now it is a common experience that most cases of CDH can be diagnosed at birth¹²⁻¹⁵ and that proper treatment will lead to the development of completely normal hips.³

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Management of intractable hiccup

SIR,—I hesitate to add to the list of drugs and other treatments of hiccups compiled by Dr B W A Williamson and Mr I M C Macintyre (20 August, p 501), but they mention methylamphetamine only to record failure in the one case they describe. I have used it to treat hiccups scores of times during the past 25 years and have rarely seen it fail to relieve the symptom. I inject the drug very slowly intravenously until the hiccups stop, usually after 6-12 mg has been given.

Unfortunately, as a consequence of restrictions introduced because of social abuse, it has become increasingly difficult to obtain the drug in this hospital, especially after normal working hours, so I now use chlorpromazine 25 mg intravenously. However, most hiccups that I see occur during or shortly after recovery from general anaesthesia for upper abdominal operations, when it can be a nuisance to the surgeon or distressing for the patient. Chlorpromazine may not be desirable at these times, but I have found that pentazocine 30 mg intravenously stops these hiccups quickly and effectively. It stops the more prolonged hiccups that occur in uraemia and the diaphragmatic irritation of pneumonia and sub-diaphragmatic infection or haemorrhage, but its short action (1-3 h) makes it less practical in these situations than chlorpromazine.

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Microangiopathy and diabetic gangrene

SIR,—In your leading article (18 June, p 1555) you assert that microvascular changes in the legs of diabetics predispose directly to gangrene. There is no functional test for the presence of microangiopathy in the leg and the histological evidence is conflicting. Nielsen¹ concluded that microangiopathy was not a cause of pedal gangrene. Du Plessis² reported

that half his patients with foot lesions had histological changes and Moore and Frew³ claimed an association between vascular changes and the presence of foot lesions, although this was true only if the most severe cases of microangiopathy were considered. My own studies have demonstrated capillary and arteriolar changes in half the diabetics studied but not more commonly in patients with ulceration or gangrene of the foot.

I believe that the evidence presently available is not sufficiently strong to justify your statement. Further, labelling a patient as suffering from "small-vessel disease" diverts attention from potentially remediable large-vessel disease.

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- ¹ Nielsen, P E, *Scandinavian Journal of Clinical and Laboratory Investigation*, 1973, **31**, suppl 128, p 229.
- ² Du Plessis, D J, *South African Journal of Surgery*, 1970, **8**, 29.
- ³ Moore, J M, and Frew, D O, *British Medical Journal*, 1965, **2**, 19.

Gastrointestinal symptoms of digoxin toxicity

SIR,—The article by Dr A Smith and Professor M D Rawlins (30 July, p 309) draws attention to the symptoms of nausea, vomiting, and anorexia as indications of digoxin toxicity and states that the digoxin dosage should be reduced if any of these symptoms occur. We would like to report our experience of assessing these symptoms with respect to the plasma digoxin concentration (PDC).

This laboratory offers a service for the measurement of digoxin in plasma and clinicians are asked to complete a specially designed request card when forwarding a blood sample for analysis. The request card includes a simple tick sheet for common signs or symptoms of cardiac drug toxicity, including gastrointestinal symptoms, together with a three-point assessment of their severity (minor, moderate, or severe).

Details of gastrointestinal symptoms and the PDC have been collated for 412 consecutive requests and are summarised in the accompanying table; symptomatic patients are those reported as having one or more of the symptoms nausea, vomiting, or anorexia at the time the analysis was requested.

The mean PDC of the symptomatic patients was significantly higher than that of the asymptomatic group ($P < 0.01$) and there was an association between the symptoms and increasing PDC ($\chi^2 25.23$; $P < 0.05$). However, there was a wide spread of results among patients complaining of the symptoms and 24% of these patients had a PDC of 1.3 nmol/l (1 ng/ml) or less. Furthermore, there was no significant difference between the mean PDC of those patients with minor symptoms and that of those displaying moderate or

severe symptoms ($P > 0.15$). These results are almost identical with our previous analysis of almost 2000 observations, based on a less detailed assay request card, in which an association between PDC and electrocardiographic signs of toxicity was shown.¹

Since the symptoms can be caused by congestive heart failure² they are often difficult to evaluate in patients who have been receiving digoxin for some time and could themselves be relieved by an increase in digoxin therapy. Indeed, our results suggest that these symptoms are encountered frequently in patients with low plasma concentrations of the drug and as a diagnostic aid they might be misleading.

In our experience the most prudent course of action when faced with a patient complaining of these symptoms is to determine the PDC, omitting digoxin therapy pending the result. Together with the evaluation of a carefully documented history and other clinical measurements we have found the PDC useful in assessing the probability of the symptoms being an indication of digoxin toxicity.

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- ¹ Holt, D W, PhD Thesis, University of London, 1976.
- ² Chung, E K, *Digitalis Intoxication*. Amsterdam, Excerpta Medica Foundation, 1969.

