country of the corresponding authors' affiliation. However, we noted a high scientific output related to cardiovascular disease in 80% (20 of 25) of DME and a low output from developing countries and DEEC. Previous studies on the geography of biomedical publications in general,[2] and of mental health[3] and HIV/AIDS[4] associated publications have reported similar findings.

Fragile research capacity, inadequate financial investment, language barriers, and exclusion of journals edited in developing countries from MEDLINE[5] are some of the factors that probably contribute to this situation. The poor research productivity of developing countries is both a consequence and a contributory factor for the widening gap between the health of the rich and the poor, and indicates the generally weak capacity of developing countries in all areas of non-communicable disease policy, advocacy, legislation, and strategy. Urgent action at global and national levels is needed to narrow this gap.

*S Mendis, D Yach, R Bengoa, D Narvaez, X Zhang

Cardiovascular Disease Program, WHO, Geneva 27, Switzerland
(e-mail: Mendiss@who.int)

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A warning about the dangers of chuna packets

Sir—Chuna (calcium hydroxide) is popularly consumed as an additive to chewing tobacco in India. Various companies have started to market the additive in easy-to-carry pouches, which are available for as little as 1 Rupee (about 2 US cents). We draw your readers' attention to a grave and previously unknown threat posed by these pouches.

In the past year, we have seen seven children, aged 3–8 years, with acute ocular alkali burns, leading to severe visual loss, caused by these packets of calcium hydroxide. The problem is that children view the pouches as toys; when squeezed hard, the calcium hydroxide paste squirts out of the packet, much like playing clay. However, if the packet bursts suddenly, chuna is sprayed around and can enter the conjunctival fornices, where the paste gets stuck and is difficult to remove. A careful search after double eversion of the upper eyelids is needed to find and remove the particles of calcium hydroxide.

Calcium hydroxide damages the ocular surface, including the cornea,[1] and a corneal limbal stem-cell transplant is often needed to restore the corneal epithelium.[2]

We feel the public should be warned about the dangers of these seemingly harmless chuna packets.

*Tushar Agarwal, *Rasik B Vajpayee*

RP Center for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi 110029, India
(e-mail: rasikvajpayee@rediffmail.com)

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Nutrition and immune function: a 1992 report

Sir—In 2001, Ranjit Kumar Chandra reported that a daily nutritional supplement, which he has patented, greatly improved the cognitive performance of elderly individuals.[1] The improvements seemed large, and some of the standard errors were statistically impossible.[2] This anomaly led us to examine a *Lancet* article[3] based on the same study, which reported large improvements in immune function and a halving of days of infection.

Here too we found problems. First, table 3 of the article gives the average values of eight immunological measures for the supplement (S) and placebo (P) groups. For each measure, it gives two p values: one for $S_{12}-S_0$ (S_{12} and S_0 being the values at 12 and 0 months, respectively), and one for $(S_{12}-S_0)-(P_{12}-P_0)$. If the two changes (from S_0 to S_{12} and from P_0 to P_{12}) are in the same direction, the second p value must be greater than the first. But in all six cases for which the changes were in the same direction and for which p values were reported, the second p value was smaller than the first. Second, the SDs of the number of days of infection of the two groups are 5 and 7 according to the text, but histograms indicate values of about 17 for each. One of us wrote to Chandra about this, but received no reply.

The article states that "all individuals approached enrolled in the study". In our experience, this has never happened. Chandra's study required blood sampling and a year of biweekly visits. The article also states that all 96 participants "were middle class". If the participants were randomly sampled from the population this outcome is unlikely even if the fraction of the population that is middle class is very high. If a population is 95% middle class, and sampling is random, the probability that 96 persons sampled will all be middle class is less than 0·01.

We have no conflicts of interest to declare.

*Kenneth J Carpenter, *Seth Roberts, Saul Sternberg*

Departments of Nutritional Sciences (KJC) and *Psychology (SR), University of California, Berkeley, CA 94720, USA; and Department of Psychology, University of Pennsylvania, PA 19104, USA (SS)
(e-mail: roberts@socrates.berkeley.edu)

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Author's reply

Sir—The comments by Kenneth Carpenter and colleagues are inaccurate and irrelevant. The *Lancet* 1992 paper was based on a randomised controlled trial whose design and statistical methods had been submitted to the journal before the study began. The manuscript was reviewed by three referees and two statisticians consulted by *The Lancet*; they were provided with the relevant raw data and their suggestions were incorporated into the third and final version that was published. The paper has been commended by experts in the field, providing "hard evidence based on a well-designed prospective trial whose results when considered in the context of the basic and intermediate endpoint clinical data now available are biologically credible",[1] and has been referred to as a "landmark study".[2]

The typographical error resulting in my use of SE instead of SD was acknowledged and published in *Nutrition*. I communicated this fact to Seth Roberts and Saul Sternberg in a letter, which they acknowledged but now deny having received. There are other inaccuracies in Carpenter and colleagues' letter. The age data are

available for the city census, and it is common knowledge that individuals approached to take part in a research study in a small community such as St John's (where I was the only clinical allergist and immunologist) invariably agree to take part and there are few dropouts. The biweekly visits for gathering morbidity data and many of the blood collections were made at the individuals' homes, causing no inconvenience to them. The middle socioeconomic stratum was chosen deliberately to minimise the effect of poverty on nutrient intake. There is often more than one valid method of statistical analysis that generally leads to the same broad clinical conclusions. The inaccurate and somewhat out-of-context comments made by Carpenter and colleagues suggest they did not read the original *Lancet* article completely and carefully.

