of disopyramide ($\pm$ SD) at 5 min were 6.8 ± 2.68 mg/l, at 15 min 4.01 ± 1.33 mg/l, and at 30 min 3.82 ± 1.21 mg/l. No serious side effects were seen, but two patients required temporary catheterisation for urinary retention and three had hot flushes for between 30 s and 6 min after the injection of disopyramide. There was no alteration in blood pressure and heart rate except in the patients with ventricular and atrial tachycardia.

Our short experience shows that the blood levels of disopyramide obtained were sufficient to suppress premature beats. It also illustrates the difficulty of assessing the drug clinically when spontaneous remission may occur. We suggest that further controlled trials need to be done to establish the effectiveness of disopyramide as a possible alternative to lignocaine in the suppression of premature beats.

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Treatment of chronic hepatitis B virus infection with ribavirin

SIR,—The new antiviral agent ribavirin (1- β -D-ribofuranosyl-1,2,4-triazole-3-carboxamide) has been used in the treatment of acute B-virus hepatitis with conflicting results. Zuniga *et al*¹ reported a significant shortening of the course of the illness and a more rapid return to normal of serum bilirubin and enzyme levels. However, Moseley² could find no difference between the response of patients treated with ribavirin and those receiving a placebo. A clearer idea of the efficacy of the drug against the hepatitis B virus (HBV) might be obtained by treating patients with chronic HBV infection and using elimination of the hepatitis B surface antigen (HBsAg) from the patient's serum as an objective criterion of anti-HBV activity.

We studied 13 patients with chronic HBV infection, diagnosed by the presence of HBsAg in the blood on three consecutive occasions at suitable intervals. One patient was an asymptomatic carrier and another had no evidence of liver disease (he suffered from recurrent respiratory infections and was deficient in complement); the remaining patients had HBV-associated chronic liver disease—one suffered from chronic active hepatitis, two from chronic active hepatitis with cirrhosis, and eight from hepatocellular cancer with or without cirrhosis. There were 12 men and one woman and all but one were Black. Ribavirin was usually given in a dose of 800 mg daily for 21 days; one patient was treated for 28 days and another received 1200 mg daily for 10 days. Blood was taken for detection of HBsAg, selected liver function tests, a full blood count, and urea and electrolyte estimation before starting the drug, at weekly intervals during the trial, and after finishing the course of treatment.

In none of the patients did HBsAg disappear from the serum during or after treatment with ribavirin. No significant changes in liver function tests or in urea and electrolyte levels were noted. However, one patient (and another not included in this trial who was given ribavirin for extensive cutaneous warts) developed mild intravascular haemolysis which disappeared after stopping the drug. The direct Coombs test was negative, as was a ribavirin-induced Coombs test.

From these results it seems unlikely that ribavirin will be effective in the treatment of patients with HBV-associated chronic liver disease or asymptomatic carriers of the virus.

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¹ Zuniga, C. B., *et al*, in *Proceedings of the 10th Congress of the Sociedade Brasileira de Medicina Tropical*, Curitiba-Parana, February 1974, abstract 118.

² Personal communication to Dr R. W. Sidwell, ICRN Nucleic Acid Research Unit, Irvine, California.

"Experience not essential"

SIR,—Your issue of 12 March (p xxv) carries an advertisement for the post of lecturer in geriatric medicine at the University of Manchester, which states: "Previous experience in geriatric medicine is not essential." Surely it cannot be possible to teach a branch of medicine in which one has had no experience. Personally, even after many years devoted to research and clinical work in geriatrics, I have found it a difficult subject to teach to medical students who have not encountered the problems of elderly patients in their previous clinical work.

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Chlorpropamide-induced hyponatraemia

SIR,—With reference to the report by Dr C. J. C. Roberts of four cases of diuretic-induced hyponatraemia (22 January, p 210), I should like to report a case in which a similar condition was induced by chlorpropamide.

A 76-year-old woman was admitted in a violently confused state, unresponsive to questions. She had a two-day history of headache and had become drowsy and confused 12 h before admission. She had been started on chlorpropamide 250 mg twice daily one week before for her recently diagnosed diabetes mellitus. Her only other treatment was Delta-Butazolidine (a combination of phenylbutazone and prednisone), which she had been taking for several years.