The sleepless child

SIR,—Dr H Jackson (20 August, p 509) attributes much childhood insomnia to "toddler negative behaviour" by which the child exerts his individuality and then goes on to enumerate treatment in the form of constructive play, hospital admission, or drugs, none of which seem appropriate to his putative cause.

Night crying must be a common complaint. Certainly I have dealt with many cases as a general practitioner as well as one as father of a 10-month daughter and another as uncle of a 20-month niece. My own hypothesis is that regular night crying is a Pavlovian conditioned reflex. The child wakes and cries (perhaps initially because of an ailment); the mother comes to him with loving attention and a drink; the child repeats his crying nightly and each time is quickly rewarded. With such regular reinforcement the reflex is soon established. It follows that the logical treatment is simply a matter of deconditioning.

It is explained to the mother how she has unwittingly trained her child to cry and that he must now be taught that crying is fruitless. On the appointed night the neighbours are warned that there will be an unusually protracted din but that this is entirely the fault of the doctor. The child cries. Father stamps in, flings down the side of the cot, slaps him once but firmly, flings up the cot side, and

Plasma digoxin concentration and incidence of gastrointestinal symptoms in 412 patients

Group	No	‰ of total	Plasma digoxin concentration (nmol/l)	
			Mean $\pm$ SD	Range
Without gastrointestinal symptoms	308	74.8	2.04 $\pm$ 1.16	0-7.3
With gastrointestinal symptoms	104	25.2	2.32 $\pm$ 1.34	0-6.6
Total	412	14.3	2.18 $\pm$ 1.29	0-6.6
Minor	59	10.9	2.52 $\pm$ 1.42	0.4-5.8
Moderate to severe	45			

Conversion: SI to traditional units—Digoxin: 1 nmol/l $\approx$ 0.78 ng/ml.

stamps out, slamming the door behind him (locking it with older children). The child screams and shouts for hour after hour until, depending on his strength and determination, eventually he subsides in a lather of sweat and exhaustion. On no account must the parents enter the room until next morning, so it must be adequately warm.

This treatment will decondition most children in one night, and indeed if toddlers attend the consultation the treatment may not even be called into play. My most remarkable case was that of a 4-year-old, who, significantly, had remained an only child, having cried nightly since birth yet delighted his desperate parents by silence after the second night. Presumably owing to the superior intelligence of *Homo sapiens* compared with *Canis* he is easier both to condition and decondition.

One of the features of our age is the loss by authority of the self-confidence to assert itself, and nowhere is this more disastrous than in the home. It is unlikely that Victorian parents needed a doctor to tell them how to deal with such a simple domestic problem, but then they had no fearfulness of psychological trauma to displace the common sense handed down to them by genetic and cultural evolution as well as acquired by personal experience.

As a postscript, my daughter and niece both fit the jargon label: mature and well-adjusted adults.

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Beta-blockers and lipid metabolism

SIR,—We note that Dr A Nilsson and his colleagues (9 July, p 126) were unable to confirm our finding that plasma triglyceride levels tend to rise during treatment with metoprolol. They suggest that our results may have been due to the patients being ambulatory outpatients (and, perhaps, by inference less truly in a fasting state), or diabetic, or increasing in weight. We would be delighted to think that there was some such reason but have not been able to find evidence of this.

Our data were obtained in an open though systematic trial on 44 (20 male, 24 female) hypertensive outpatients aged 34-70 (mean 55) years. The patients received careful instructions to fast after 9 pm on the previous day, not to smoke, not to drink tea or coffee, but to take their antihypertensive medication with a little water on the morning on which blood for fasting lipids was to be taken, usually in association with a glucose tolerance test. The tests were done before metoprolol was started, after 3-4 months on metoprolol, and in many cases again after one year on metoprolol.

Of the 44 patients, 15 were untreated non-diabetic hypertensives, eight were non-diabetic hypertensives taking a diuretic alone which did not control their blood pressure adequately, and 21 were taking a non-selective β -blocker (17 of these on a diuretic also). Of these 21 patients, 15 had a diabetic tendency (blood sugar: fasting >5.6 mmol/l (>100 mg/100 ml); 2 h after 50 g glucose >6.7 mmol/l (>120 mg/100 ml) on non-selective β -blocker therapy and six were non-diabetics but had had side effects limiting the dose of the non-selective β -blocker. The dose of the diuretic was kept constant; non-selective β -blockers were replaced by an equivalent dose of metoprolol which was then increased if necessary for optimum blood pressure control. The daily dose of metoprolol ranged from 50 to 600 mg/day. Patients not previously treated with a β -blocker were started on metoprolol 25 mg twice daily and the dose was increased as dictated by blood pressure control.

As shown in the accompanying table the fasting triglyceride level showed a significant rise after three months' treatment with metoprolol in each of the four groups of patients. The rise was maintained after one year, though the numbers in two groups became too small for significance testing by the Wilcoxon signed rank test. Student's paired *t* test was significant at $P < 0.05$ levels for both these groups. Thus a diabetic tendency or diuretic therapy seemed to play no part in the findings.

