fication on this point would be welcome, as well as how the actual trial tablets compare with the commercially available. Since comparative trials of different drugs are now more common it seems important to report not only the relative merits of various drugs tested but also the absolute merits in terms of the variables used, as well as to pay close attention to all aspects of methodology.—I am, etc.,

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Potassium Deficiency during Treatment with Brinaldix K

SIR,—We wish to report four cases of severe potassium deficiency seen recently in this hospital in patients receiving Brinaldix K.

Case 1.—A 48-year-old woman was admitted to hospital with weakness, depression, and lassitude. For four months she had been known to be hypertensive, with an impaired creatinine clearance (12 ml/min), and had recently developed cardiac asthma. In addition to clonidine 0.1 mg four times daily for her hypertension she had been receiving digoxin 0·25 mg daily and Brinaldix K two tablets daily for three weeks. Severe hypokalaemia was found (see table) and treated by withdrawal of Brinaldix K and addition of Sando-K, with return to normal values over the following three days. In spite of the impaired renal function and hypokalaemia, no electrocardiographic features of digitalis toxicity were found.

Case 2.—A 69-year-old woman known to be hypertensive for six months was admitted to hospital with extreme weakness, nausea, and postural hypotension. Her hypertension was at the time being treated with clonidine 0.1 mg twice daily. She had been taking digoxin 0.25 mg daily for several months, and on admission showed gross electrocardiographic evidence of digitalis toxicity, with coupling and ST-segment depression. Electrolyte estimations confirmed marked hypokalaemia. For one month prior to admission she had been receiving Brinaldix K one tablet daily. This was discontinued after admission, and potassium supplements added, with return of serum potassium values to normal levels in seven days and disappearance of digitalis intoxication in three days.

Case 3.—A 79-year-old woman was admitted to hospital having been found on her kitchen floor, where she had presumably been for some hours. She was not hypothermic. Six weeks previously she had been discharged from hospital after treatment for congestive cardiac failure with frusemide. On return home her diuretic was changed to Brinaldix K two tablets daily. When readmitted asymptomatic hypokalamia was found. Her diuretic was changed to frusemide and Slow-K added, with return to normal of plasma potassium levels in five days.

Case 4.—A 58-year-old woman was readmitted to hospital with congestive cardiac failure and chronic obstructive lung disease. She had been discharged one week previously following a period of treatment for the same condition. In hospital she had received frusemide and Slow-K, and this was replaced by Brinaldix K on her discharge. Electrolytes prior to discharge had been normal. When readmitted asymptomatic hypokalaemia was found and reverted to normal values in three days upon withdrawal of Brinaldix K and administration of potassium supplements.

The use of potassium supplements together with diuretic therapy is widely accepted as necessary. It is perhaps less well appreciated that to be fully effective potassium should be given in the form of chloride. Potassium deficiency due to diuretics is often accompanied by hypochloraemic alkalosis. Potassium in the form of bicarbonate may aggravate the alkalosis and thereby worsen the hypokalaemia in spite of the administration of potassium ions.[1]

Each Brinaldix K tablet contains clopamide 20 mg and potassium 12 mEq but only 3·4 mEq of chloride ions. The remaining anion is present as bicarbonate. Clopamide 60 mg is more potent than bendrofluazide 7·5 mg[2], so that it is likely that the patient receiving Brinaldix K is receiving a greater effective amount of diuretic than with other combined diuretic and potassium preparations. We believe that this combination of a more potent diuretic dose together with inadequate chloride and significant bicarbonate content carries a risk of induced hypokalaemia. A striking feature in our patients was the short duration of treatment with Brinaldix K, and the knowledge from previous attendance that prior to receiving Brinaldix K hypokalaemia had not been present in spite of other diuretic and potassium therapy being administered.

While in general deprecating the use of combined diuretic and potassium preparations, we accept that there are some indications for their use, but we feel that in its present form Brinaldix K should not be used in preference to the non-effervescent preparations containing a thiazide with potassium as chloride in a slow-release form. As Brinaldix K is an effective diuretic and pleasant to take, we feel that the chloride content should be increased and the bicarbonate reduced or omitted.—We are, etc.,

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1 Welt, L. G., in *Pharmacological Basis of Therapeutics*, ed. L. S. Goodman and A. Gilman, 4th edn., p. 794. New York, MacMillan, 1970.
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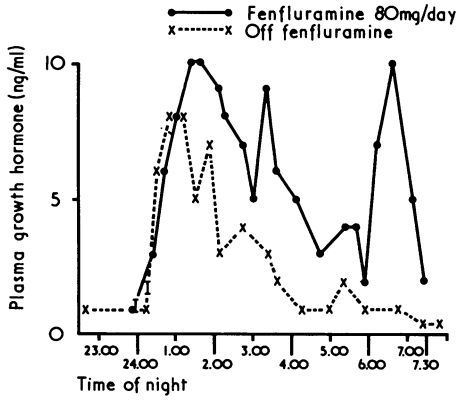
Case	Serum Electrolytes (mEq/l.)			Blood mg/100ml Urea	Dose of Clopamide (mg/day)	Duration of Treatment with Brinaldix K (weeks)	Reversal Time of Hypokalaemia (days)
	Na	K	Cl				
1	140	1·6	85	75	40	3	3
2	136	1·8	85	67	20	4	7
3	139	2·6	93	31	40	6	5
4	140	2·6	94	42	20	1	3

