indicate that the individual concerned is consuming milk, though it is possible that high titres may indicate a greater consumption of cow's milk. If this is the case, this should be verifiable experimentally. The true inference of the study may be that an increase in the prevalence and severity of M.I. is associated with a greater consumption of cow's milk.

On this continent respiratory and gastrointestinal disorders in babies are often due to untoward reactions to cow's-milk proteins. Similar reactions to cow's milk can often be detected in parents and siblings.[7] For this reason I have made a practice, when taking histories of babies suspected of having cow's-milk sensitivity, of asking the parents whether other members of the family consume large quantities of milk, for such individuals not uncommonly have similar symptoms to the baby's. I also ask whether any member of the family refuses to drink milk, since such individuals are naturally spared symptoms present in the affected child. Analysing responses, I was surprised to find that an aversion or even hatred of milk is relatively common in mothers, being present in over 20%, whether or not the child itself is upset by milk.[8] By contrast, 8·7% of fathers and 3·7% of siblings dislike milk. It seems, therefore, that some time between childhood and child-bearing, many women on this continent take an aversion to cow's milk. In the not too distant past, when air stewardesses served nothing stronger than coffee, tea, or milk to their passengers, I sometimes asked stewardesses which was the preferred drink of their passengers. I was repeatedly told that men chose milk while women preferred coffee. It may well be that this aversion to cow's milk by many women plays a part in their relative freedom, when compared with men, from M.I., and possibly also to their increased longevity. Is there a corresponding difference in attitudes towards milk on the part of men and women in England?

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DIET AND CORONARY HEART-DISEASE

SIR,—In one of his lectures to the American Philosophical Society, Sir Peter Medawar[9] quoted the story of the Reverend Sydney Smith, a famous wit, who while walking with a friend through the narrow streets of old Edinburgh came upon two housewives having a furious argument from high-up windows on opposite sides of the street. "They can never agree," said Smith to his companion, "for they are arguing from different premises."

In his letter (June 29, p. 1340) Sir John McMichael gives several references in support of his view that dietary-induced increases in serum-lipids play no role in the pathogenesis of coronary-artery disease. However, none of the authors whom he quoted were quite as ready to reject the evidence in favour of the lipid hypothesis as he appears to be. Thus, although Stehbens[10] considers that hæmodynamic factors play a major role in the pathogenesis of human arteriosclerosis, he acknowledges that this does not exclude the possibility that dietary and serum lipids influence lipid accumulation in the arterial wall. Blumgart et al.[11] stated that their results did not disprove the role of cholesterol in the production of atherosclerosis but simply demonstrated that hypothyroid-induced hypercholesterolæmia was not in itself sufficient to produce coronary atheroma. And although the National Heart and Lung Institute Task Force on Arteriosclerosis[12] did not recommend a single, major national study in the general population of the U.S.A., it did recommend the continuance of smaller, well-controlled clinical trials to determine whether lowering of blood-lipids by diet or drugs would result in a decreased incidence of clinical disease. It also proposed that intensive efforts be made to identify individuals with hyperlipoproteinæmia, who are at high risk from vascular disease.

The truth will eventually out, but this is more likely to be achieved sooner rather than later if there is objective discussion of all the available evidence. Surely is it not time that those involved in the clinical management of coronary-artery disease and those interested in the pathogenesis, detection, and possible prevention of atheroma quit their respective premises and start a constructive dialogue?

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THE BRAN HYPOTHESIS

SIR,—No hypothesis on diverticular disease can be complete without mention of bowel infections, in addition to roughage and sugar, as mentioned by Dr Yellowlees (June 22, p. 1282). At the same time as the consumption of sugar has risen since 1815, so the incidence of bowel infection has gone down in this country while it still remains high in most of the underdeveloped countries. It also affected our troops who were stationed in those countries during the war. Many of those who were stationed in the Middle East or India for any considerable time during the war have never had to take a purgative since then. On the other hand, these individuals have lived on the typical diet of Western Europe. They would serve as a useful control group to show whether it is essential to have large amounts of roughage in one's diet, whether sugar plays an important part, or whether diverticular or other diseases which are said to be due to low roughage content of the diet are less frequent in those who have suffered from chronic dysentery during their war service.

