The study was performed while in receipt of a thrombosis research grant from Manchester Regional Hospital Board. We are also indebted to Manchester Family Planning Clinics, who sent the women for testing, and Dr. W. Lye, of Dista Products Ltd., for supplying the Dista Sequential preparation used in this study.

—We are, etc.,

L. POLLER.

JEAN M. THOMSON.

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Asparaginase

SIR,—In your leading article (24 May, p. 465) you state: "Asparaginase is now known also to affect normal cells, particularly those of the thymus and lymphoreticular system. Whether this effect, which has so far been seen only in animals, will prove an added hazard to therapy in man is not yet known."

I recently treated a patient with acute lymphoblastic leukaemia who developed a profound leucopenia following asparaginase treatment. The findings in life and the post-mortem examination strongly suggested that the normal cellular elements of the bone marrow, as well as leukaemic cells, had been depressed. A detailed report on this patient by Dr. M. J. Oehlers, Dr. W. Fetwadjeff, and myself will be published elsewhere.—I am, etc.,

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Acute Infective Gastroenteritis

SIR,—I should like to comment on the letter by Dr. Mary J. Wilmers and others (31 May, p. 573) advocating the wholesale use of neomycin and other antibiotics in their gastroenteritis ward with the expressed purpose of preventing cross-infection with pathogenic *Escherichia coli*.

They give as their rationale the failure of careful barrier nursing techniques to contain cross-infection with these organisms. We have developed a system of barrier nursing at this hospital which has proved highly effective,^{1,2} but it must be emphasized that in order to operate the system efficiently it is essential to have properly constructed and equipped cubicles and a sufficiency of nurses for both day and night duty.

There are a number of possible disadvantages and dangers in the indiscriminate use of suppressive antibiotic treatment in babies. (1) It may engender in the minds of doctors and particularly nurses a false sense of security. Dr. Wilmers and her colleagues continue to get periodic bouts of cross-infection despite the approach they are recommending. (2) This practice encourages the emergence of resistant strains of *E. coli*. (3) Neomycin and antibiotics such as oxytetracycline may have undesirable and occasionally serious side-effects in small babies.

The question of whether or not to use antibiotics for babies seriously affected with gastroenteritis is a separate and debatable

matter. For the last four years or more we have seriously restricted the use of antibacterial preparations in our gastroenteritis unit, and have found rather to our surprise that very ill infants not given antibiotics generally respond promptly and well to accepted measures directed at restoring and maintaining electrolyte and fluid balance coupled with skilled nursing.

Needless to say, faced with an outbreak of hospital-acquired gastroenteritis in a paediatric unit or maternity department, it would be folly not to use an appropriate antibiotic in an attempt to stem the spread of infection.—I am, etc.,

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Contaminated Chloroform

SIR,—For at least 15 years we have used analytical grade chloroform for the extraction of the dithizone complex with lead when estimating this metal in biological fluids. During the last few weeks these estimations have given anomalous values which have appeared to be too high. Careful investigation ruled out contamination of the apparatus as a cause. The source of the error has been traced to certain batches of chloroform labelled as being suitable for use with dithizone and free from metallic impurities. Some batches of chloroform gave a red colour with dithizone which was equivalent to a positive error of 20 µg. of lead/100 ml. whole blood.

The impurity can be removed from the contaminated chloroform by washing with 10% sulphuric acid. The washings give an apparent lead content of 1.9 µg. of lead in 100 ml. of contaminated chloroform, in the presence of citrate/cyanide buffer. The metallic impurity is not lead, as by taking the same amount of wash liquor and omitting the cyanide buffer, the complex gives an optical density of 1.75 at 520 mµ in 0.5 cm. cells in 10 ml. of chloroform. It should be noted that if the contaminated chloroform is used to "delead" cyanide buffer solution then the cyanide becomes contaminated with the impurity which is not removed by dithizone.

Similar high optical densities can be obtained in the presence of thiosulphate, of iodide, and of citrate buffers. Thus, severe interference can be expected in the measurement of copper, cadmium, cobalt, and zinc when contaminated chloroform is used in the dithizone methods for these elements.

It is strongly recommended that laboratories which use chloroform for the extraction of dithizone metal complexes should test each batch of every consignment of chloroform before it is used in micro-analytical methods. It appears that the chloroform became contaminated during the filling process owing to a faulty filling line.—We are, etc.,

R. C. BROWNE.

J. STEEL.

R. W. ELLIS.

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Health,
University of Newcastle upon Tyne.

