Dr Wharton Comments:

We thank Dr deSa for his interest and also acknowledge the useful comments sent to us by other doctors. Dr deSa makes a number of points. He agrees with our conclusion of a 'need to describe an Asian population with details of their subethnic structure' but takes us to task for not subdividing the population further than we did. We accept this criticism but would point out that many obstetric and paediatric papers concerning Asian immigrants in Britain have not made any subdivision at all. We certainly did not automatically classify mothers of the Islamic faith as Pakistanis and all Hindus/Sikhs as Indian. As Dr deSa infers religion does not always indicate geographical origin. Various boundary changes have occurred and at partition the people had some time to decide on which side of the boundaries they would reside—for example a Punjabi may come from Pakistan and be Moslem, or from the Indian Punjab, where the major religion is Sikhism. While a Gujerati generally comes from Gujerat State in India and is a Hindu (Hindu is a Persian word meaning Indian) parts of Pakistan, (a predominantly Moslem area) are also called Gujerat.

Regarding our Indian patients we commented that interpretation of secular changes was difficult and that any further studies should be in a centre with more Indian births than Sorrento. However, other information is available. One third of our Asian patients come from India (compared to a national average of 46% Asian births to mothers coming from India) about equally divided between Sikhs from the Indian Punjab and Gujerati Hindus from Gujerat itself.

We agree with Dr deSa’s reference to religious differences and eating taboos. We have commented elsewhere on the different dietary patterns of the 4 subethnic groups attending Sorrento (Pakistani Moslem, Punjabi Sikhs, Gujarati Hindus, Bangladeshi Moslems), and detailed observations of their food customs, recipes used, and nutrient analysis are in press. Briefly, there were the expected major differences in food practices between the different religious groups, for example Moslems not eating pork, Hindus not eating beef, but nevertheless we often found that meals eaten by Moslems from different parts of Pakistan showed as much variation as the difference between some Moslem and Sikh or Hindu meals. Using the weighed and recall method of dietary assessment we found that the pregnant Pakistani mothers consumed less food during the second trimester than the Gujerati, Hindus, and Punjabi Sikhs attending the hospital.

We explained why 1978 Pakistani and Bangladeshi mothers were 'lumped together' and commented that the results from the Pakistani mothers were also analysed separately but this led to no change in the conclusion drawn. Few Bangladeshis (8% of our Asian patients) attend Sorrento anyway.

We are uncertain whether Dr deSa suggests that our Pakistani patients should be divided into 4 subgroups. He will probably know that people from the Indian subcontinent who come to this country tend to retain their identity by congregating in smallish groups according to place of origin, kinship, and religion. Pakistani mothers attending Sorrento come almost exclusively from a small area of north east Pakistan—Mirpur (Azad Kashmir) and the Pakistani Punjab. The secular increase in birthweight therefore, is very unlikely to be due to a genetic change in the population. Environmental factors must play an important role.

It is too easy to claim that a larger series, presumably multicentre, would solve the problem. The numbers would be larger but standardisation would be more difficult and more importantly, geographical spread of maternal origin would probably be wider.

An explanation of the context of this study may help to clarify the position. It was one of a series describing the problems of the Asian mother and her baby at Sorrento, which reached the following conclusions. Babies of similar gestational age, born to Asian mothers at Sorrento are lighter than those of European mothers of similar height and parity. Many of these light babies have anthropometric and biochemical changes suggesting intrauterine marasmus (reduced skinfolds and raised plasma triglyceride in cord blood) and they are therefore unlikely to be small normals. In view of the secular increase in birthweight of Pakistani babies their lighter weight is unlikely to be due to genetic factors alone; environmental factors operating before and during the pregnancy play an important role (this study). One environmental influence during pregnancy is under-nutrition. Food customs and observed food intakes (on average only 1700 kcals per day, which is less than many civil servant mothers eat in Pakistan) might easily lead to nutritional stress. Mothers of light babies have anthropometric evidence of nutritional stress—reduced deposition of fat in the second trimester—and in these stressed mothers (but not others) a protein energy supplement improves birthweight.

