Total faecal calcium is then given by

$$f = (d + s)(1 - \alpha) + s' \quad (1)$$

The discussion is simplified by taking $s + s' = 287$ mg./day, the value found by Dr. Rose and his colleagues, and $s' = 40$ mg./day, the value derived by Heaney.¹ Equation (1) then reduces to

$$f = (d + 247)(1 - \alpha) + 40$$

$$\text{or, } \alpha d = (d - f) - 247\alpha + 287 \quad (2)$$

Equation (2) is plotted for various values of α and d in the Figure. At constant α values αd on $(d - f)$ is a family of straight lines with gradient unity. The line degenerates to a point, V, at $\alpha = 0$. XY and UT represent the lines for $\alpha = 1$ and $\alpha = 0.5$. At constant d values αd on $d - f$ is a family of straight lines radiating from V ($\alpha = 0$). VW and VY represent the lines for diets of 300 and 1,000 mg./day and α values from 0 to 1.

As the figure shows, αd on $d - f$, when both α and d vary, represents an area, not a single line. This area shrinks to a straight line if s is independent of α . The line then obtained is VZ, the regression line of Dr. Rose and his colleagues.

$$\alpha d = d - f + 287$$

The two interrupted lines represent the upper and lower deviations of the data of the authors.

The authors did not give the range of d studied nor the values of α found, but if d ranged from 300 to 1,000 mg. and α between 0 and 0.5, then all the results obtained would be included in the small shaded triangle, most of which falls within the lower deviation from the mean line. So, two radically different assumptions about the secreted calcium are about equally well confirmed by the data when they are presented as a regression of αd on $d - f$. Therefore, it seems unjustified to accept the conclusion of Dr. Rose and his colleagues.

The danger of trusting correlation coefficients is well illustrated by the other correlation demonstrated by the authors (see their Fig. 5, line B). The correlation coefficient is again 0.95 but the correlation is spurious because it leads to an impossible conclusion. The equation of line B is

$$\alpha d = 0.82(d - f) + 250 \text{ mg./day}$$

When $\alpha = 1$ —i.e., when dietary absorption is complete—the equation reduces to

$$d = 0.82d - 0.82f + 250$$

$$\text{or, } f = 300 - 0.22d.$$

—i.e., f is still dependent on d . This is absurd because if all the dietary calcium is absorbed none can appear in the faeces—i.e., if $\alpha = 1$, f cannot be dependent on d . This does at least suggest that the correlation in Fig. 4 which is equally good is equally spurious.

It is interesting and possibly significant that Dr. Rose and his colleagues' Fig. 5, referring to isotope given with a whole day's milk seems more compatible with my hypothetical figure than their Fig. 4. The gradient of VY is 0.80; line B in Fig. 5 (really a narrow triangle) has a gradient of 0.82. This may suggest, and I put this forward very tentatively, that absorption measured after an overnight fast is an overestimate compared with that averaged over a whole day. The authors may be able to confirm this.

I conclude that the results of Rose *et al.*, when presented differently, are likely to be quite compatible with those of the authors I quoted.—I am, etc.,

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Hookworm Infections Acquired in Britain

SIR,—The letter from Professor J. J. C. Buckley and Mr. F. R. N. Pester (10 July, p. 106) recording hookworm infection in two children acquired in this country compels a reappraisal of the possibility of its more widespread dissemination. In a consecutive series of 139 adult male immigrants applying for employment I found 49 (approximately 36%) were excreting hookworm ova.

When washed hookworm ova are placed in 5% formol saline growth and active movements of the embryos continue for five hours or more at room temperature. If the ova were protected by being embedded in a mass of faeces their survival would presumably be much longer.