On examination she was normotensive and the only abnormal findings were confusion, diminished reflexes, and bilateral extensor plantar responses. Her plasma sodium concentration was 118 mmol (mEq)/l, chloride 79 mmol (mEq)/l, and blood glucose 8.4 mmol/l (150 mg/100 ml). Standard bicarbonate, plasma potassium and creatinine, serum cortisol, and blood urea levels were all within normal limits. Brain scan and chest x-ray were normal. On the second day, serum osmolality was 258 mmol/kg and urine osmolality 346 mmol/kg. This is consistent with the syndrome of inappropriate antidiuretic hormone (ADH) secretion.

All drugs were stopped and within 10 days she had made a complete clinical and biochemical recovery. By the fifth day the plasma sodium had risen to 134 mmol/l and plasma chloride had fallen to 90 mmol/l.

Chlorpropamide-induced syndrome of inappropriate ADH secretion was reported by Weissman *et al*¹ in a series of five women who presented with symptoms of hyponatraemia. They postulated that 4% of people taking chlorpropamide are at risk of hyponatraemia, though Epstein *et al*² dispute this figure. Considering the severe symptoms that may arise from hyponatraemia, screening of patients

receiving thiazide diuretics or being over-hydrated for urinary tract infections or urological investigations seems indicated if they are also taking chlorpropamide, though I think this is the first symptomatic case to be reported in England and it seems less common than was originally supposed.

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¹ Weissman, P. N., Shenkman, L., and Gregerman, R. I., *New England Journal of Medicine*, 1971, **284**, 65.

² Epstein, S., *et al*, *New England Journal of Medicine*, 1972, **286**, 785.

Hexachlorophane—yes or no?

SIR,—In response to your leading article (5 February, p 337) and the subsequent correspondence, we have a number of comments.

(1) Hexachlorophane (HCP) is an effective skin antiseptic that has been used for 30 years as a surgical scrub and skin cleanser and has been found to be a highly effective agent in the control of staphylococcal infections and epidemics. There are adequate scientific and epidemiological data to support the use of HCP, and its marked activity against Gram-positive organisms is well documented. Immediately after the use of HCP was restricted a report from the US Center for Disease Control (CDC)¹ illustrated the dramatic rise in staphylococcal infection when HCP was discontinued for baby bathing. The rate of infection rose from a documented 1 case per 1000 births to 6 per 1000. This included serious staphylococcal diseases such as impetigo, enterocolitis, bacteraemia, and osteomyelitis. More recently Hyams *et al*² reported an increase in staphylococcal colonisation from 2.2% in HCP-bathed infants to 6% in non-HCP-bathed infants. This was followed by an epidemic of *Staphylococcus aureus* infection in the latter group which was controlled with HCP. Similar evidence from the United Kingdom is reported in the letter from Dr Beryl Corner and her colleagues (5 March, p 636). The US Food and Drug Administration (FDA) and the CDC recommend that nurseries consider HCP bathing to control an outbreak of Gram-positive infection and the American Academy of Pediatrics also endorses this procedure.

(2) As to the establishment of a "benefit to risk ratio" for HCP, we would point out that there is no evidence of neurotoxicity resulting from the use of HCP as a surgical scrub or as a skin cleanser by adults or by teenagers and children, who before the regulatory restrictions used 3% HCP extensively to treat acne and other skin conditions. An examination of 135 stillborn infants and infants dying in the neonatal period³ showed that there was no significant difference in the neurological findings in infants bathed in HCP at birth compared with infants not bathed in HCP. Plueckhahn's⁴ experience of 81 756 live births is impressive evidence for the lack of deleterious effects on growth and development of the babies bathed with pHisoHex and also for the lack of any deaths associated with HCP. Even in inherently high-risk patients, such as premature infants, the evidence for HCP neurotoxicity is not absolute, and the interpretation by Professor E. G. McQueen and Mr D. G. Ferry (5 March, p 637) of Plueckhahn's data ignores that author's clear evidence that three or more bathings with 3% HCP are required

for the development of any neurotoxicity, and also that hyperbilirubinaemia is a contributory factor.

