	Control Group		Treated Group		P
	No.	Mean ± S.E.M.	No.	Mean ± S.E.M.	
Total anuric period (diuresis <100 ml/day) (days) ..	19	10·58 ± 1·14	21	8·43 ± 1·66	>0·2*
Total oliguric period (diuresis <500 ml/day) (days) ..	17	15·59 ± 1·77	17	11·94 ± 1·26	>0·05*
No. of dialyses	22	6·09 ± 1·15	20	5·50 ± 0·72	>0·5†
Time to reach spontaneous decrease of blood urea (days)	22	22·05 ± 2·41	19	19·53 ± 1·69	>0·2*

*Student's *t* test.
†Mann and Whitney test.

differences between the two protocols utilized. (1) They used higher doses of frusemide—2,000 mg in repeated daily doses until dialysis became unnecessary. (2) It is not stated in their series whether patients treated with frusemide were similar to the controls in all respects—for example, aetiology and severity; were the two patients with obstructive uropathy and acute glomerulonephritis in the treated or control group? (3) What was the mode of randomization? The very disparate numbers of patients treated with frusemide (39) and without (19) during the second period (1969-72) is disturbing, particularly if "treatment was allocated on an alternated patient basis." As suggested a few lines below this statement, the explanation for this difference is perhaps that some patients were excluded from the control group because they had received frusemide before referral to the hospital. If so, the two groups become dissimilar and cannot be submitted to further statistical evaluation.

Since the results of our strictly randomized study do not confirm a beneficial effect of frusemide in established acute renal failure, we do not agree with the conclusions reached by Dr. Cantarovich and his colleagues.—We are, etc.,

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Correction of Serum Calcium Measurements

SIR,—It will not be long before the clinicians at this hospital read the two articles on the above subject (15 December, p. 640 and p. 643) and ask when I intend to correct my serum calcium measurements for the patient's serum albumin level. This will put me in somewhat of a dilemma. For a measured serum calcium of 8·0 mg/100 ml and a serum albumin level of 3·8 g/100 ml corrected calcium level, according to Dr. E. M. Berry and his colleagues (p. 640), would be 8·7 mg/100 ml, yet according to Dr. R. B. Payne and his colleagues (p. 643) it would be 8·2 mg/100 ml. Should I therefore give them both corrections and let them exercise their clinical freedom in choosing which correction best suits the clinical situation?—I am, etc.,

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Acute Pancreatitis and Diabetic Ketoacidosis in Hypothermia

SIR,—In their paper reporting the apparent association of acute pancreatitis and diabetic ketoacidosis with hypothermia Dr. D. Maclean and his colleagues (29 December, p. 757) fail to mention whether arterial or venous samples were used for the measurement of serum amylase and blood glucose levels. Conclusions drawn from venous samples taken during hypothermia are notoriously unreliable because of stagnant blood flow in the cold.[1] The mean serum amylase value for the series ±1 S.D.) was 386 ±556 Somogyi units/100 ml and that of blood glucose 149 ±158 mg/100 ml, indicating a huge scatter of values. Because of this scatter it is likely that these means would not be significantly different from means of values measured in a control group of subjects with normal body temperatures.

Even acid-base calculations made from arterial samples can be misleading unless corrected to what they would be at normal body temperatures.[2] It is generally accepted that acidosis is not usually severe during hypothermia but may be during rewarming.[3] It is likely to be dangerous to the patient if measures are taken because of diagnoses made from biochemical estimations subject to error due to cold.—I am, etc.,

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Effect of Viruses on Lymphocyte Reactivity

SIR,—Studies of lymphocyte sensitization in health and disease continue to appear in large numbers. The important observations made by Miss Elizabeth Thompson and others (22 December, p. 709) are therefore most timely, since it is not widely appreciated how exposure of lymphocytes (both in humans and experimental animals) to certain common viruses may greatly influence their reactivity to antigens. The phenomenon first obtruded itself in the M.R.C. Demyelinating Diseases Unit in Newcastle in early 1972, when the occurrence of an influenza epidemic was accompanied by wildly random results in the macrophage electrophoretic mobility test.[1 2] Between 25 January and 2 March all normal guinea-pigs within the colony used to prepare macrophages for the test were found to be sensitized to P.P.D. as well as to encephalitogenic factor (E.F.). A description of what occurred has been published,[3] and the episode led to a systematic study of the manner in which guinea-pig lymphocytes reacted to the above antigens after injection with some common viral vaccines. It was found that cellular sensitization occurred not only to the specific inoculum but also to P.P.D. and to E.F., and indeed in lesser degree to other apparently unrelated antigenic stimulants.[4]

