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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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.,

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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 follow-up domiciliary investigation is to be published.³—We are, etc.,

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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