I received the patent for the multinutrient 4 years after publication, and have derived no financial benefit from it.

Ranjit Kumar Chandra

Case Postale 111, CH-3963 Crans-sur-Sierre, Switzerland
(e-mail: nutres2002@yahoo.com)

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Fatal drowning of children in whirlpool baths in Japan

Sir—Japanese people have traditionally bathed in extremely hot water. In the past few years, whirlpool baths have become popular and, by 2000, about 400 000 whirlpool baths had been sold in Japan. However, fatal accidental drowning in these baths has become a nationwide problem. In 2000, 3429 people, including 38 children younger than 10 years, drowned in whirlpool baths. A recent fatal accident in a whirlpool bath highlights the need to prevent drowning of children in Japan.

A healthy 6-year-old Japanese girl had been bathing alone in a whirlpool bath when her hair became trapped in the suction intake and could not be released. After 15 min, the girl's mother found her with her head beneath the water and her hair trapped in the suction intake. Although the mother cut the girl's hair and removed her from the water, she was in cardiopulmonary arrest. Despite aggressive resuscitation attempts, she was pronounced dead and forensic investigation showed the cause of death was drowning.

The police investigated this accident; when they placed a hairpiece near the suction intake, they saw that it was immediately sucked in and could not be pulled out by a force of 10 kg. According to an investigation by the Ministry of International Trade and Industry of Japan, in December, 2000, two 7-year-old girls and one 6-year-old girl had died in similar accidents.

To prevent such accidents, the National Consumer Affairs Center of Japan requested that manufacturers of whirlpool baths install covers on all intakes to prevent hair from being trapped. Furthermore, they warned customers not to allow young children to bathe unattended. After this warning, no similar accidental drownings have occurred.

**Masahito Hitosugi, Hitoshi Kawato, Kazumi Matsushima, Toshiaki Nagai, Shogo Tokudome*

Department of Legal Medicine, Dokkyo University School of Medicine, Tochigi 321-0293 Japan
(e-mail: hitosugi@dokkyomed.ac.jp)

Early postnatal undernutrition in preterm infants and reduced risk of insulin resistance

Sir—Atul Singhal and colleagues (March 29, p 1089)[1] propose that early postnatal undernutrition in children born preterm could have beneficial effects on insulin resistance later in life. However, this notion conflicts with the Barker hypothesis and that proposed by Ong and Dunger,[2] which indicates that perinatal growth failure leads to obesity, insulin resistance, and cardiovascular disease in adults.

Although the published works reviewed by Ong and Dunger[2] refer to infants born small for gestational age as a result of intrauterine growth retardation, we believe that preterm newborns could be thought of as exteriorised fetuses. When pronounced postnatal growth deceleration occurs in these exteriorised fetuses, they become smaller at term-equivalent post-conceptional age than their term-born peers. This situation might be analogous to small for gestational age in term newborns.

Associations between birthweight and disease-risk markers, such as insulin resistance, are apparent from childhood, especially when low birthweight is followed by rapid postnatal weight gain and childhood obesity.[2] However, insulin resistance has also been documented in children born small for gestational age who did not achieve catch-up growth as compared with short normal-birthweight controls.[3]

Singhal and co-workers[1] used weight velocity at 2 weeks' postnatal age and body-mass index at adolescence as surrogates for overall somatic growth. Without data on the growth in head circumference as well as length in the early postnatal period, and the height attained in adolescence, the overall somatic growth and the presence or absence of postnatal growth deceleration and subsequent catch-up growth and adiposity remain unknown. Since catch-up growth often takes place during the first few years of childhood, diet beyond the neonatal period is likely to exert a greater effect on catch-up growth. The association between weight velocity at 2 weeks of age and insulin-resistance in adulthood is fascinating.

It is noteworthy that the fasting 32–33 split proinsulin concentration in the adolescents born preterm, fed nutrient-enriched diet, and with greater weight gain at 2 weeks of age was not statistically different from that of the healthy term-born control group—ie, insulin sensitivity of the adolescents born preterm and fed nutrient-enriched diets was normal as in controls. By contrast, the lower fasting 32–33 split proinsulin in the adolescents born preterm and fed the lower-nutrient diets would seem subnormal, given that fasting glucose and insulin concentrations were not significantly different between the groups.

Since proinsulin is converted to insulin in vivo, the proinsulin/insulin ratio, together with glucose tolerance test, could yield additional information—eg, an increased proinsulin/insulin ratio could suggest impairment in proinsulin to insulin conversion as is associated with ageing.[4] Conversely, a decreased ratio could suggest more efficient conversion in the presence of insulin resistance, as reported in some children.[5]

Because rapid somatic growth takes place during the last trimester of gestation, early neonatal under-nutrition is difficult to reconcile with long-term benefits in preterm infants. We would argue that nutritional management needs to achieve normal growth variables and a normal body composition without increasing the risk of type 2 diabetes in adulthood.

**Melinda Y Yeung, John P Smyth*

*Department of Pharmacy, Liverpool Hospital, Liverpool, New South Wales, Australia (MYY); Trevor Mann Baby Unit, Royal Sussex County Hospital, Brighton, UK (JPS)
(e-mail: melinda.yeung@swsahs.nsw.gov.au)

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