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Acanthamoeba keratitis and contact lens wear

SIR—Nigel Morlet and colleagues (Aug 9, p 414)[1] describe the increasing incidence of contact-lens related acanthamoeba keratitis in patients at Moorfields Eye Hospital, London, and suggest that a unique combination of circumstances in the UK may explain the unusually high incidence of the disease relative to other developed countries. They suggest that the domestic water-supply systems may be a source of acanthamoebae that contaminate contact lenses and their storage cases. Acanthamoeba cysts are impervious to inorganic chlorine at up to 50 parts per million,[2] and they may be incorporated in the biofilm within water pipes and on contact lenses. Corneal isolates have been shown to be indistinguishable from those of the domestic water supplies and storage case.[3] However, the prevalence of acanthamoeba in domestic water sources and its contribution to the aetiology of acanthamoeba keratitis have not been assessed in other regions of the world.

We treated the first case of contact-lens associated acanthamoeba keratitis in Hong Kong in 1993, and have subsequently seen five further cases at our hospital. In a recent case, we examined domestic water supplies at the patient's home. We examined his contact lenses and carrier cases, samples of domestic water, and swabs from the hand basin and bath at his home. We observed acanthamoeba cysts by light microscopy on the contact lenses, and obtained positive cultures from the lens and carrier cases only. Subsequent examination of domestic water samples and swabs from the hand basin and bath from homes of ten members of our laboratory staff did not yield any evidence of acanthamoeba.

Our findings highlight the need for further investigation of domestic water supply as a potential risk factor for acanthamoeba infection. The supply of domestic water in the high-rise buildings typical of Hong Kong often comes from a tank located on the building's roof, suggesting that the risk factor of domestic water may also be important in Hong Kong. Reports suggest that acanthamoeba keratitis is an emerging disease in south and east Asia[4] where there has been an increase in the use of contact lenses.[5] With substantial cultural, social, environmental, and climatic differences between Asia and elsewhere, we believe studies to determine risk factors for this disorder are a matter of urgency.

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Iodination of irrigation water and infant mortality

SIR—Robert DeLong and colleagues (Sept 13, p 791)[1] suggest that iodine supplementation of irrigation water in areas of severe iodine deficiency reduces infant mortality, the effect being more pronounced in the neonatal period. However, the evidence for an effect is weak; the data suggest a sudden fall consistent with the exact timing of the intervention in only one area, which does not have the lowest baseline urinary iodine.

Bakechi was the least iodine-deficient area; addition of potassium iodate (PI) to irrigation water in 1993 coincided with a reduction in neonatal mortality from 63·7 per 1000 births during the years preceding the intervention (1988–92) to 36·9 per 1000 births in 1993–95 (relative risk [RR] 0·58 [95% CI 0·38–0·86]). A similar fall was recorded in the Bakechi control area, but it occurred earlier (from 54·6 per 1000 births in 1988–89 to 35·4 in 1990–95).

In Long Ru, the most iodine-deficient area, repeated addition of PI to one canal over 2 years (1992–93) did not lower neonatal mortality, which showed no significant change between 1988–92 and 1993–95 (26·2 and 19·9 per 1000 births, respectively, RR 0·76 [0·18–2·42]). If 1992 is reassigned as an intervention year, the rates before and after the intervention are 23·0 and 26·5 per 1000 births, respectively.

Finally, in Tusala, neonatal mortality fell from 23·0 to 6·4 per 1000 births between 1992 and 1993 (RR 0·28 [0·07–0·87]), 1 year before the introduction of PI to the irrigation canal and 2 years after the introduction of iodised-oil capsules to pregnant women and children in 1990–91.[2]

DeLong and colleagues also use logistic regression, comparing rates before and after intervention (as above), and allowing for an overall trend and for the control areas. This method shows a significant effect in Tusala, but ignores the problem to which we allude—the numbers of deaths falling sharply a year before the intervention. One cannot obtain the statistical significance of the PI effect in the other areas from table 2, but logistic regression for each area separately, which we carried out, shows no significance for them. The effect difference between Bakechi and Tusala is significant in table 2, showing non-uniformity by area, although results are equivocal for both when compared with Long Ru.

One therefore cannot draw firm conclusions. In studies without random allocation of interventions to treatment and control groups, interpretation is greatly aided by use of a greater range of outcomes. Support for an association would have been enhanced if trends in more immediate outcomes, such as dietary or urinary iodine, or sheep production and income, were shown to be consistent with the timing of the intervention. The declining birth rates in all areas (significant at p=0·01) are only one indication of fundamental changes this society is undergoing, which may be unrelated to the intervention.

