haematocrit usually falls. This may be seen in patients after admission with hypoxia, stroke, and myocardial infarction and after the cessation of smoking.

The fall in haematocrit commonly seen in these patients in the days after admission is usually attributed to the correction of dehydration. I believe this is usually an unacceptable explanation for such haematocrit changes: the total body-water deficit would need to be considerable, and clinically obvious, if this was the case; and haematocrit can increase rapidly after acute stress, the speed of which is too fast for dehydration to be an explanation. Thus haematocrit, red-blood-cell mass, and plasma volume should not be interpreted independently from cardiovascular control. Many investigators appear to view red-blood-cell mass and plasma volume as independent variables, and independent from cardiovascular control. I believe not only that this is illogical but also that there is substantial evidence to the contrary.

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JAMES P. IBSSERT


AWARENESS OF HYPOGLOCAEMIA IN DIABETES

SIR,—To continue the correspondence (Sept 26, p 748; Oct 17, p 919) about whether human insulin produces more hypoglycaemia than other insulins I report a case which illustrates the danger of inadvertent changing from one species to another even if this is from pork to human insulin. This patient, a 73-year-old woman, had been an insulin-dependent diabetic for five years. She was well controlled on 'Mixtard' and had no hypoglycaemic problems with a regimen of around 20 units in the morning and 14 at night. However, when she attended her pharmacist she was told (erroneously) that pork mixtard was no longer being made and that she should change to human mixtard. This was done and thereafter she had a series of severe hypoglycaemic attacks, some of which required the use of intravenous dextrose. The dose of insulin had not been changed nor had the site of insulin injections. It has been long recognised that patients should not be inadvertently changed from beef to pork insulin because of the danger of hypoglycaemia. Unfortunately Novo (pork) and Nordisk/Welcome (beef) appear to be encouraging a particularly dangerous practice with their withdrawal of insulins. I suspect that other pharmacists and doctors are confused by their advertisements.

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A. C. BURDEN

ORAL CONTRACEPTIVES AND BREAST CANCER

SIR,—By the courtesy of the editor of the British Journal of Cancer and the authors, the Committee on Safety of Medicines (CSM) has been able to review the paper by McPherson and colleagues which is published this week.1

This paper adds to the considerable body of knowledge which has now accumulated on this subject. At least eight substantial case-control studies in which the possible relation between oral contraceptive use and breast cancer was investigated have been published since 1980. Most of these studies, including the largest of them, the American Cancer and Steroid Hormone (CASHE) study, have provided no cause for concern. Some, however, have raised questions about a possible adverse effect of prolonged oral contraceptive use early in life.

McPherson and colleagues' paper suggests that there may be a 2.5-fold increase in the risk of breast cancer in women up to 45 years of age who have had 4 or more years of oral contraceptive use before their first full-term pregnancy. The authors point out that their data do not directly reflect upon the use of the modern low-dose oral contraceptive pills. This study found no association between oral contraceptive use after the first pregnancy and breast cancer either in women under 35 years of age or in older women. The paper by McPherson and colleagues extends the results published in a Lancet letter in December, 1983, which were fully considered by the CSM at that time.

The CSM has considered the latest results in the light of all the current evidence. The committee will continue to monitor studies still in progress but agrees with McPherson et al that the newly reported findings do not indicate the need to change at this time advice on the use of current oral contraceptive agents. Thus, the CSM remains of the view that women receiving oral contraceptives should be prescribed a product with the lowest suitable content of both oestrogen and progestagen.

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A. W. ASSCHE, Chairman


*Further details of the paper referred to are given on p 1286.—Ed. L.

6-MERCAPTOPURINE DOSAGE

SIR,—Dr Lennard and Dr Lilleyman (Oct 3, p 78) ask whether children with lymphoblastic leukaemia are given enough 6-mercaptopurine. They suggest that the drug should be administered to myelo-suppression rather than by a set dosage. Titration of mercaptopurine dosage to leukopenia has been a standard practice in some centres for decades.1 The question is whether this practice improves remission duration and cure rate. The evidence is not clear. There are no published comparative studies of mercaptopurine alone given to patients with leukaemia in more versus less myelosuppressive dosage. When administered as one component of a combination drug regimen half dosage was associated with shorter median remission duration than full dosage.2 On the other hand, the Pediatric Oncology Group found no difference in outcome for children with "good prognosis" acute lymphoblastic leukaemia in remission on mercaptopurine plus methotrexate whose white-blood-cell counts were maintained at 1500-3000/μl versus 3000-4500/μl.3 Although the hypothesis and the practice of "titration to toxicity" of mercaptopurine are reasonable their validation in patients remains to be demonstrated. However, there is another reason for titration to toxicity that does not require verification. When children with acute lymphoblastic leukaemia experience haematological relapse the physician needs to know whether it is the result of inadequate dosage of drug or resistance to drug at tolerable dosage. If the patient has been receiving maximum tolerated dosage, one can feel secure that the relapse is due to resistance rather than inadequate dosage. This knowledge is helpful both for accepting the misfortune of relapse and for planning a second attempt at cure.

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DONALD PINKEL


WHAT MAKES SOME CHILDREN SHORTSIGHTED?