Not only do cells from subjects exposed to banal viral infections develop unusual reactivity, but they appear to be "on edge" in the sense that they undergo "spontaneous" transformation in vitro to a greater degree than normally. Such irritability of the cells may persist for some weeks and may indeed occur in the presence of an influenza epidemic even when the subject concerned has not suffered obvious clinical infection.[5]

From the experience gained in the winter of 1971-2 it was possible by introducing the most rigorous discipline in the animal house and laboratories (especially the wearing of masks and removal of workers with "colds") to prevent a recurrence of the troubles in the winter of 1972-3. Inadvertent guinea-pig exposure to infections may be monitored by measuring the response of peritoneal exudate cells to P.P.D. or E.F. in the manner described by Sundaram *et al.*[6] and Diengdoh and Turk.[7] A rise above 1·5% in macrophage slowing should be regarded as unacceptable. Recent studies of the sensitivity of lymphocyte-antigen interaction to the presence of linoleic acid[8-10] will very probably also be highly susceptible to the same errors.

All who hope to achieve consistent and meaningful results while working with lymphocyte reactivity, especially during the winter months, must be prepared to exercise the greatest care in the supervision of animal stocks and should at least inquire about recent exposure of human subjects to influenzal infections.—I am, etc.,

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Incidence of Postpartum Deep Vein Thrombosis in the Tropics

SIR,—I refer to the articles by Mr. M. A. Hassan and others and by Mr. O. B. Williams and others on postoperative deep vein thrombosis (3 March 1973, pp. 515 and 517) and the letter from Mr. K. R. Orr (9 June, p. 615) which suggests a low incidence of this phenomenon in Vietnam. Since the incidence of postpartum thromboembolic complications in Thailand is also supposed to be rare, 41,056 clinical charts from the Chulalongkorn Hospital for the years 1970-71 were analysed retrospectively to determine the occurrence of postpartum thromboembolism (see table).

The prevalence of postpartum thromboembolic complication was 1·7 per 10,000 deliveries. The results of a similar study at

	No. of Cases	No. per 10,000 Deliveries
Superficial venous thrombosis	1	0·25
Deep vein thrombosis	2	0·5
Pulmonary embolism	3	0·7
Cerebral thrombosis	1	0·25
Total	7	1·7

the Mayo Clinic[1] indicated a prevalence of 134·7 per 10,000 deliveries. This apparent low prevalence of thromboembolism in the Thai series could be due to one or more of the following factors. (1) The period of postpartum hospitalization in Thailand is only two to three days. No cases occurring three or more days after delivery would be detected. The Mayo Clinic study showed that 34·4% of cases occurred three or more days after delivery. Thus the present study may have underestimated the prevalence of thromboembolism. (2) There may have been a failure to diagnose or record thromboembolism owing to diagnostic bias on the part of the physicians, especially in mild cases. It is noteworthy that the prevalence of superficial venous thrombosis was only 0·25 per 10,000 deliveries in the Chulalongkorn study, whereas it was 118·1 per 10,000 deliveries in the Mayo Clinic study. This suggests under-notification of mild cases. (3) The prevalence of postpartum thrombosis may be lower in Thailand owing to nutritional or ethnic factors.

The results indicate that while postpartum thromboembolism does occur in Thai women, the prevalence is lower than in the United States. However, the prevalence shown in the table is undoubtedly an underestimate owing to the short period of hospitalization and diagnostic artefacts. Studies are in progress to detect clinical and occult postoperational thromboembolism in Thai women using the ^{125}I-fibrinogen uptake test.—I am, etc.,

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1 Aaro, L. A., and Juergens, J. L., *American Journal of Obstetrics and Gynecology*, 1971, **109**, 1128.

Breast Milk Substitute

SIR,—The recent article by Dr. A. T. Willis and others on a planned "breast milk substitute" (13 October, p. 67) is an example of the type of tunnel-vision simplicism which can only amaze and dismay.

This group's earlier investigations into the protective functions of human milk in the maintenance of a *Lactobacilus bifidus* flora, a low faecal pH, the inhibitory effect of lactoferrin, etc. are very important contributions to the rapidly increasing knowledge concerning host resistance factors in breast milk.[1] From this background, Dr. Willis and his colleagues have pursued the valuable, but circumscribed, holy grail of a breast milk substitute (or cow's-milk-based "formula") geared to the production of acid stools and to a bifidogenic effect on intestinal flora. These aims are indeed important and desirable. At the same time, they represent once again an attempt to "humanize" a cow's milk formula based on one or two considerations only. In the past such ventures have often been related to major proximate principles or to mineral balance. The present authors approach the problem mainly from an anti-infective point of view, and, as they concede, the nutritional and metabolic implications of this particular mixture are left rather indefinite. One wonders, for example, if they are aware of the outbreak of pyridoxine-related convulsions that occurred in infants fed on another "formula" some 20 years ago[2] or of the vitamin E haemolytic anaemia story.[3]

The type of study described in this paper does have importance, as perhaps introducing a degree of artifical chemotherapy into artificial feeding, which may have particular value in some circumstances, especially where environmental hygiene is poor and the risks of diarrhoea and other infections are great. However, the dangers of an approach geared to the solution of a single problem need stressing. Human milk is an exceedingly complex mixture of over 100 different nutrients and of large numbers of protective substances. Research work into the least inappropriate cow's milk formula invariably poses problems because the investigators almost necessarily focus on trying to reach a "solution" of one problem, whether this be a bifidogenic effect or a reduction in curd-tension or increased calcium absorption.

