ticular form. A number of patients are excluded from these results on the grounds of "advanced diseases or other reason." Those exclusions rise as high as 354 out of 892 patients seen with cancer of the hypopharynx (p. 33), so that a considerable element of selection appears to be taking place.

If in future editions of this useful book figures are also given as described by Macdonald,¹ Berkson and Gage,² or MacComb,³ the appropriate corrections can be made when necessary to make these results comparable with other series.—I am, etc.,

Hull,
Yorks.

R. G. WILLIAMS.

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Hookworm Infection

SIR,—I was pleased to read your leading article about hookworm infection. (28 December, p. 788). You state that the overall rate of infection in people coming from overseas is unknown, but 8% of immigrant school children examined in Bradford showed hookworm ova in the stools.

In Cwmbran, immigrants working at catering establishments and some others have been investigated for helminths and organisms since 1965. The Chinese from Hong Kong have been very co-operative and anxious to ensure that they are not infected. The following Table, although the number investigated is small and includes adults and children, may be of interest.

Immigrants Investigated for Hookworm and Whipworm 1965-7

	Hong Kong	India and Pakistan
Total number of immigrants	44	11
Number infected with hookworm	9	4
Number infected with whipworm	24	3
Number infected with both parasites	8	3

You will observe that infection with hookworm varies from one-fifth to one-third of those investigated.

Some immigrants seen and treated in 1965 had been resident in this country for four years. Complaints of abdominal pain were made before treatment in some cases. No immigrant appeared to suffer from anaemia. The incidence of infection varied with social class; restaurant owner/managers and professional persons, for example, doctors and surveyors, were not infected. The four children examined and treated have gained in weight and height since arriving in Cwmbran.

I had always assumed that the hookworm infection was *A. duodenale*. One dose of 5 g. of buphenium hydroxynaphthoate has been sufficient to clear the stools of ova. The treatment of whipworm is more difficult. All Chinese investigated have been treated and the infection eliminated, either by one or two courses of buphenium hydroxynaphthoate, 5 g. nightly for 5 nights, or by referring to

hospital for treatment with dithiazanine iodide. The latter course was necessary in the case of two children.

You state that infection with hookworm in people who have never been out of this country is unusual. Even so, I consider that all immigrants should be investigated and treated to ensure that they are not infected with parasites. One outbreak of whipworm infection in this country in 1968 is known to me. This was of 17 cases at a hospital for the care of the mentally subnormal. The original source of the infection was not elucidated.—I am, etc.,

H. G. JENKINS.

Public Health Department,
Cwmbran, Mon.

Peritoneal Dialysis Assembly

SIR,—We wish to draw your attention to the fact that there is at the present time satisfactory apparatus commercially available for the delivery and drainage of peritoneal dialysis fluid.

Baxter Laboratories Ltd. have developed a complete range of equipment for this procedure, which comprises Dianeal solutions, a Y-type administration set with drainage tubing, catheter, and 3-litre drainage bag. This equipment is designed to relieve the hospital staff of the time-consuming assembly procedures which were described by Mr. R. W. Lloyd-Davies and his colleagues (21 December, p. 757).—We are, etc.,

J. A. WHEELER-BENNETT,
Medical Director.

P. IRVING.

Baxter Laboratories Ltd.,
Thetford, Norfolk.

SIR,—I have seen the letter from Baxter Laboratories Ltd. on this subject. The total cost of their Br61L Y-type administration set with drainage tubing and their 3-litre drainage bag (R-61D) is 25s. 6d. This is twice the cost of the set that is made routinely in the Central Sterile Supply Department of St. Thomas's Hospital. Each set takes but five minutes to make up, and, furthermore, meets our requirements for single-litre exchanges only. I think it is important to stress the ease of making up such equipment from standard components, together with their low cost to the National Health Service, considering the amount of dialysis being carried out at the present time.—I am, etc.,

R. W. LLOYD-DAVIES.

Department of Urology,
St. Thomas's Hospital,
London S.E.1.

Solvents for Ear Wax

SIR,—I have been not a little surprised to find no reference made, other than by Dr. H. G. Morris-Jones (28 December, p. 835), to the use of sodium bicarbonate as a preparatory instillation before syringing.

I was taught to use this very many years ago, and have done so ever since with only one complete failure. Sodium bicarbonate is not, of course, a solvent, but as a preparatory agent it is in my experience unrivalled. Apart from the incident previously mentioned, the

only difficulties I encounter are in those patients who have got an accumulation of desquamated epithelium or whose meati are excessively endowed with hairs. The strength that I advise is half a teaspoonful dissolved in half a cupful of warm water.—I am, etc.,

H. G. WATSON.

Bakewell,
Derbyshire.