SIR.—Reading ability is associated with myopia,1 and the association is specific to reading ability per se rather than to intelligence or achievement in general.2 The direction of causation is controversial: does excessive near-work of scholarship cause myopia? or do myopes choose to read and so become more scholarly?3 A biological theory argues for a non-causal association, a single pleiotropic gene causing both myopia and better reading ability.4 These hypotheses can be distinguished by examining longitudinal data. If reading causes myopia then there will be a greater cross-lagged correlation between reading at one age and myopia at a subsequent age than vice versa. With non-causal association the cross lagged correlations will be similar.


Correlation between reading ability and distance vision at ages 7, 11 and 16 in cohort of children in National Child Development Study.

Solid arrows for cross-lagged correlations indicate inferred direction of causation between reading and distance vision.

The National Child Development Study (NCDS) assessed reading in a cohort of children at ages 7, 11, and 16, using specially developed tests, and measured distance vision by Snellen chart at 6 m. Near vision was assessed at ages 11 and 16 with the near-vision test card at 25 cm. Some aspects of these data have been presented elsewhere. For the present analysis distance vision was considered in the better eye, and children without 6/18 vision in at least one eye at one age on either distance or near-vision tests were included. Myopia, defined as distance vision worse than or equal to 6/12, was present in 2.3% of 6268 7-year-olds, 4.6% of 11-year-olds, and 7.7% of 16-year-olds. The figure shows correlations and cross-lagged correlations between reading ability and distance vision at ages 7, 11, and 16. At 11 and 16 there is a negative association between reading and distance vision, an association which is reversed at age 7. There is a higher correlation between reading at one age and distance vision at a subsequent age, than vice versa (Pearson-Filon r 7–11: p < 0.001; 11–16 p < 0.001). We may infer that these data are more compatible with reading causing myopia than vice versa and that the causal influence continues beyond early childhood through into adolescence.

These results suggest that early childhood experience (up to age 7) does not cause the reading-myopia association, and that the association continues to develop into adolescence. The role attributed to unpatterned vision in early development by your Oct 31 editorial seems unlikely to explain such findings, and suggests a more direct effect of continued accommodation upon the geometry of the optic globe.

I thank the National Children's Bureau for permission to reanalyse these data and the ESRC Study Archive for providing the data.

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I. C. McMANUS


Sir,—From your editorial of Oct 31 it appears, as usual, that both nature and nurture have a part to play in the development of myopia. However, the eyes are nurtured not only by diffuse unpatterned light, as described, but also, not surprisingly, by their nutrient supply. More than 25 years ago I had the unusual opportunity to study refraction on large numbers of tribespeople in different parts of Tanzania. In one area there had been severe famine some years earlier and the subjects for examination were chosen so that they would have been in utero or infants at the time of the famine. They might thus be expected to be among those most likely to show refractive errors if malnutrition was capable of influencing the growth of the eye. Our results, summarised in 1980, were consistent with such a hypothesis. In 1960 I showed the data to Arnold Sorsby, to whom your editorial refers, at the Royal College of Surgeons in London and he remarked that he had never seen such a high rate of high myopia (over +4D) in any population, not even among the Japanese. It is probably significant in this regard that there has been a 50–70% decrease in the incidence of myopia among the Japanese in recent years. This has coincided with better nutrition and increase in height, a relation previously demonstrated in migrant Indians.

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DONALD S. MCLAREN


Sir,—On July 22, 1987, J. R. G. Turner, a geneticist at Leeds University, wrote a letter to The Times, an extract from which follows:

"The need for so many white Europeans to wear glasses—peoples from other continents have much better eyesight—probably results from the adoption of agriculture by their ancestors in the neolithic: a short-sighted farmer can live, a short-sighted hunter will starve along with his short-sighted children."

Your Oct 31 editorial does not mention racial differences in myopia. Are there hard data to support Dr Turner's suggestion?

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CYRIL A. CLARKE

Sir,—Your Oct 31 editorial asks if the prevalence of myopia is increasing. The US Public Health Service conducted visual acuity screening in urban schoolchildren in 1923–24 and in the 1960s and 1970s. There are no comparable community surveys which include retinoscopy. The familiar Snellen E chart includes the 20/70 (6/21) level, and in adolescents and young adults, corresponds to about 1.0D of myopia, a deficiency significant enough to require correction for driving and sports. In surveys of young people born in 1907–08, 1936–44, and 1949–53, 6.3%, 11.3%, and 22.1%, respectively, were 20/70 or worse in the right eye.

While visual acuity and, presumably, myopia thus appear to have been worsening over the course of the century, children born after 1949 seem especially vulnerable. These were among the first to be reared in the presence of television. Since children often view television from the floor immediately in front of the screen, a visual distance of about 50 cm, the experience would be much like reading but for much longer periods. (Among contemporary college students, who had access as children to colour television 24 hours a day, contact lenses for myopia appear almost as common as shoes.)

Your editorial also raises the question of reading as a contributor to myopia. A nineteen-state survey in 1939–40 of semiletter farm families on Federal assistance, at a time when rural electrification was just being completed, revealed that of the 15–19-year-olds, only 1.5% of males and 2.3% of females were 20/70 or worse in the "better eye". These percentages suggest the lower limits of myopia in young people who read very little if at all.

While the cause of myopia remains a puzzle, the predominant use of the eyes in childhood, whether for farming and hunting or for reading and television, appears to play an important role.

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5. Green M, Vauxley JB. Physical impairment of members of low-income farm families: 11,490 Persons in 2,477 farm security administration borrower families, 1940. Publ Health Rep 1944; 59: 1163-85.