clined to insignificant levels in nine-month-old infants in all population groups, is, to say the least, a highly irresponsible one. Wide variations in this regard are to be expected. A blanket public-health policy of combining vaccinations with vitamin A administration cannot be justified on the basis of such loose assumptions.

**OTHER STUDIES**

It may also be recalled that other authors had earlier reported that simultaneous massive dose vitamin A administration along with immunisation (even where live vaccines were not involved) had conferred no special advantage from the immunological point of view. Thus Brown et al. found that large doses of vitamin A failed to enhance antibody response to tetanus toxoid in children. Bhashkaram et al. found that with DPT, adequate antibody response to antigenic challenge could be obtained even in sub-clinically deficient vitamin A children, without vitamin A administration; and had argued that "vaccination programmes in poor communities with widespread vitamin A deficiency could still achieve the expected beneficial results" in the absence of vitamin A administration.

These authors saw no special advantage in combining immunisation with massive dose vitamin A administration. They considered the marginal increase in antibody titres following on vitamin A administration in these subjects as possibly of no "functional significance in terms of additional benefits to the host". On the other hand, these authors found in the same subjects who had received massive doses of vitamin A with DPT, a significant decrease in salivary S_9, and had speculated that "large doses of vitamin A could be having some adverse effect on the epithelium of the mucosa". While the validity of this speculation remains to be proved, this could possibly explain the reports of increased mortality from respiratory diseases in children who had received massive doses of vitamin A^2. Certainly these reports, to say the least, are by no means supportive of the policy of combining massive dose vitamin A administration with EPI.

Incidentally, while Semba et al. at long last chose to investigate the question of the possible effect of massive doses of vitamin A on immunological response, no attempt has been made thus far to address the other doubt I had raised regarding the possibility that retention of vitamin A following on a massive dose might be poorer when it is administered along with EPI, than when given independently.

**FONTANELLE BULGING**

It may be relevant at this point to draw attention to yet another side-effect of massive vitamin A dose administration in early infancy. De Francisco et al. had observed that nearly 12 per cent of infants given 50,000 IU in early infancy had developed fontanelle bulging following vitamin A administration. Later they showed that even with a lower dose of vitamin A (25,000 IU), this phenomenon was observed. Drawing attention to the possible dangerous implications of this finding I had said:

"One-third of infants in South Asia are of low-birth weight to start with and show signs of psychomotor deficits at birth. Our attempt must be to help them overcome these initial handicaps. Subjecting these poor infants to repeated episodes of increased intracranial tension could contribute to further retardation of their brain development. A significant part of the overall development of the brain takes place in the post-natal period. It has been estimated that as many as 6,000 to 10,000 synaptic connections between neural cells, which determine behaviour and overall mental development, take place in early infancy.

"Before any procedure is recommended for adoption, especially on a public health scale, its safety must be established beyond reasonable doubt. We have no studies whatever on the effects of repeated episodes of raised intracranial tension on the development of the brain in the post-natal period, especially in infants who start their lives with psychomotor deficits as a result of intrauterine growth retardation.

"It is quite possible that careful studies could show that infants who had been subjected to massive dose administration in early infancy and who had shown bulging of fontanelles as a result, exhibit evidences of retardation with respect to some aspects of brain development in their childhood.

"It is strange that a wholly unnecessary procedure, the safety and validity of which has not been adequately tested and proven, and which could undermine the confidence of poor communities in EPI, is sought to be promoted."

Thus far, this warning has also been ignored; fontanelle bulging following on massive dose vitamin A administration in early infancy in a considerable proportion of infants (a third of whom are low-birth-weights to start with) has been sought to be dismissed as of no consequence! Indeed it is being claimed in total disregard of the basic principles of Physics (Pascal's Law) that fontanelle bulging does not reflect pressure on the brain!

It is to be hoped that a conscientious group of scientists will address this issue also with the same competence and objectivity as Semba et al. had done with respect to the question of impairment of immune response following on vitamin A administration. Even without this, on the basis of current evidence, and on the basis of practical logistic considerations, combining vitamin A administration with EPI (a programme of proven value) is an imprudent and potentially harmful procedure.

**COMMENT**

It is an accepted axiom in medical and public-health practice that new procedures and new drugs should be first subjected to carefully controlled trials and their safety should be established beyond doubt, before they are recommended for general use.

Here, however, is an instance where this sequence was blatantly reversed! Recommendations for the general use of an untested procedure and the actual implementation of such recommendations had preceded the safety test. The test here had been undertaken long after the recommendations were implemented, and only after doubts and fears about the procedure were repeatedly raised — possibly in the hope of allaying doubts and assuaging fears. It has, however, turned out that the test had served to confirm the fears and doubts that had been expressed.

While Semba et al. deserve to be complimented on the objectivity of their effort and on having publicised their results widely, the fact remains that several thousands of normal poor children in Asia and Africa had been subjected to an untested procedure which
on the basis of the present evidence was unnecessary, undesirable and potentially harmful.

It is reasonable to expect that many of the thousands of unfortunate infants whose response to immunisation could have been impaired because of the simultaneous administration of vitamin A, might indeed have suffered greater morbidity and many more might have died in their childhood due to lack of adequate immunological protection despite vaccination, as compared to the fortunate ones who had 'escaped' the vitamin A administration misadventure. The 'international experts' who had advocated and pushed this untested programme on poor developing countries, taking advantage of their weak, vulnerable and pliable health administrations, bear a heavy responsibility in this regard and must answer for this. Equally to blame are the gullible health agencies of those developing countries which were too heavy handed and dubious 'advice' of interested 'external advisors', much to the serious detriment of their own children. In the event that any child which had received the polio vaccine in its infancy along with a massive dose of vitamin A happens to develop polio, despite vaccination, the blame would rest squarely on the shoulders of the national and international groups who had advocated and pushed for combining vitamin A administration with vaccination. The victims and their families will be legally entitled to adequate compensation.

All this raises serious ethical issues and leads to the unfortunate suspicion that children of poor developing countries are being used as human guinea pigs by groups funded (directly or deviously) by powerful pharmaceutical interests of the First World for their commercial benefit, with the covert support and connivance of some international agencies (both of the 'true-blue' and 'self-styled') varieties. Most certainly, unethical adventures of this kind would neither have been permitted nor indeed even attempted in First World countries.

The credibility of international agencies once looked up to as the guardians of peoples' health stands seriously eroded. The 'guardians' of yesterday now need to be guarded against!

To conclude: EPI is a programme of proven life-saving value. On the other hand, vitamin A deficiency is by no means a major public-health problem in infancy. Evidence points to the conclusion that massive dose vitamin A administration in infancy could at best be of doubtful value and possibly potentially harmful especially when combined with EPI. Under the circumstances it will be immoral to continue to combine EPI with massive dose vitamin A administration.

The message to the massive vitamin A dose lobby is loud and clear: Hands off EPI! Hands off infants!

References