Management of Coronary Artery Disease

SIR,—In the article on the management of coronary artery disease (4 January, p. 37) the following comment appears in relation to propranolol: "The dose, however, required to control angina sometimes far exceeds that needed to effect complete beta receptor blockade. Propranolol must therefore exert other actions which contribute to its beneficial effect in this disease, and one of these is a quinidine-like depressant action on the myocardium."

There are two points in this paragraph which require comment in order to prevent confusion in the minds of your readers. Firstly, the dose of propranolol to produce "complete beta receptor blockade" is entirely arbitrary, being dependent on the pre-existing level of stimulation, as is the case with all competitive antagonists. Assessment of beta-blockade may be determined by the extent to which the response to a specific beta receptor stimulant is reduced—for example, isoprenaline tachycardia, or physiological responses to exercise or tilting. Determination of the level of sympathetic stimulation or myocardial noradrenaline release is not a practical possibility at the present time, and there is no way of knowing how closely a provoked response in volunteers matches that present in patients with angina. Secondly, the inference from a difference in dose levels that beta receptor blockade is not the mechanism of action in angina is only tenable if clear-cut differences in dose levels have been shown.

Analysis of seven clinical studies in which isoprenaline tachycardia (0.03 µg./kg.) was used to determine beta-blockade shows the mean dose of propranolol to abolish the response to be 0.12±0.02 mg./kg. intravenously. In four clinical evaluations of intravenous propranolol in 67 anginal patients, objective improvements were observed in 62 patients, with respect to exercise tolerance or E.C.G. changes at a mean dose level of 0.08 mg./kg. In single oral dose trials it was found that 50 mg. propranolol reduced exercise tachycardia to 75% of the reduction observed after sympathectomy.¹ In three clinical single-dose studies objective improvements in exercise E.C.G. patterns were observed in all of 42 anginal patients following the mean dose of 50 mg. propranolol—that is, 0.7 mg./kg. in both contexts assuming a mean body weight of 70 kg.

In chronic trials it must be remembered that dosage recommendations (q.d.s.) are intended to provide 24-hour blockade of sympathetic beta receptor activity as opposed to the short-term effect (up to 2 hours) in the single-dose studies. This is particularly important for a drug with an estimated half-life of only 2-3 hours. In 11 chronic oral trials involving 221 anginal patients 169 showed objective improvements in effort tolerance or E.C.G. at a mean daily dose of 159 mg. (or 2.3 mg./kg.). In 17 double-blind trials 279 anginal patients from a total of 370 had subjective improvements on a mean daily dose of 162 mg. If one assumes that self-dosing provides effective blood levels of the drug for 18

hours per day the average hourly oral intake corresponds to less than 10 mg./hour or 0.15 mg./kg./hour. Bearing in mind that the intravenous dose to produce evidence of beta-blockade was 0.12 mg./kg. it cannot be argued that there is a gross discrepancy between the doses required to control angina and "effect complete beta receptor blockade." The suggestion that anginal relief must be due to some other property of propranolol is not tenable in face of the present evidence.

While it is true to say that a "quinidine-like depressant action on the myocardium" is a property shared by propranolol and verapamil, it is equally fair to comment that reduction in peripheral resistance is a property shared by verapamil and nitroglycerin. Preliminary studies with the D-isomer of propranolol (which does not block beta receptors but has equivalent local anaesthetic action²) indicate that it has no effect on exercise tolerance whereas I.C.I. 50,172 (which blocks beta receptors but has no local anaesthetic activity) is qualitatively equal to propranolol.³—I am, etc.,

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Coronary Disease and Competitiveness

SIR,—It is appropriate that you should start the new year by drawing attention to the excellent studies of Hinkle¹ and his group on the epidemiology of coronary disease among the employees of Bell Telephone in the United States (4 January, p. 1), specially in view of the fact that the results of this research are broadly similar to those in two earlier surveys in large American industries.^{2,3}

Other facts must, however, be taken into account if this work is to be put in perspective. To begin with, Hinkle is at pains to emphasize that what is true of a cohort of men who spend their lives in a single industry, which in effect shelters them from some of the vicissitudes of life, may well not be true of those who are self-employed or change their employers (as opposed to taking different jobs offered by a single employer). In this regard it may be relevant that the overall mortality within the Bell group of companies is much lower than in the United States as a whole.⁴

Then there have been well-designed surveys undertaken by Cassel and Tyroler^{5,6} in North Carolina, and by Syme and his associates in North Dakota^{7,8} and the San Francisco area in California,⁹ which indicate that both improvement in social status and changing from a rural to an urban way of life are separately associated with an increase in the risk of developing coronary heart disease. One interesting aspect of this work is that it seems that the consequences are the same whether a rural community becomes urbanized by the introduction to it of new industry or a countryman leaves his home to seek employment in the town. Like much epidemiological research, the results of these studies are open to different interpretations, but the authors themselves seem to be of the view that competitiveness does cause coronary heart disease.