The controversy over absorption of HCP through the skin and central nervous system toxicology should be placed in proper perspective and, as pointed out in your leading article, "the reasonable conclusion seems to be that . . . the data on treatment and blood level in neonates are so heterogeneous that they should be taken only as a general indicator and that blood concentrations in animals are a poor guide to those in man."

After almost seven years of regulatory restriction one has yet to see any major deleterious effect when HCP is used in the recommended way. It is interesting to note that in Victoria, Australia, the Executive Committee of the National Health and Medical Research Council has recommended that HCP be removed from its restricted status and placed in a freely available category.

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¹ US Center for Disease Control, *Morbidity and Mortality*, vol 21, No 30, 29 July, 1972.

² Hyams, P J, et al, *American Journal of Diseases of Children*, 1975, **129**, 595.

³ Gowdy, J M, and Ulsamer, A G, *American Journal of Diseases of Children*, 1976, **130**, 247.

⁴ Plueckhahn, V D, and Collins, R B, *Medical Journal of Australia*, 1976, **1**, 815.

Brewer's yeast and diabetes

SIR,—With reference to your note about the insulin-potentiating effect of yeast extracts (Any Questions? 4 December, p 1366) I recently noticed an early paper by a Bristol physician, Dr W Bird Herepath, who claimed to have successfully treated a case of diabetes with yeast in 1853.¹

Before treatment the patient had been voiding urine of specific gravity 1.044 and containing 850 grains of sugar per pint. Within two days of employing brewer's yeast (given in a dose of one tablespoonful two to three times daily in milk) the specific gravity of the urine had sunk to 1.020 and the sugar to 300 grains per pint. After a further six weeks there was no glycosuria and the patient rapidly recovered his original weight.

Dr Herepath concluded that yeast worked by fermenting glucose in the stomach, thus preventing excessive absorption into the blood. In the light of modern thinking it seems likely that his patient's diabetes was caused by a depletion of chromium which was corrected by giving yeast.

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¹ Herepath, W B, *Journal of the Provincial Medical and Surgical Society*, 28 April 1854, p 374.

*Our expert writes: "It is interesting that the antidiabetic action of brewer's yeast was noted as long ago as 1853. Brewer's yeast is the richest natural source of "glucose tolerance factor," a trivalent chromium complex. American investigators have produced improvement of glucose tolerance in adult diabetics by adding chromic chloride to their diets.¹⁻³ The chromium complex formed from the inorganic salt exerts its hypoglycaemic action by potentiating the effects of insulin. Brewer's yeast, therefore, has no significant

therapeutic effect on the untreated, insulinopenic juvenile diabetic, although it may facilitate the response to exogenous insulin. Dr Herepath's patient was almost certainly a mild maturity-onset diabetic. The excellent response to yeast supplementation makes one wonder if he simultaneously recommended a reduction of carbohydrate intake. The importance of dietary restrictions in the treatment of diabetes was realised at the end of the 18th century and about the middle of the 19th century Bouchardat introduced the idea of fasting days for diabetics. This advance was well publicised and probably reached the ears of most practising physicians. The role of chromium in human diabetes is by no means resolved. There is no evidence that depletion actually causes diabetes; it may, however, aggravate pre-existent disease."—Ed, *BMJ*.

¹ Glinsmann, W H, and Mertz, W, *Metabolism*, 1966, **15**, 510.

² Levine, R A, Streeten, D H P, and Doisy, R J, *Metabolism*, 1968, **17**, 114.

³ Hopkins, L L, and Price, M G, *Proceedings of Western Hemisphere Nutrition Congress*, Puerto Rico, 1968, vol 2, 40.

Metabolic and cardiotoxic effects of salbutamol

SIR,—We have been following with interest recent publications on this subject but wish to refer specifically to one statement made by Dr A J Johnson and others (19 March, p 772). We fully endorse the view there expressed—namely, that salbutamol should normally be given by *slow* injection when the intravenous route is used. Our literature and packaging are clear on this point. Any suggestion that rapid intravenous injection may be generally acceptable is not of our making and is not supported by evidence available to us.