Relapsing Amoebic Colitis

SIR,—The report by Drs. S. R. Kanari and R. Knight (7 June, p. 613) will, I hope, stimulate awareness of the possibility of amoebic disease in patients who have lived or served abroad.

Army personnel have been particularly at risk in certain campaigns. In 1965 I diagnosed amoebic colitis in over a dozen soldiers who had been infected at the same source in Borneo, but there were many others, both British and Australian, who were at risk. Should any of these attend doctors, military or civil, with a complaint of piles, or recurrent diarrhoea, or rectal bleeding, it is to be hoped that amoebiasis will be considered. My patients were frequently referred with "piles." In the acute case I noticed that the abundant mucus always contained myriads of tiny bubbles; it was almost effervescent. I have not seen this described and it may not be of significance, but in that particular outbreak led me to repeated searching and examination of the specimens myself in the laboratory if a negative report was received from a technician.

As has been pointed out many times, the geographical history is the most important clue to the possibility of "tropical disease."—I am, etc.,

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Neonatal Serum Bilirubin Estimation

SIR,—Dr. T. Hargreaves (17 May, p. 448) indicates that false "low" results could occur using a diazo-coupling method during serial estimations of neonatal bilirubin levels and be reported as "normal" results, thus leading to complications arising over any proposed treatment by exchange transfusion.

Recently, while comparing two methods for the estimation of serum bilirubin levels in neonates, using a micro spectrophotometric method,¹ and a diazo-coupling method,² both methods were found to be in close agreement, the spectrophotometric method tending on average to be 1 mg.% higher than the comparable diazo results. However, in one case, a premature jaundiced infant, there was a marked discrepancy between results obtained using both methods, the diazo method producing consistently higher values than the spectrophotometric method over a period of several days (see Table). After careful rechecking of both methods, further inquiries resulted in the information that the baby was being treated with the antibiotic ampicillin (50 mg. twice daily). During a subsequent exchange transfusion samples of blood before and after transfusion were obtained and the serum separated, 2 ml. was acidified and extracted with ethyl acetate. The extract was evaporated to dryness and the residue subjected to two-dimensional chromatography, first in isopropyl alcohol, ammonia, water (80:10:10) overnight, and secondly in Anisole/acetic acid (70:30) for five hours. The chromatograms were dried, sprayed with 10% sodium carbonate, redried, and developed in diazotized *p*-nitro aniline to detect phenolic compounds. Both pre- and post-transfusion chromatograms developed an intensely staining orange/red spot which did not appear to correspond, position-wise, to any known phenolic acid and was presumed to be either ampicillin or a metabolite of ampicillin. On stopping treatment with ampicillin the marked discrepancy between the diazo and spectrophotometric values for the bilirubin levels which had occurred reverted to the expected level. Blood was also taken from full-term in-

infants and adults who were taking ampicillin, but no detectable amounts of ampicillin were found after chromatography.

Marked Variations in Serum Bilirubin Levels Between Spectrophotometric and Diazo-coupling Methods when Applied to Serum from One Premature Infant on Ampicillin 50 mg. (Twice Daily)

Day	Time	Diazo Method mg./100 ml.	Spectrophotometric Method mg./100 ml.	Difference
1	09.30	10.5	9.5	-1.0
2	09.30 12.00	18.0 14.0	12.1 12.8	+5.9 +1.2
3	09.30 pre-transfusion post-transfusion	22.4 19.4 9.2	15.0 15.5 8.3	+7.4 -3.9 -0.9
4	09.30 12.00 15.30	19.4 19.4 15.6	13.7 14.7 14.7	-5.7 -4.7 -0.9
5	09.30 Taken off drug 12.00	18.4	14.2	+4.2
6	11.30	16.0	13.1	+2.9
7	09.30	14.0	14.5	-0.5

Work by Stewart and Harrison¹ has shown in rats that ampicillin after absorption is excreted very rapidly into the bile, and that bile levels can read 40-times peak serum concentrations. It could perhaps be suggested in certain premature infants with perhaps bile duct obstruction and/or liver enzyme deficiencies that serum levels of ampicillin could build up to levels which could produce a "falsely high" bilirubin result when estimated by a diazo-coupling reaction as opposed to a direct spectrophotometric measurement of bilirubin.