The real trouble is that all of us are apt to forget the full implications of the fact that coronary heart disease is not only multifactorial in its causation, but, as knowledge stands at the moment, seems to have a more complicated aetiology than any other disease. Certainly the generally accepted risk factors only play a relatively small causal role when the disease is considered as a whole.^{10,11} This means that almost all the many putative "causes" which have been put forward in the literature could have a part to play in some cases at least.

Payne¹² has criticized much of the research in this field in the following words: "The hypothetical influences, which it is desired to investigate, are restricted to one or, at most a very few [previously selected areas], and the effects recorded as measures to these influences are similarly restricted. In other words, a small piece of the ecosystem is being chopped out for study on the implied hypothesis that the rest of the system has no influence on what happens in that piece." If we are to get any further in our understanding of this important disease, "thinking simple" is no longer likely to be of much help.—I am, etc.,

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- ¹¹ Truett, J., Cornfield, J., and Kannel, W., *J. chron. Dis.*, 1967, 20, 511.
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Mandrax and Methaqualone

SIR,—I would like to point out that the clinical observations I reported in my letter (11 January, p. 122) do not refer to the effects of methaqualone alone, but to the combination of methaqualone and diphenhydramine (Mandrax). My experience has been restricted so far to this particular combination. Though methaqualone is the most active of the two components I have no personal evidence to claim that on its own it is responsible for the

effects I described. May I add that in the last month three cases of accidental overdose of methaqualone and diphenhydramine (Mandrax)—all in young people with a previous history of heroin abuse—have come to my notice.—I am, etc.,

R. DE ALARCON.

Medical Research Council,
Clinical Psychiatry Research Unit,
Graylingwell Hospital,
Chichester, Sussex.

Vaginal Candidiasis

SIR,—We do not agree with Dr. M. J. V. Bull's claim (11 January, p. 120) that an increased incidence of vaginal candidiasis in patients on contraceptive steroids is already well-established. Much of the data incriminating oral contraceptives in this respect is based on observations on highly selected and sometimes very small populations. The risk is as yet not fully assessed; it may not apply equally to all the available preparations and may have been over-emphasized.

In a prospective study of 291 women attending a family planning clinic, of which 104 patients were taking oral contraceptives, we were not able to demonstrate a significantly higher incidence of *Candida albicans* in the vagina of patients who were on the pill. *C. albicans* was isolated from the vagina of 10.7% of this total population and 13.5% of patients on oral contraceptives; other yeasts were isolated from an additional 6.9% of the total population studied.¹ One hundred and sixty-six of these 291 women were re-examined after one year and 99 after a second year; there was no evidence that patients on oral contraceptives had been significantly more liable to develop a vaginal discharge than other women, and the numbers of isolations of *C. albicans* were of a similar order to those from the first samples collected. Women with *C. albicans* on one occasion were significantly more likely to have this present a year later than were women with no yeasts on the first occasion ($P < 0.003$), regardless of their contraceptive method. There is evidence that a compound of predominantly oestrogenic activity may have exerted some influence on vaginal candidiasis, but this could only be established with certainty by a study of a much larger population than that available to us.²

Our observations relate to women taking combined oral contraceptives and are not necessarily relevant to patients using sequential preparations. An analysis of the following domiciliary investigation is to be published.³—We are, etc.,

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DELIA F. MORRIS.

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Remuneration of Clinical Teachers

SIR,—The University Grants Committee's proposal to assimilate non-professorial clinical teachers with honorary consultant contracts on to the point on the N.H.S. consultant scale which was nearest to the salary these were paid on 1 October 1968 (*Supplement*, 18 January, p. 21) discriminates most unfairly against those who are at the top of the present university scale—that is, those who have already suffered the greatest loss in income and superannuation because of the differences

that have existed hitherto between the two scales. While a newly appointed non-professorial honorary consultant (senior lecturer or reader) will now rightly reach the top of the N.H.S. scale in 10 years, an honorary consultant appointed, for example, in 1948 (as two of us were) will not reach the top of this scale until 1971—23 years instead of 10.

The U.G.C.'s proposals are clearly at variance with the spirit not only of the Prices and Incomes Board's report but also that of