Fenfluramine and Growth Hormone Release

SIR,—Mr. W. R. Sulaiman and Dr. R. H. Johnson (12 May, p. 329) describe the effect of a single intravenous injection of 20 mg of fenfluramine on the metabolic response to exercise lasting 20 minutes and report a suppressive effect of this drug on the secretion of growth hormone normally encountered in response to exercise. They then suggest a hypothalamic site of action for the drug and draw inferences for clinical practice.

We would remind them of almost completely contrary evidence[1] presented in a symposium report from which they quote two references. This other study involved obese patients—to whom fenfluramine is commonly administered. The dose was 40 mg orally four times daily for one week before repeating the exercise study. Plasma growth hormone concentrations showed striking increments with exercise, and these were even greater on the drug—"the differences between the mean values . . . when fenfluramine was added were statistically significant at 1½, 2½, and 4½ hours after the start of the period of exercise." Again contrary to Mr. Sulaimain's and Dr. Johnsons' findings, changes in blood glucose and the plasma concentration of insulin were not found during periods of exercise more prolonged than those they used.

Furthermore, the most vigorous and consistent secretion of growth hormone occurs during natural sleep. Having previously mentioned that chronic intake of fenfluramine, far from suppressing growth hormone secretion during sleep, may lead to increased plasma levels,[2] we now show in the accompanying figure an example where plasma levels (in ng/ml) were consistently higher throughout a night, in the case of a man who had received oral fenfluramine for over two months, than was the case six weeks later when he had been off fenfluramine for a month. Blood was withdrawn without disturbing sleep, using a venous catheter technique.[3]



In studying the mode of action of a drug such as fenfluramine it would seem important that the conditions of administration should resemble as nearly as possible those in which it is commonly used.—We are, etc.,

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1 Brockie, B. K., Brown, P., Ahmed, N. E. L., Shirling, D., and Strong, J. A., *South African Medical Journal*, 1971, **45**, Suppl. (June), p. 26.
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Transmission of Trichuris trichiura

SIR,—Dr. D. M. Lynch and others (14 October 1972, p. 73) described the incidence

of *Trichuris trichiura* infection in hospitals for the mentally subnormal in the U.K. and reported the successful treatment of patients with difetarsone. This note describes the location of the major source of infective eggs of this parasite in one of the hospitals surveyed, Cell Barnes Hospital, St. Albans, and reports the activity of chloropicrin against the eggs.

In a search for the source of infection, the only site within the buildings where fully embryonated eggs were encountered was in the laundry, at a point between the intake of dirty linen and the first wash. However, it was thought unlikely that these numbers of eggs were responsible for the heavy infections seen in some wards. Eggs were also found elsewhere throughout the buildings, but none showed signs of development to the infective stage.

Small soil samples of 1 or 2 g were taken from the play areas of two heavily infested wards, nos. 18 and 1, but no eggs were found. However, because infection with *T. trichiura* via the soil has been accepted for many years as the mode of transmission in the tropics, it was decided to investigate further the possibility that soil from the playgrounds could be the source of infective ova. A 25-lb (11·3-kg) sample of top soil was taken from the play areas of ward 18 and ward 1 and the eggs extracted by a semi-mechanical sieving and sedimentation technique described by Beer[1]. In the sample from ward 18, where the parasite has been known to be present for a number of years, approximately 10,000 fully infective eggs of *T. trichiura* were recovered. In the sample from ward 1, into which infested patients were moved only one year ago, 2,000 fully infective eggs were recovered. In a follow-up examination in which 1-in (2·5-cm) layers were taken from an area approximately 8 in (20·3 cm) square, down to a depth of 12 in (30·5 cm) in ward 18 and 15 in (38·1 cm) in ward 1, infective eggs were randomly distributed in each of the layers. In ward 18, 100-2,000 eggs were found per layer and in ward 1, 25-500 eggs were found per layer.

