and achieve better results than the officially appointed health professionals. Many of the health targets set for 1990 were achieved without incurring the expense of providing a new water supply, additional food, or new sanitation methods—the total cost of the project being about Rs 6 per head per year.

The Mandwa project also showed that the interest of the health professional does not always coincide with the interest of the people. The professionals prefer to retain power over the local people and keep medical treatment shrouded in mystery. Moreover, it seems that few trained health workers, however well intentioned, can discriminate between education and intelligence and hence establish a rapport with the local people.

Perhaps the reason that the Mandwa experiment and other similar projects remain isolated experiments that have had little impact on the health service of India lies in the opposition from the people who hold the power in rural communities. Resistance to anything that changes the status quo is considerable.

This seems the only explanation for the fact that almost four decades after independence half the population in India remain below the poverty line, 30 of every 1000 children who are born die within the first year, and diseases that can be prevented and controlled continue to take their toll. It may also explain why, despite there being a school in every village, about 60% of the population (75% of women) are illiterate. This is profoundly important for the link between female literacy and health is clear: in

Bihar and Uttar Pradesh where female literacy is 14%, the infant mortality rate is 177. By comparison, in Kerala female literacy is 65% and the infant mortality rate is 42.

Sadly even well intentioned doctors see health as an isolated problem rather than as a subsystem of the social, economic, and political structure of the country. Even with the best of intentions most voluntary agencies with their purely humane approach often help to create an even greater dependence among those whom they serve.

The Mandwa experiment may either be seen as a failed community health project or as an experiment that shows that simple knowledge and technology can help poor people to overcome their fears and develop self reliance. Before health can be improved appreciably, however, education, especially of women, must be improved. Furthermore, the economy must be developed and the political will generated to effect change.

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Clinical Topics

Immunisation of preterm infants

We received this letter from Dr S Lingam and colleagues in the Department of Child Health, Redbridge Health Authority, Children's Centre, Barkingside IG2 6YG, and asked four people to respond to it.

The value of routine immunisation against diphtheria, pertussis, tetanus, and poliomyelitis is well known.^{1,2} At present in the United Kingdom primary immunisations are started at age 3-4 months, but there are no firm guidelines for the timing of the first injection in preterm infants. We therefore asked paediatricians with special interest in the care of the newborn to state their own practice.

The British Association for Perinatal Paediatrics allowed us to send questionnaires to its members asking them to state their current practice in immunising preterm infants. We sent out 167 questionnaires and received 105 (63%) replies.

The results showed that 33 (31.5%) recommended that immunisation start at 3-4 months, making no allowance for the preterm birth; 39 (37%) recommended immunisation after full correction for the preterm birth—that is, 3-4 months after the expected date of delivery; and 33 (31.5%) recommended immunisation after half correction for the preterm birth.

The American Academy of Pediatrics states that: "DPT (diphtheria, pertussis, and tetanus) and OPV (oral poliovirus vaccine) can be administered to prematurely born infants at the appropriate chronological age. If the infant leaves hospital at 2 months of age both DPT and OPV can be given on discharge or at 2 months of age."³

A study of antibody response in preterm infants immunised at 2 months against diphtheria, pertussis, and tetanus showed that protective antibody levels were not produced until after the second injection.⁴ Thus early immunisation is important. There was no

increase in side effects; only 15% of preterm babies needed antipyretics compared with 54% of term infants, and no convulsions, collapse, or apnoea were seen. The preterm infants were given the standard dose of 0.5 ml of diphtheria, pertussis, and tetanus vaccine.

A second study showed that after the second injection with diphtheria, pertussis, and tetanus vaccine 100% of preterm infants developed antibody to diphtheria, tetanus, and pertussis, and the incidence of side effects was again low.⁵ It thus seems that preterm infants can safely have their first immunisation from 8 weeks after birth without correction for preterm birth, and immunisation for them should start at 3-4 months, as for babies born at term.—SUNDARA LINGAM, CHRISTINE MILLER, JANE PATEMAN, and RICHARD BEAVER.