The fact is that all mammal milks are both highly complex and differ greatly from one another—their numerous constituents are species-specific and in balance with one another. Planned alterations of ingredients in the mixtures that constitute cow's milk formulas to achieve a particular specific purpose are only too likely to lead to further unappreciated metabolic imbalances and other interference phenomena. The literature is full of such examples—pyridoxine-dependent convulsions have already been mentioned. The manufacturers of so-called "breast milk substitutes" kid themselves. There is no way at all for cow's milk to be transmuted into human milk. Minor changes and tinkering can certainly make cow's milk formulas more acceptable, safer, and metabolically tolerable. However, these modifications are inevitably at partial and gross levels, as becomes increasingly evident as recent scientific work continually adds to knowledge of the complex nature and species specificity of the very large number of interrelated constituents and nutrients found in all mammalian milks.[4]—We are, etc.,

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1 Hanson, L. A., and Winberg, J., *Archives of Disease in Childhood*, 1972, **47**, 845.
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Rheumatoid Arthritis

SIR,—Your leading article on rheumatoid arthritis of the temporo-mandibular joint (18 August, p. 369) credits Sir Archibald Garrod with the introduction of the term rheumatoid arthritis. This, of course, is incorrect by one whole generation, since it was Sir Archibald's father, Sir Alfred Baring Garrod, who coined the term and nicely described the disease in 1859.[1]—I am, etc.,

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1 Garrod, A. B. *The Nature and Treatment of Gout and Rheumatic Gout*. Walton and Maberley, London, 1859.

Possible Hazard of Methacrylate Monomer

SIR,—The letter from Dr. R. Routledge (24 February 1973, p. 487) on a possible hazard to workers manufacturing contact lenses may be relevant to orthopaedic surgeons. The author suggested that the inhalation of methyl methacrylate monomer might be potentially dangerous. The increasing use of this material in the insertion of artificial joints subjects not only the orthopaedic surgeon but the anaesthetist and, especially, the scrub nurse to repeated inhalation of the monomer. Its sweet smell is already well known in our theatres.

As a result of the warning we have adopted the simple expedient of applying suction to the air immediately about the bowl of methacrylate while the monomer is being mixed with the polymer. It has proved easy to remove the smell of the vaporized monomer almost completely by this means. The introduction of a Charnley tent into the orthopaedic theatre of Frimley Park Hospital will allow us to include a small sterile exclusion cupboard with vacuum extractor at its apex within the tent. We hope by this means to reduce the inhalation of monomer by the theatre staff to a minimum. —I am, etc.,

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Preleukaemic Syndrome and Marrow Hypoplasia

SIR,—Your leading article (22 December, p. 691) mentions that a hypocellular bone marrow has been found in about a quarter of the reported cases of preleukaemia. We have recently seen two patients with marrow hypoplasia in whom there were haematological features resembling those of acute leukaemia.

The first patient was an 8-year-old boy who presented with prolonged bleeding on dental extraction and was found to have pancytopenia, haemoglobin 4·7 g/100 ml, leucocytes 2,000/mm^3 (neutrophils 20%), and platelets 10,000/mm^3. The blood smear showed lymphoid cells with atypical features, some containing nucleoli and resembling lymphoblasts. Bone marrow aspiration showed marked hypocellularity, the predominant cell being the atypical lymphoid cell seen in the peripheral blood. He was treated with blood transfusion, steroids, and antibiotics and over a period of 18 months underwent remission. There has been no further clinical or haematological evidence of leukaemia.

The second patient was a 20-year-old woman who developed pancytopenia while being treated with sulphasalazine for ulcerative colitis. She presented with a haemoglobin 10·8 g/100 ml, leucocytes 2,600/mm^3 (neutrophils 20%), and platelets 40,000/mm^3. Bone marrow showed an increased cellularity, myeloid:erythroid ratio 7:1 and 30% atypical promyelocytes, some with nucleoli. Three days later the peripheral blood leucocyte count had risen to 4,000/mm^3 and platelets to 120,000/mm^3. Repeat bone marrow aspiration still showed increased cellularity but with a myeloid:erythriod