As pica is commonly practised by subnormal patients and has been frequently observed at Cell Barnes Hospital, it would appear that infection with *T. trichiura* is principally via the soil. Development of these eggs to the infective stage in soil would be a comparatively slow process in the U.K., where the mean ambient temperature is lower than 20°C, as ova require more than 120 days at 15°C and up to 57 days at 20°C before becoming infective.[2]

As far as could be determined from a search of the literature, there appeared to be no compound that was effective against ova of *T. trichiura*. The compound chloropicrin (trichloronitromethane) is used commercially on a contract basis for the treatment of soil nematodes and seemed worthy of evaluation in the laboratory. The large numbers of *T. trichiura* eggs required for this work were not readily available, so we used the more easily obtainable ova of the very closely related species, *T. suis* of the pig[3]. Eggs of *T. suis* in lots of 10,000 were exposed to serial ten-fold dilutions of chloropicrin in water for 24 hours, washed thoroughly, and incubated at 30°C for five days. In repeated experiments 1/1,000 dilutions completely inhibited embryonation, while 1/10,000 was without effect. A similar experiment was undertaken using eggs which had been incubated previously for 14 days, and again a 1/1,000 dilution arrested development of the larvae.

The evidence suggests that chloropicrin should be evaluated for sterilization of the soil in the areas responsible for reinfecting patients. It is known that the eggs of *T. trichiura* can survive for many years in the soil, and failure to sterilize the soil will result in repeated reinfections over long periods. Treatment of soil should therefore be undertaken at the same time as treatment of the patients.—We are, etc.,

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1 Beer, R. J. S., *Parasitology*, 1972, **65**, 343.
2 Dinnik, J. A., and Dinnik, N. N., *Meditsinskaya Parazitologiya i Parazitarnye Bolezni*, 1937, **6**, 603.
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Gram-negative Bacilli on Hands

SIR,—In their interesting report on the skin bacteria of hospital staff (9 June, p. 580) Drs. Johan N. Bruun and Claus O. Solberg conclude that "Gram-negative bacilli should be regarded as frequent members of the resident flora" and that the incidence of "hand-carriage" of such bacilli is increased by the use of hexachlorophane soap. The data presented do not, however, support these conclusions.

Though "coliforms" and other Gram-negative bacilli were isolated from the washed hands of 110 out of 624 staff members, only eight of these consistently yielded Gram-negative bacilli over a period of several months. These "persistent carriers" yielded identical strains throughout this period in only six cases, and five of these individuals actually had clinical paronychia and chronic "skin irritation."

The colonization of skin by Gram-negative bacilli is rare except in areas that are already diseased or damaged.[1 2] In contrast to true carriage, the hands of members of staff frequently yield large numbers of Gram-negative bacilli which are repeatedly acquired from the hospital environment.[3] Drs. Bruun and Solberg have previously shown that the regular use of hexachlorophane preparations is far more effective at preventing the transient contamination of skin by hospital strains of *Staphylococcus aureus* than by Gram-negative bacilli.[4] They have not however shown that Gram-negative bacilli are permanent members of the flora of healthy skin.—I am, etc.,

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Hepatitis-associated Antigen in Chronic Hepatitis

SIR,—We have previously shown a clear difference in the incidence of hepatitis-associated antigen (H.A.A.), as determined by complement fixation, between chronic persistent and aggressive hepatitis.[1] These findings could be explained either on the basis of an aetiological difference between the two forms or because of failure of the technique employed to demonstrate the antigen in all of the cases.

Since then we have studied 66 cases of biopsy-proved chronic hepatitis by both complement fixation (C.F.) and radioimmunoassay (R.I.A.). The latter method gave positive results for H.A.A. in five cases which had been negative by complement fixation. Moreover, we were able to confirm our previous findings of a sharp difference in the incidence of H.A.A. in the two forms of hepatitis (classified according to De Groote *et al.*[2]) (see table).

Therefore it is likely that, in a region like ours (Campania, South Italy) in which there is a high incidence of H.A.A. in chronic liver diseases,[3] chronic aggressive hepatitis is in the vast majority of cases related to virus B, which seems to be associated with only a limited number of cases of chronic persistent hepatitis.—We are, etc.,

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1 Carrella, M., del Vecchio-Blanco, C., and Coltorti, M., *British Medical Journal*, 1972, **2**, 169.
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Disease	No. of cases tested	No. H.A.A.-positive	
		C.F.	R.I.A.
Chronic aggressive hepatitis	42	31 (73·8%)	33 (78·6%)
Chronic persistent hepatitis	24	3 (12·5%)	6 (25·0%)

Androgens and Exercise

SIR,—Dr. J. R. Sutton and others have reported (3 March, p. 520) significant increases in serum androgens in response to maximal exercise in athletes and normal male students. We have recently obtained results on serum androgens in immobilized patients which may illustrate the converse effect.

During investigation of a new radioimmunoassay kit for serum androgens (Sorin, Italy) a series of determinations were conducted on serum specimens surplus to requirements for requested biochemical tests on male inpatients, together with serum from healthy male volunteers. Our results are shown in the table.

Group	No. Tested	Serum Androgen Concentration (ng/ml)	
		Mean	Range
Healthy men	4	4·4	3·6-5·0
Ambulant male patients ..	4	5·5	2·8-9·4
Immobilized male patients	15	0·6	0·2-1·5

Serum androgen levels in the normal men and in the ambulant male patients were all within previously reported normal ranges,[1] but were markedly depressed in immobilized, severely ill male patients. The mechanism of