative rate associated with a 1 mmol/l increase in plasma cholesterol concentration was 0.98 (95% confidence interval 0.83 to 1.16). For suicide the corresponding relative rate was 0.87 (0.66 to 1.15). Adjustment for employment grade, a marker of socioeconomic state, did not materially alter these results.

Other prospective studies have not found a consistent relation between cholesterol concentration and violent death.^{3,4} The size of our study means that it is unlikely that a large true effect has been missed. A direct behavioural effect of low cholesterol concentration might be expected particularly to affect suicide. Though the lowest rate was seen in the fifth quintile, the highest rate was in the fourth quintile and there was no consistent trend in the risk of suicide with cholesterol concentration.

Dr Muldoon and colleagues suggest that associations between serum cholesterol concentration, neuronal function, and behaviour could explain the relation between cholesterol concentration and deaths due to violence. We examined the association between serum cholesterol concentration and hostility in a second cohort of London civil servants. Hostility was indexed by the Cook-Medley hostility scale,⁵ a component of the Minnesota multiphasic personality inventory. This scale has predicted mortality due to violent causes in some^{6,7} but not all⁸ studies. The correlations between serum cholesterol concentration and hostility score were negligible, being 0.016 ($p=0.3$, $n=4246$) for men and -0.005 ($p=0.8$, $n=1742$) for women. Examination of hostility score by decile of cholesterol concentration showed

that, even at the lowest concentrations, there was no association with hostility. Furthermore, there was no relation between hostility and concentrations of apolipoprotein A or apolipoprotein B. These results were independent of employment grade.

Though some forms of aggression may be missed by using the Cook-Medley scale, our data do not support the notion that low serum cholesterol concentration has a direct effect on behaviour and in turn increases the risk of violent death. It may be more rewarding to investigate the influence of dietary changes or drugs used in the intervention studies than to focus on a possible direct effect of low serum cholesterol concentration.

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SIR,—Dr Matthew F Muldoon and colleagues have been too cautious in interpreting their results.¹ The results showed a higher total mortality during interventional treatment (albeit not significant). This was made up of a 14% reduction in mortality from coronary heart disease and a 44% increase in mortality from cancer. In addition, there was a 78% increase in mortality from causes unrelated to disease. Despite these findings they conclude that a reduction in cholesterol concentration tended to be associated with a reduction in mortality from coronary heart disease ($p=0.06$) and that there was "no consistent relation" between reduced cholesterol concentration and mortality from cancer (although the crude change in mortality from cancer was significant; $p=0.01$). They went on to "launder" the results until they found a significant effect on mortality from coronary heart disease and had eradicated the effect on mortality from cancer.

The first duty of authors is to report their results, however unpalatable they may be. Manipulation of data to explain what the authors construe as aberrant findings or exceptions should be the province of the discussion, and such discussion cannot be used as an excuse to report the principal findings as the exact opposite of what the results have shown.

In this case the authors were highly selective

Age standardised mortality/1000 person years (number of deaths) by quintile of plasma cholesterol concentration

	Plasma cholesterol (mmol/l)					χ^2 For trend (p value)
	≤ 4.11	4-73	5-27	6-05	> 6.05	
All violent deaths	0.29 (16)	0.34 (21)	0.27 (15)	0.33 (20)	0.31 (18)	0.00 (0.96)
Suicides	0.12 (7)	0.14 (9)	0.11 (6)	0.17 (10)	0.07 (4)	0.50 (0.48)