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Streptococcus mutans endocarditis—a trap for the unwary

SIR,—We would like to draw attention to the difficulties we have recently independently encountered in our respective laboratories in the recognition of *Streptococcus mutans*. In both instances the organism was initially discarded as a diphtheroid.

One patient, a man of 61, was admitted to the Whittington Hospital with a history of a flu-like illness, known congenital aortic valve disease, and features of congenital syphilis. He had been given co-trimoxazole by his general practitioner and four blood cultures on admission were sterile. Ten days later a "diphtheroid" was grown from a further blood culture and was initially dismissed as a contaminant. In view of the strong clinical possibility of endocarditis further blood cultures were then performed, all of which grew the "diphtheroid." Empirical treatment had already been started with penicillin and gentamicin when a culture of the "diphtheroid" in glucose broth revealed it to be a chaining streptococcus subsequently identified by the Streptococcus Reference Laboratory as *Str mutans*.

The second patient, a woman of 81, was admitted to St Thomas's Hospital with a history of increasing breathlessness and malaise and known mitral valve disease. Blood culture on admission grew a "diphtheroid" from one of two blood culture bottles which was dismissed as a contaminant. In view of continuing fevers and anaemia four further blood cultures were performed, from all of which

the "diphtheroid" was isolated. It was soon recognised as a streptococcus when Gram-stained films were made from broth cultures. The Streptococcus Reference Laboratory confirmed that it was *Str mutans*.

This non-haemolytic streptococcus is responsible for 14% of cases of streptococcal endocarditis¹ and is therefore likely to be only rarely encountered in any laboratory. It was originally described in 1924 by J K Clarke,² who recognised its morphological variation dependent on the pH of the medium. For those, like ourselves, previously unaware of this classic description of *Str mutans* we would suggest that no "diphtheroid" should ever be regarded as a contaminant in a blood culture until a Gram-stained film has been made from a broth culture.

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¹ Parker, M T, and Ball, L C, *Journal of Medical Microbiology*, 1976, **9**, 275.

² Clarke, J K, *British Journal of Experimental Pathology*, 1924, **5**, 141.

Cord blood IgM and suspected congenital rubella

SIR,—Professor J E Banatvala and Dr Jennifer M Best (22 January, p 228) and Dr J B Pattison (p 228) comment on our short report on "Importance of IgM determination in cord blood in cases of suspected rubella infection" (1 January, p 23). We concluded that in the second case reported, in which the maternal titre of rubella haemagglutination inhibition antibodies at the 8th week of pregnancy was 1/16 and at the 38th week >1/512, reinfection and viraemia had occurred with infection of the baby, proved by a high titre of rubella antibodies in the IgM fraction of the baby's cord blood. In both samples of this mother's serum we found only IgG rubella antibodies.

Professor Banatvala and Dr Best suggest the possibility of a primary infection in the 8th week of pregnancy. I think that this chance is minimal, for up to now we have always found IgM rubella antibodies in a primary infection; perhaps because we obtain a high concentration of the IgM fraction by using the Amicon filter. As for the rubella antibodies in the IgM fraction of the cord blood, they suggest a possible false-positive reaction by contamination of the IgM fraction through aggregated IgG. I do not think this is possible since heat inactivation was performed after fractionation. Moreover, we examined every fraction by the Mancini method to see whether contamination had occurred; not a trace of IgG could be detected in the IgM fraction with this method. Storage or bacterial contamination as causes of false-positive reactions can be excluded by the fact that fractionation was performed within 8 h after the withdrawal of blood. Contamination during fractionation was avoided by the use of sodium azide in the elution buffer.

Dr Pattison also suggests that a primary infection of the mother was possible, the rubella IgM antibodies having disappeared by the 38th week of gestation, and that the titre of 1/16 found at the 8th week of gestation could have been caused by non-specific inhibitors. As no α - or β -lipoproteins could be