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TRANSFUSION OF FRESH BLOOD IN THE NEWBORN

SIR,—Dr Baum and others (June 8, p. 1162) strongly advocate small replacement transfusions of fresh blood for infants with respiratory-distress syndrome. Use of members of the hospital medical and nursing staffs as a "walking donor" programme for such patients also has achieved a degree of popularity in this country. Although acknowledging a degree of empiricism in their espousal of this form of transfusion, the authors' promotion of this procedure is based on the need of the newborn for freshly drawn blood to improve tissue oxygenation.

Such "walking donor" programmes invariably remove control of transfusion of blood and blood components from the transfusion service of the hospital. As a result, appropriate pretransfusion compatibility testing often is waived, hepatitis testing of donors may be performed only sporadically, and necessary records cannot be maintained. Moreover, use of the syringe transfusion method precludes the convenient preparation of red blood-cells (packed cells), the component most needed by such infants.

The Committee on Standards of the American Association of Blood Banks has reviewed such programmes from the

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8. Gerrard, J. W., MacKenzie, J. W. A., Goluboff, N., Garson, J. Z., Maningas, C. S. *Acta pædiat. scand.* 1973, suppl. 234.
9. Medawar, P. B. Induction and Intuition in Scientific Thought. London, 1969.
10. Stehbens, W. E. *Proc. R. Soc. B*, 1974, **185**, 357.
11. Blumgart, H. L., Freedberg, A. S., Kurland, G. S. *Am. J. Med.* 1953, **14**, 665.
12. Arteriosclerosis: Report by National Heart and Lung Institute Task Force; 1971, vol. II.

standpoints of patient needs and patient safety. It must be appreciated that blood anticoagulated with C.P.D. will maintain suitable levels of 2,3-diphosphoglycerate for at least the first week of storage. Furthermore, use of such relatively fresh blood drawn into integral transfusion sets in a closed system permits preparation of requisite volumes of red blood-cells for the infant and thereby provides more effective improvement of tissue oxygenation per volume transfused. Such blood will be no less beneficial to the patient in terms of needed coagulation factors than freshly drawn blood. Should the infant manifest deficiency of labile factors, such as factor VIII or platelets, treatment with specific components is required.

It is strongly recommended that replacement transfusion of these infants can be accomplished safely and effectively through techniques which comply fully with the widely accepted standards.[1] This implies that the hospital blood bank or transfusion service administer the examination and selection of the donor, withdrawal of the donor blood, performance of necessary pretransfusion tests, and storage of the blood in the laboratory until the time of the transfusion. This ultimately will be of greatest benefit for the patient.

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KVEIM REAGENT

SIR,—Your editorial (June 15, p. 1205), which stated that the Kveim-Siltzbach test remains a "safe simple outpatient technique for segregating sarcoidosis from other confusingly similar granulomatous disorders", raises premature hopes, because Kveim antigen is not available for clinical use in most parts of the United States. Moreover, Finland [2] has suggested that the U.S. Food and Drug Administration would not be justified in approving clinical use of the Kveim test reagent "because of the difficulties in preparing, standardizing, preserving, and uniformly replicating and monitoring the specificity . . .". On the other hand, mysteries concerning the immunology of sarcoidosis appear to be rapidly unfolding, and enthusiasm for the investigative use of Kveim antigen should not be dampened.

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THE MEGAVITAMIN SCENE

SIR,—Shortly after reading the Dialogue (June 15, p. 217) we encountered an interesting clinical finding caused by heavy self-administered vitamin therapy.