References


D J DeSa
Children’s Centre, General Hospital, 700 William Avenue, Winnipeg, Manitoba R3E 0ZE

Correspondence 567
Loperamide toxicity in severe protracted diarrhoea

Sir,

We read with interest the paper by Sandhu et al. on loperamide in severe protracted diarrhoea¹ paying particular attention to the doses they used. In an earlier paper² they reported using doses of loperamide of up to 4 mg/kg with impressive results, and in this one, although 5 out of the 6 children described received less than 1 mg/kg/day, I was treated with 3.8 mg/kg/day. We should like to report the case of an infant age 4 months with severe diarrhoea caused by a short bowel syndrome who exhibited signs of central nervous system toxicity when treated with such a dose of loperamide. We believe this to be the only account of such toxic effects following a course of loperamide in this therapeutic range.

This infant had necrotising enterocolitis in the neonatal period necessitating resection of the greater part of his ileum. An anastomosis between the proximal and terminal small intestine left 38 cm of small bowel measured from duodeno-jejunal junction to ileocaecal valve. Loperamide was prescribed first at 6 weeks of age at a dose of 6 mg/day increasing to 18 mg/day over the next 10 weeks. It had little effect on the volume or frequency of the infant's stools which were watery, offensive, and passed 7 to 11 times per day. His weight was 4.5 kg at 16 weeks.

One week after a dosage of 18 mg/day had been reached the infant became hypothermic, peripherally 'shut off', and grey and suffered a generalised convulsion lasting 3 minutes that was controlled with intravenous diazepam. After the convulsion he remained irritable and subconvulsive with increased muscle tone in all limbs, brisk tendon reflexes, and writhing movements when disturbed. Both pupils were constricted, the anterior fontanelle soft, his temperature 35.5°C, respiratory rate 20, and pulse rate 90 per minute. Full biochemical and bacteriological screens were negative. He was treated with intravenous gentamicin, fluocoxacillin, and metronidazole for 3 days, and given a single intravenous dose of pyridoxine 12 hours after the convulsion. Oral loperamide was stopped. For 24 hours after the convulsion he was irritable, subconvulsive—especially when disturbed, hypothermic, and unwell, but he made a full recovery and has had no further convulsions since withdrawal of loperamide. He is now 9 months old, has 1 to 2 bowel actions per day, and is growing well on oral Wysoy and a mixed lactose free diet. He is developmentally and neurologically normal with a weight of 6.4 kg.

In 1981 Friedli and Haenggeli described a 4 month old infant who suffered opiate like toxic effects, reversed by naloxone, after a single accidental overdose of 10 mg (3 mg/kg) loperamide³ and the signs exhibited by our infant were similar to those described. The dose of loperamide taken by our patient at the time of his convulsion was 4 mg/kg/day, actual body weight. We suggest that caution should be observed when prescribing loperamide in this dosage range, and that opiate like poisoning be included with ileus as a potential adverse effect of loperamide.

References


L T Weaver, S W J Richmond, and R Nelson
Children’s Clinic, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP

Dr Sandhu and co-workers comment:

We were interested to read the letter of Weaver, Richmond, and Nelson, and agree that the symptoms in the patient that they describe were probably caused by the high doses of loperamide used. As we have previously stated, the drug should be used with caution particularly in sick infants.

There are, however, a number of points which should be borne in mind. First, in patients with life threatening protracted diarrhoea loperamide can be dramatically effective. Secondly, over 95% of an oral dose is metabolised during its 'first pass' through the liver and this process renders the drug virtually non-toxic to the central nervous system. Thus in theory loperamide in large doses could be toxic in patients with liver dysfunction, and in this context it would be important to know whether liver function was impaired in the patient reported by Weaver et al. Thirdly, since loperamide is an