A consultant epidemiologist

When answering questions on immunisation from colleagues I have been impressed by the lengths to which they will occasionally go to find either a contraindication to giving a routine vaccine or some reason for putting it off. If we are to attain "Health for All" by the year 1990 it is important that we do not allow spurious contraindications to interfere with achieving the high vaccination rates required in infancy. Although I tend to encourage vaccination if at all possible, the issue of prematurity has found me unusually vacillatory. The evidence suggests that chronological age is more important than gestational age for antibody response, but the guidelines of the Department of Health and Social Security¹ and the World Health Organisation² do not give guidance on the issue. As 5-10% of babies are preterm or of low birth weight even in this country, the problem may be a sizable one. Because the chances of

an infant acquiring diphtheria, polio, or tetanus in this country are remote, the only reason for giving diphtheria, pertussis, and tetanus and polio vaccines at the usual time in preterm children would be for pertussis. Hence if a whooping cough epidemic were imminent or in progress I would advise immunisation against diphtheria, pertussis, and tetanus and polio starting at 3 months of age, especially as a preterm infant would be at special risk of a serious complication from whooping cough. At other times a correction for preterm birth could be made. The small studies by Bernbaum and others, which have been quoted by Dr Lingam and colleagues, should reassure me that the counsel to those advised to vaccinate without adjusting for prematurity has a scientific basis.⁵

Nevertheless, there are several possible reasons now for advocating immunisation of preterm infants without allowing for gestational age. Postponing vaccination, even for a month or two, runs the risk of the parent not bringing the child back, whereas if the infant is still in hospital when the first dose of vaccine is due one could take advantage of this. Moreover, the interesting finding in the papers quoted of lower preimmunisation concentrations of IgG antibody, which may in part explain the decreased side effects of the first dose of vaccine in the preterm infants (but not of subsequent doses), suggests that the preterm infant is more vulnerable to these infections, pertussis in particular, than the full term infant. It is, however, possible that the immunity acquired by the infants whose final antibody levels were measured, in the quoted papers, only two months after the third dose might not be as persistent as that in the full term infants, and a longer period of follow up with more subjects might be appropriate before firm conclusions are reached about routine immunisation against diphtheria, pertussis, tetanus, and poliomyelitis in premature infants.—NORMAN NOAH

A professor of child health and a community paediatrician

Since July 1983 it has been the policy in the neonatal units in Nottingham to recommend that all preterm infants start their immunisations at 3 months after the actual date of delivery rather than the expected date. If the infant is still in the unit and is well the first triple immunisation is given in the unit at 3 months, or as soon as possible after this. Contraindications as suggested in the Department of Health and Social Security memorandum are taken into consideration. The first polio immunisation is given on the day of discharge to avoid any risk of passage to other infants. If the infant leaves the unit before 3 months a comment is made in the discharge summary, encouraging the start of the immunising schedule at 3 months and stating whether or not we consider that there are any neonatal contraindications to pertussis vaccine.

These decisions were based on the evidence that infants are able to mount satisfactory immune responses soon after birth, and there was no reason to suppose that preterm infants would be any less capable of this at 3 months of age. We are concerned, like the authors, that preterm infants are particularly at risk from pertussis infection. In order to confirm that this immunisation schedule provides a satisfactory response, however, we are currently studying a group of preterm infants and are particularly interested in the very immature (that is, under 30 weeks' gestation). These very immature infants may have limited immunological competence, but they are also more vulnerable to the infection. Their immune responses are being measured after the third triple injection (or diphtheria and tetanus) and again before their preschool booster. We were encouraged by the results reported by Bernbaum and others.⁵—DAVID HULL and CONNIE PULLAN

A consultant paediatrician

Dr Lingam and colleagues advance a strong case for the immunisation of preterm infants at 3-4 months of postnatal age, quoting recent literature from the United States. I remain unconvinced, however, about the immunological response to vaccination in infants with very low birth weights, especially those who have received prolonged intensive care. The publication cited states that

"the mean birth weight and gestation was 1320 g and 31 weeks respectively, and all the babies were in a stable condition at two months of age when immunisation was commenced."

In my neonatal intensive care unit many very low birthweight infants remain unstable for longer than two months and are smaller and of earlier gestation than in this series. There is little information available on the effects of prolonged neonatal intensive care, with frequent pulmonary infections and often several blood transfusions, on the maturation of the immune system. To be certain that all babies respond adequately more extensive studies are needed, consisting of immunisation of a cross section of infants with varying severity of illness and at different postnatal ages.

Although many infants of 28-30 weeks' gestation have an unremarkable postnatal course and could, according to the literature cited, be given immunisation at 3-4 months of age, I cannot recommend this as routine. The organisation of a system where some very low birthweight infants are immunised against diphtheria, pertussis, and tetanus at 3-4 months and others who have been particularly ill receive it later would be confusing. In Tower Hamlets, as in most districts, immunisation is carried out at infant welfare clinics, and for various reasons the postnatal course may not be known at the clinic. Notification of birth, however, ensures that gestation is known. I now recommend that babies of 32 weeks' gestation or more receive diphtheria, pertussis, and tetanus vaccine at 3-4 months of postnatal age, whereas those of less than 32 weeks' gestation have their first injection delayed by one to two months—that is, half correction for preterm birth. Thus I believe that the possible immunological disadvantage of immunising a previously very sick infant should recede, and this is a simple method to administer.

