susceptibility to thromboembolism seems likely to be established within the first few months. Obviously it is important to know if there is a critical period of a few months (for argument's sake, between 24 and 36 weeks after commencement, corresponding to the critical period during pregnancy) after which the incidence of thromboembolism falls abruptly, or if the risk remains at the same level throughout the period of taking the pill (full allowance being made for age-dependency). In other words, if the 10 cases of thromboembolism occurring within 6 months of starting the pill are disregarded, do the remaining 16 cases constitute a significantly high incidence of the disease? Drs. Vessey and Doll's comments on this point would, I feel sure, be welcomed.—I am, etc.,

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Phenylketonuria

SIR,—Your leading article entitled "Screening Tests for Phenylketonuria" (16 March, p. 656) opens with the statement that "detection and treatment of phenylketonuria early in infancy can prevent severe and permanent intellectual impairment." This opinion, and also the underlying assumption that hyperphenylalaninaemia is incompatible with normal mental development, should be kept open, for some ambiguities must still be resolved.

As you point out, recent challenges of the efficacy of dietary treatment have been contested by E. S. Brown and H. A. Waisman[1] and by M. E. O'Flynn and D. Y. Y. Hsia.[2] However, Brown and Waisman do not cast doubt on the existence of phenylketonuria without mental retardation; and O'Flynn and Hsia, while recommending dietary treatment, emphasize that "the therapeutic value of the low-phenylalanine diet remains to be proved by means of a control study."

Concerning your statement that "atypical phenylketonuria," as described by L. I. Woolf *et al.*,[3] requires dietetic treatment in infancy, I should like to mention that both cases described by Woolf *et al.* showed normal mental development during infancy without treatment. One continued normal into adulthood; the second had epileptic seizures, starting at the age of nine years.

In regard to legal requirements of mass screening for phenylketonuria in the United States, the Children's Bureau[4] announced in November 1966 that 37 States had enacted legislation, with Connecticut starting its programme on 1 January 1966. Since these laws are aimed at prevention of mental retardation, they may well exert some legal pressure toward dietary treatment. Thus control studies of therapy must consider legal as well as ethical restraints. In spite of growing evidence for the need for further study of the indications and the efficacy of dietary treatment, the opportunity for evaluation may well have passed in the United States.

Recent reports underscore again the variability of biochemical and clinical manifestations in phenylketonuria, and the possible hazards of the diet.[5–7] Reversible retardation of growth and motor and mental development, epilepsy, and hypochromic anaemia have occurred during dietary treatment, and some fatal outcomes have been reported. In the light of these facts action should not freeze further research, and legislation should allow for evaluation and review.—I am, etc.,

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Intramuscular Injections

SIR,—The subject of the optimum site for intramuscular injections is of great importance, so it is as well that from time to time various points of view continue to be expressed. I am sure few, if any, will disagree with Mr. W. H. Beesley (13 April, p. 116) that the lateral aspect of the thighs should always be used in preference to the buttocks or the deltoid. I think, however, those who have been subjected to a prolonged period of intramuscular injections at frequent intervals will disagree that there is usually less discomfort in the thigh than in the buttock. I would say the buttock is by far the more comfortable site. It is true if the injection is given into the thigh the patient does not have to sit on the site, but on the other hand repeated injections under the tight fascia lata may lead to stiffness of the muscles and pain on flexing the knee.

The point in writing this letter is not to disagree with the optimum site of injection, as I am sure the thigh should be routinely used, but to point out that in my experience it is not correct to say the thigh is less uncomfortable than the buttock, and that there are occasions when the buttocks may have to be called into play if intramuscular injections are required for any length of time. If, then, nurses cease to be taught the correct technique of injections into the buttock and the dangers stressed, when the occasion arises when such an injection has to be made both the nurse and patient will be at a grave disadvantage.—I am, etc.,

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SIR,—In a letter to you (27 April, p. 241) Professor S. D. Rubbo and Dr. Joan F. Gardner mention the use of skin preparations such as tincture of iodine or 0.5% chlorhexidine in 70% alcohol before injections, as they "will effectively destroy vegetative contaminants and assist the removal of any spores." However, this is not so in practice, as I have shown.[1] In this paper I showed evidence that at best "virtual" sterility could be produced in 15 seconds, but that the average time between swabbing and injection was about five seconds.[2] According to Lowbury[3] the maximum temporary reduction in the number of organisms detectable on the skin is approximately 80%, whatever method is used, although Price[4] and Story[5] obtained a complete kill of all skin flora after 30 seconds' swabbing. The mechanical effects of swabbing are also discussed, and no good evidence found that they are of benefit in producing sterility.

By all means avoid the buttock for intramuscular injections of adrenaline or colloidal iron, but I do not believe that swabbing of the skin as normally performed will make any injection in any way safer. I have dispensed with routine skin preparation before all injections for several years now, with no ill effects, and would commend this practice to be adopted universally.—I am, etc.,

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Birth Asphyxia

SIR,—In the article on respiratory disorders in newborn infants (27 April, p. 228) the use of intravenous sodium bicarbonate was recommended for the correction of severe metabolic acidosis. It was implied that oral administration was unsuitable because of slowness of onset of effect and the dangers of regurgitation and inhalation. While the intravenous route should be used wherever possible, circumstances may render this impracticable—for example, in domiciliary practice when the doctor is not immediately available.

We are carrying out studies to compare the efficacy of oral and intravenously administered sodium bicarbonate, and preliminary results suggest that a useful degree of correction can be obtained within one hour by the oral route. In some cases the administration of oral sodium bicarbonate has been followed by almost complete correction of severe metabolic acidosis within three hours of birth despite evidence of impaired respiratory compensation. The oral dose (approximately 1 mEq/lb. (500 g.) bodyweight of sodium bicarbonate) appears to be well tolerated and there has been no significant regurgitation. Further studies are in progress, but meanwhile we think it is perhaps too early to dismiss the use of the oral route altogether.

Incidentally, the dose of 10 ml. of 5% sodium bicarbonate recommended in the article would contain 6 mEq and not 12 mEq as stated. Our results suggest that 10 ml. of 5% sodium bicarbonate—that is, 6 mEq—gives an adequate initial correction in the full-term infant.—We are, etc.,

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*** A dose of 10 ml. of 5% sodium bicarbonate would contain 6 mEq and not 12. —ED., *B.M.J.*