It therefore seems a possibility that temporary camping sites, construction sites, or any place where the contents of pail or chemical closets are dumped or buried could be potential sources of infection under suitable climatic conditions.—I am, etc.,

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Absence of Carcinogenic Properties of Propranolol in Mice

SIR,—Alderlin (pronethalol) has been shown to produce thymic lymphosarcomata and reticulosos in mice,¹ and it has been suggested that this may be related to the production of a reactive ethyleneimine as a transient breakdown product.² Inderal (propranolol) is probably broken down in much the same way, but the resulting intermediate product would be expected to be much less reactive and therefore might not produce tumours. This hypothesis is supported by an experiment on similar lines to those of Alcock and Bond¹; there is no significant difference between mice treated with propranolol and a control group.

Specific pathogen-free mice of the Alderley Park strain were used. The drug was given by stomach tube for ten months and for a further nine months was administered in the diet as follows: 30 male, 29 female mice given 150 mg./kg. by tube for 10 months and 0.2% in diet for nine months; 28 male, 28 female mice given excipient only by tube for 10 months and control diet for nine months.

During the 19-month period of treatment there was no significant difference between the animals given propranolol and the control group. The incidence of tumours was equal and fitted into the pattern with which we are familiar in this strain of mice. In the series reported by Alcock and Bond¹ thymic tumours began to appear 75 days after the start of treatment with pronethalol and by the end of the experiment 11.1% of the animals had died with thymic tumours.

With the observation that pronethalol caused tumours in mice its use in man was necessarily restricted, although there is no evidence that any species other than mice are susceptible. No tumour attributable to it was seen in rats dosed with the drug (0.2% in the diet) for 18 months. Apart from giving reassurance that propranolol is free from this hazard, these experiments highlight how relatively minor structural changes can alter toxicity as well as pharmacological activity.—We are, etc.,

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Scared to Death?

SIR,—We would like to report a case of an apparently healthy middle-aged woman dying with massive adrenal haemorrhage, following a relatively minor operation, who was subsequently found to have had forebodings of death.

Mrs. A. B., aged 43, mother of five children, was admitted to North West River Hospital, Labrador, on 18 March 1965. She had been complaining of severe stress incontinence for several months. She had been treated during the past three years for anxiety which responded well to reassurance and mild sedation with phenobarbitone, 30 mg., three times daily. There was no relevant past medical history. On examination she was found to be in good health. Vaginal examination revealed a moderately large cystocele and urethrocele. On 19 March anterior colporrhaphy was performed under general anaesthesia. The premedication was pethidine, 100 mg., and atropine, 0.65 mg.; induction with intravenous thiopentone, 400 mg., and Flaxedil (gallamine triethiodide), 40 mg.; maintenance with nitrous oxide, oxygen, and a trace of trile, accompanied by intermittent intravenous pethidine to a total of 80 mg. The operation, which lasted less than one hour, was straightforward with minimal blood loss. Her blood-pressure remained around 120/70 throughout the operation, and pulse and respiration were normal. She regained consciousness before leaving the theatre. One hour later she became shocked and her systolic blood-pressure fell to 70 mm. Hg. She remained conscious, but shortly afterwards complained of severe pain in the left hypochondrium. Methedrine (methamphetamine) was immediately given, 15 mg. intravenously, and 15 mg. intramuscularly, and the foot of the bed was raised. As the blood-pressure showed no response Aramine (metaraminol), 10 mg., was given intramuscularly. An infusion of dextran, 500 ml., with hydrocortisone, 100 mg., was started. Despite continuous infusion with metaraminol and hydrocortisone no improvement was obtained and intranasal oxygen was required as the patient became cyanosed. The pain was partly controlled by injections of morphine, 16 mg., given on three occasions. The E.C.G. was normal. Her condition deteriorated and her temperature rose to 103.6° F. (39.8° C.) by midnight, when she became comatose. She died at 5 a.m. on 20 March.

At post-mortem examination the adrenal glands showed extensive haemorrhage. Petechial haemorrhages were found in the stomach, ileum, liver, and in the skin of the nose. There was no other pathology.