The outcome measures were economical to measure. A community randomised controlled trial, with power to detect a realistic effect,[3] would enable iodinisation to be assessed unequivocally with only these outcomes. It would give more certain inference for these outcomes alone, but other

outcomes would be needed for a deeper understanding.

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SIR—The study by Robert DeLong and colleagues[1] shows that correction of iodine deficiency may have a major effect in reducing infant mortality. Their findings lend support to the WHO's efforts to make iodine one of the two micronutrient deficiencies (the other being vitamin A) that requires action on an international scale.

It is salutary that, almost a century ago, McCarrison[2] carried out a similar trial, the results of which are pertinent to the study reported by DeLong et al. McCarrison was convinced that endemic goitre was attributable to faecal contamination of the drinking water, and carried out a controlled trial at the Lawrence Military Asylum (later the Lawrence Royal Military School), in the Punjab, which was in what was then North India. Goitre was prevalent among both the boys and girls attending the school and McCarrison intervened by treating the water supply with a chemical antibacterial agent. As male chauvinism was not politically incorrect at that time, it was the water to the boys' school that was treated while the girls' school acted as the control. The trial proved a success, goitre prevalence decreased among the boys but not the girls and lent support to McCarrison's thesis that faecal contamination was the root cause of the goitre. However, the chemical treatment of the water supply was with a mixture of potassium iodine and potassium iodate. Nevertheless, McCarrison argued that it was the antibacterial effect of the iodine and not its thyroidal effect that led to the reduction of the prevalence of goitre. Some years later he supported this interpretation by a comparison with children attending a sister school, the Lawrence Memorial Royal Military School, at Lovedale in the Nilgiri Hills of South India.[3] (These observations have a particular poignancy for me because I attended both the Lawrence schools as a child, albeit some years after McCarrison carried out his experiments.)

In regions where infant mortality is high, one of the important causes of death is diarrhoeal disease. Is it possible that some of the fall in infant mortality noted by DeLong can be attributed to chemical decontamination of the water or was the quantity of iodate added to the water too low to allow this explanation? Could McCarrison and DeLong et al both be correct in their disparate interpretations? Bacterial contamination of the water is thought to bind the iodine, making it unavailable for absorption, and the fall in infant mortality may be due, in part, to a reduction of diarrhoeal disease.

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Authors' reply

SIR—With respect to C Ronsmans and T F de C Marshall, analysis of each township separately sacrifices power relative to the full model used in our analysis. The effect of iodination on neonatal and infant mortality in Tusala is highly significant, as is that effect when data from all townships are combined. Tests of the other two townships separately do not show a significant effect of treatment. For Long Ru, this is not surprising; with the smallest population and so few deaths in any year, even a large true effect of treatment would probably be swamped by stochastic effects. As we noted, the apparent effect of iodination in Bakechi is smaller than in Tusala; indeed, it is not statistically significant. A smaller effect would be expected there, since Bakechi is the least iodine deficient of the towns studied. There may be a real but more modest effect, but with a sample size too small to show this clearly. Clearly, variations in early mortality over time and among the townships involve more than iodine availability. As we noted, mortality in Bakechi was much higher than in the other towns, and that difference cannot be attributed to iodine deficiency. Other determinants of mortality may have changed over the period examined, and may have changed differentially in the communities. The secular decline in mortality in Bakechi seems somewhat steeper than in Tusala, and this may help to obscure, statistically, the effect of iodination.

Despite the heterogeneity in response, the demographic and physiological data support a substantial effect of iodination on early mortality in this region.

Intermediate outcomes have been published elsewhere.[2] They show increased iodine in soil, crops (five-fold), animal thyroid glands (three-fold), and urine of women of childbearing age (median rose from <10 to 55 μg/L during 3 years in Long Ru); sheep production grew because of decreased neonatal mortality, with a 5% increase in mean family income due to animal sales alone; mean height, weight, and head circumference increased in children aged 2–6 years in the 3 years after iodination. We agree that these factors strengthen the association with decreased infant mortality, and allow a deeper understanding of the outcome.

The declining birth rates may well indicate changing conditions; but may also relate at least in part to the fall in infant mortality (lower early mortality results in longer birth intervals and lower fertility, mainly because infant deaths truncate the period of postpartum infecundity.

Differences between the scope of our study and that of Cobra and colleagues[2] should be emphasised: these workers randomised for individual iodine supple-mentation 617 infants age 6 weeks, who were followed to age 6 months. Our intervention encompassed townships during 3 years, surveying 14 806 births; it was also a controlled trial, controls being contiguous villages entirely comparable with the treated areas.

The description by P O D Pharoah of McCarrison's intervention is fascinat-ing. In our work, iodine concentrations in irrigation water increased only during the 2 weeks of dripping and were too low to be bactericidal.[3]

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