One of us examined a visitor from the United States who appeared to be quite healthy but his urine was of an unusual vivid yellow colour. It caused a cloudy greenish-yellow reduction of Benedict's solution, but testing for glucose by 'Clinistix' was negative. These findings suggested the presence of some reducing substance other than glucose. Inquiry then revealed that the patient had been taking a 1 g. effervescent tablet of ascorbic acid daily for some two years as a prophylactic against colds. Biochemical examination showed that the urine contained 158 mg. of ascorbic acid per 100 ml. After cessation of ascorbic-acid consumption for 4 days, the patient's urine was of a normal pale straw colour and the ascorbic-acid content had fallen to approximately 0·09 mg. per 100 ml. or probably not more than 0·2 mg. per day.

The patient was advised that his money was quite literally going down the drain and that there was no sound evidence that ascorbic acid prevented the catching of colds. Josiah Coleman was said to have made his fortune from the mustard left on people's plates, and the ascorbic-acid manufacturers must equally benefit from the discriminating excretory powers of the human kidney.

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PENICILLINASE PRODUCTION BY HAEMOPHILUS INFLUENZAE

SIR,—Several of your correspondents have referred to the occurrence of ampicillin-resistant *Hæmophilus influenzae*.[1-4] Often this resistance is difficult to detect and marked variations are reported in the concentrations of antibiotics needed to inhibit these resistant strains. We have further examined some of the strains of *H. influenzæ* isolated during the study carried out to determine the prevalence of resistant strains.[5] It is apparent that the minimum inhibitory concentration (M.I.C.) of ampicillin required for resistant strains is higher than for sensitive strains, but considering the problems of ensuring a uniform inoculum and the exacting growth requirements of *H. influenzæ* there can be overlap of concentrations for sensitive and resistant strains.

The strains of *H. influenzæ* examined were isolated in Stafford. The production of penicillinase was tested for using an inoculum equivalent to a 3 mm. colony emulsified in 0·2 ml. of benzylpenicillin at 10,000 units per ml. in 0·05 *M* phosphate buffer pH 6·5. Penicillinase activity was detected using the starch iodine tube decolorisation technique of Foley and Perret.[6] Of the 16 strains tested as possibly ampicillin-resistant strains, 5 were producing penicillinase. In Stafford M.I.C.s were found to range from 1·0 to 2·0 μg. per ml. for non-penicillinase producers and 2·0 to 16·0 μg. per ml. for penicillinase producers. In London the ranges were 0·125–1·0 μg. per ml. and 2·0–4·0 μg. per ml. respectively. Thus there was an overlap of M.I.C.s in the Stafford results and only a small difference between the two groups when tested in London.

There may, of course, be mechanisms of resistance other than penicillinase production, but it seems that a simple test for penicillinase production may be more clear-cut than determination of M.I.C.s of penicillins against *H. influenzæ*.

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AMPICILLIN-RESISTANT HÆMOPHILUS INFLUENZÆ MENINGITIS

SIR,—We were very interested in the letter from Dr Thomas and his colleagues (Feb. 23, p. 313) reporting meningitis caused by ampicillin-resistant strains of *Hæmophilus influenzæ* type b, because we had seen a patient with this condition a few weeks previously.

A female infant of six months was admitted to hospital with signs of meningitis some ten days after an upper-respiratory-tract infection. Lumbar puncture revealed a cloudy cerebrospinal fluid from which *H. influenzæ* was isolated. On routine sensitivity testing on chocolate agar, no zone of inhibition could be detected around a 2 μg. ampicillin disc, although some inhibition of growth was noted around a 10 μg. disc. Dr D. C. Turk kindly confirmed the ampicillin resistance, reporting a minimum inhibitory concentration of between 4 and 6 μg. per ml., and that the strain belonged to type b.

1. Standards for Blood Banks and Transfusion Services. American Association of Blood Banks, 1974.
2. Finland, M. *in* Controversies in Internal Medicine, II (edited by F. J. Ingelfinger and others); p. 360. Philadelphia 1974.

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2. Turk, D. C. *ibid.* 1974, i, 453.
3. Clymo, A. B., Harper, I. *ibid.*
4. Price, E., Boswell, P. A. *ibid.* p. 937.
5. Williams, J. D., Cavanagh, P. *ibid.* p. 864.
6. Foley, J. M., Perret, C. J. *Nature*, 1962, **195**, 287.