I would like to emphasise that I consider it essential that preterm infants are protected against pertussis, and recommend it for all infants except those who have obvious evidence of severe brain damage.—R J HARRIS

A clinical lecturer in paediatrics

The confusion over the timing of immunisations for preterm infants, highlighted by Dr Lingam and colleagues, is symptomatic of the confused state of childhood immunisations in the United Kingdom. We greatly need a body with the authority of the American Academy of Pediatrics, whose "Red Book" on paediatric infection has become the unofficial guide to immunisation

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policies in the United States. Hopefully, the new British Paediatric Association and Joint Committee on Vaccination and Immunisation (BPA/JCVI) Liaison Group, chaired by Sir John Badenoch, which first met in July 1985, will achieve this authority.

There is little evidence on which to base policies about the immunisation of preterm babies. Indeed, immunisation of term infants is started at 3 months largely on empirical grounds. Immunisation at or soon after birth is unsatisfactory, probably because of interference by maternal antibodies.^{7,8} Antibody production improves with age, but protection against pertussis is required before 6 months as it is infants under this age who are most at risk.

Preterm infants will receive less maternal antibody than term infants, so there may be less interference with endogenous antibody production. Neonatal antibody production is thought to depend more on exposure to antigen than on maturity, as preterm infants immunised on their expected date of birth produce higher titres of antibody than term infants immunised at birth.⁹ Studies suggest that preterm babies will produce antibodies after the second immunisation if immunisation is started two months postnatally.⁵ The problem with assessing the response to immunisation against pertussis is that none of the antibodies measured against various pertussis antigens has been correlated with protection, and clinical studies are needed.

In the absence of such studies our policy in Oxford is to immunise preterm babies from 3 months postnatally. This policy is in line with the Red Book recommendations and also with the views of the BPA/JCVI liaison group; we recognise that it is based on limited evidence.—DAVID ISAACS

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Lesson of the Week

Acute adrenal crisis precipitated by thyroxine

V FONSECA, R BROWN, D HOCHHAUSER, J GINSBURG, C W H HAVARD

It is well recognised that in patients with pituitary insufficiency thyroid hormone replacement without concomitant adrenal steroid replacement may precipitate an acute adrenal crisis.¹ It is less widely appreciated that similar problems may arise during treatment of primary myxoedema if the patient also has unrecognised or subclinical adrenocortical disease. We report on two patients with primary hypothyroidism in whom thyroxine replacement precipitated an acute Addisonian crisis.

Case reports

CASE 1

A 47 year old woman had presented elsewhere three years previously with a history of lethargy. No clinical or biochemical abnormality had been detected. Her symptoms persisted, and two years later a low serum thyroxine concentration and a raised serum thyroid stimulating hormone concentration were recorded. Plasma urea and electrolyte concentrations were normal. She was prescribed thyroxine 50 µg daily, increasing to 100 µg after two weeks, but felt ill and dizzy, lost weight, and stopped taking the

An unfavourable response to treatment with thyroxine in cases of unequivocal hypothyroidism may reflect the coexistence of another, underlying condition

thyroxine, attributing her symptoms to it. Over the next few months she was seen by several doctors; low serum thyroxine and raised serum thyroid stimulating hormone concentrations were found each time, and she was advised to resume taking thyroxine. Initially she took it only intermittently because it made her feel unwell within a few days, but eventually, because of repeated medical persuasion, she took it continuously for two months. During this period she became progressively more unwell, lost 10 kg in weight, and was confined to bed, unable to cope with daily activities; menstruation, however, continued. She then stopped taking thyroxine and was referred to this hospital.

On examination she was thin and pale; there was no pigmentation of the cheek or skin. Secondary sexual characteristics were well preserved. Her blood pressure was 110/70 mm Hg both recumbent and standing. Systemic examination did not elicit any abnormality. Investigation showed: plasma urea concentration 8 mmol/l (48 mg/100 ml) (normal range 4-7 mmol/l; 24-42 mg/100 ml), sodium 137 mmol(mEq)/l (138-145 mmol/l), potassium 4.4 mmol(mEq)/l (3.6-4.8 mmol/l), and glucose 5.1 mmol/l (92 mg/100 ml). Blood was taken for estimation of serum concentrations of thyroxine and thyroid stimulating hormone, and an adrenal stimulation test was performed using tetracosactrin 0.25 mg intramuscularly.

During the next two weeks she felt increasingly unwell and restarted taking thyroxine 100 µg daily of her own accord. Two days later she was admitted to hospital as an emergency. Her pulse rate was 100 beats/min and her blood pressure 90/60 mm Hg. Plasma urea concentration had increased to 10.5 mmol/l (63 mg/100 ml) and potassium to 5.1 mmol/l while sodium

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