I feel, therefore, that a spectrophotometric method is quick and easy to perform, requires the minimum amount of serum, and probably suffers less from interference from extraneous sources than do colorimetric methods which depend on "diazo-coupling" reactions.—I am, etc.,

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Vitamin C and the Elderly

SIR,—In their paper "Vitamin C Supplementation in the Elderly" (17 May, p. 416), Dr. J. Andrews and others make the point that an average of nine months' supplementation with ascorbic acid is required with doses of 40 mg. or 80 mg. daily to bring the ascorbic acid content of leucocytes in elderly people to levels comparable with those found in younger people.

It is important to stress that with larger daily doses of ascorbic acid this process can be considerably accelerated. In a study carried out on long-stay geriatric hospital patients¹ it was shown that daily supplementation of the diet with 200 mg. of ascorbic acid achieved levels well above those

of the average younger person, within three months—as shown in the accompanying table. These high levels of ascorbic acid in leucocytes were maintained throughout the period of supplementation.

Period of Supplementation with 200 mg. Ascorbic Acid Daily	Mean Leucocyte-Ascorbic Acid Level of 40 Long-stay Geriatric Hospital Patients ($\mu\text{g.}/10^9$ W.B.C.)
0 months	13.6
3 months	43.4
6 months	56.5
9 months	54.0
12 months	57.9

Average level in younger people—26 $\mu\text{g.}$ ascorbic acid/ 10^9 W.B.C.

We suggest that if dietary supplementation with ascorbic acid is to be used in elderly people then the dose should be 200 mg. daily, at least for the first month.—We are, etc.,

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Pin or Prosthesis?

SIR,—Your correspondents (10 May, p. 384, and 31 May, p. 575) on the controversial subject of "Pin or Prosthesis?" (26 April, p. 201) have aligned themselves in favour of one method versus the other. I am writing to suggest that the two methods may not be mutually exclusive and that there is a place for both.

It seems to me that in such a multifactorial problem as fracture of the neck of the femur no one method has clearly emerged as superior to others in every respect, and that to treat all cases by one method regardless may not be best for the individual patient.

Those who favour prosthetic replacement in patients over 70 years of age wax more enthusiastic the older the patient. The prosthesis is less likely to fail from wear and it is thought that the greater early mobility obtained automatically improves the ultimate prognosis. I feel that there is an "end-point" and that the prognosis of the older, frail patient is better with fixation than replacement. The one certain advantage of the prosthesis is that non-union and avascular necrosis are precluded. This advantage is less important in the elderly and has to be paid for if one believes that prosthetic replacement is a more "shocking" operation than nailing.

It may be that too much is expected of the patient with the prosthesis in situ, who is then considered "cured." She may well be allowed to use her prosthesis rather more, soon after a major operation, than is good for her general health. In addition, the change of environment to home surroundings soon after operation, attractive as it sounds, must place another physical and emotional burden on a person with already low reserves. The patient with frail fixation is not "cured." She can be allowed to sit out just as early, since there is no risk of dislocation, and to make more gradual progress at her own rate. Her rehabilitation is more gradual and probably better suited to her

age and condition. I think this may be one reason why elderly patients with prostheses do very well or very badly while those with fixation probably on average fare better, although making a slower and less spectacular recovery.—I am, etc.,

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SIR,—I cannot agree that fractures of the neck of the femur are still best treated by trifin nails (26 April, p. 201). As long ago as 1954 Haboush¹ demonstrated convincingly that shaft fixation was essential and that the so-called bull's-eye position with the nail in the anatomical axis was comparatively ineffective. Moreover, nails have to be hammered in and some femoral heads do not take kindly to this pile driving. A screw is far less damaging.

As a result of laboratory experiments and clinical experience I consider that patients who are suffering from senile osteoporosis or rheumatoid arthritis are best treated by immediate prosthetic replacement—total if the patient has a reasonable expectation of life, partial if he is decrepit. This statement is made despite the figures published by G. A. Hunter.² In his series of 94 cases infection supervened 21 times. The only conclusion your leader writer can draw from these figures is that in Hunter's series the sepsis rate was high.

Patients whose hips are considered mechanically sound are in my opinion best treated by internal fixation with a sliding pin. This is a difficult operation and requires scrupulous attention to detail. A successful case three years after injury is shown in the Figure. Yet a biopsy from the centre of the femoral head taken at the time of internal fixation showed dead bone. It is therefore possible that the viability of the cancellous bone in the femoral head is less important than its mechanical strength. It may well be that avascular necrosis of the head of the femur is in the nature of a crush fracture which may affect dead as well as living bone. Investigation of the specific gravity of femoral head biopsy specimens from the centre of the