The mean weight gain in the four groups shown in the table was of the order of 0.1-0.5 kg and was not statistically significant. Seven diabetic patients had a significant improvement in glucose tolerance after changing from a non-selective β -blocker to metoprolol,¹ but they nevertheless showed a significant rise in plasma triglycerides after three months (0.31 mmol/l (27.4 mg/100 ml)) and one year (0.56 mmol/l (49.6 mg/100 ml)) on metoprolol.

We have no reason to think that the patients were less careful over fasting while taking metoprolol. It may be of significance that our patients took their drugs at the usual time on the morning of the test—that is, 1-2 h before blood was drawn; possibly therefore we were observing an acute rather than a chronic effect. Dr Nilsson and his colleagues do not state whether their patients took the drug on the morning of the test. We hope that others also will make observations on triglyceride levels in patients treated with metoprolol and other β -blockers.

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¹ Waal-Manning, H J, *Drugs*, 1976, **11**, suppl 1, p 121.

Fasting plasma triglyceride concentrations before metoprolol and change after 3 and 12 months' treatment

Previous treatment	No of patients	Before metoprolol (mean; mmol/l)	Change with metoprolol (mean $\pm$ SE; mmol/l)		Dose of metoprolol at 3 months (mean and range; mg/day)
			3 months	1 year	
None	15	1.06	+0.24* $\pm$ 0.099	+0.39* $\pm$ 0.167 (3 dropouts)	159 (75-450)
Diuretic alone	8	1.78	+0.38* $\pm$ 0.150	+1.03** $\pm$ 0.360	219 (50-450)
Non-selective β -blocker; patients with diabetic tendency	15	1.56	+0.59** $\pm$ 0.149	+1.12 $\pm$ 0.578 (6 dropouts)	330 (50-450)
Non-selective β -blocker; non-diabetic patients	6	1.13	+0.87* $\pm$ 0.196	+0.31 $\pm$ 0.161 (2 dropouts)	275 (50-600)

Wilcoxon's signed rank test: * $P < 0.05$; ** $P < 0.01$.

Conversion: SI to traditional units—Triglyceride (as triolein): 1 mmol/l $\approx$ 88.6 mg/100 ml.

Perinatal and infant mortality

SIR,—You published the official figures for perinatal and infantile mortality for 1976 (20 August, p 527). Some of your readers might be interested to see how they compare with the 1973 figures given in the Court Report,¹ (vol 2, table C3). This cannot be done on a national basis except for Wales, since in 1973 the figures were for England and Wales and in 1976 they were for England alone. However, the English regional figures are comparable. Scotland was left out of the Court Report.

	Perinatal mortality per 1000 births		Infantile mortality per 1000 births	
	1973	1976	1973	1976
Wales	21.45	19.0	16.36	13.6
Northern Ireland	—	22.3	20.90	18.3
England (RUAs)				
Northern	21.77	19.1	17.72	15.1
Yorkshire	22.89	18.4	19.95	15.0
Trent	21.05	19.2	16.05	14.7
East Anglian	17.37	13.9	13.66	11.6
NW Thames	19.20	16.9	15.31	13.9
NE Thames	20.40	16.6	16.57	13.4
SE Thames	19.55	17.4	15.02	14.8
SW Thames	18.80	14.8	16.17	12.7
Wessex	20.65	15.1	14.58	12.7
Oxford	17.04	13.8	13.74	12.9
South-western	18.99	16.1	15.04	12.9
West Midlands	23.63	21.1	19.14	15.7
Mersey	24.57	19.5	20.05	14.2
North-western	23.44	18.7	19.18	15.7

There is considerable overall improvement.

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Committee on Child Health Services, *Fit for the Future*, vol 2, table C3. London, HMSO, 1976.

Effect of calcium deposition on copper IUDs

SIR,—Recent work by Dr Christine Gosden (22 January, p 202) and Dr E Chantler (30 July, p 288) and their co-workers have suggested that progressive incrustation of copper intrauterine contraceptive devices (IUDs) by calcium or protein-containing deposits causes a decline in the rate of copper release and hence, presumably, in contraceptive efficacy. But the amount of such incrustation at a given time since IUD insertion shows much individual variation,^{1,2} and metallic ions do diffuse through similar deposits on orthopaedic implants (Mr J R Newton, 6 August, p 387). What are the clinical implications of this work?

Unfortunately the paper by Mr Newton and his colleagues (22 January, p 197) is inconclusive. As Dr I Sivin showed (6 August, p 387), the non-random allocation of subjects at two years' copper IUD use to a "continuation group" and a "replacement group" led to differences between them which may have biased the comparison of the pregnancy rates. Moreover, the pregnancy rate among the 183 women who elected to have their Copper 7 replaced at 24 months was subsequently unbelievably low—no pregnancies at all for the next 21 months. Such a low rate has not been described in any previous IUD study. It cannot be entirely explained by the fact that some of the more fertile women initially recruited would have dropped out for reasons such as pregnancy during the first two years and hence been excluded from both the groups subsequently compared. However, the pregnancy rate in the third year among the "continuation group" was not significantly different from that of all the acceptors in the