Correspondence

Letters to the Editor should not exceed 500 words.

Mammography as a Screening Test for Breast Cancer

SIR,—Your leading article on mammography as a screening test for breast cancer (27 August, p. 484) is very welcome, as it shows that some attention is being focused on an important technique which has achieved considerable acceptance outside this country, but relatively little within it.

We feel, however, that your leader writer has emphasized the technical difficulties and failed to stress the implications, and that the relatively recent New York survey should have been considered with earlier work done in Philadelphia, New York, and Detroit,[1-4] especially the Philadelphia survey in which a ten-year follow-up has been completed and modern methods of localization of small carcinomas developed. Pick-up rates would appear to be between two to four per 1,000 cases screened, and they compare favourably with other screening surveys, such as those for anaemias, diabetes, chest lesions, and cancer of the cervix.[5-7] It would seem therefore on statistical evidence alone that more effort directed towards the early diagnosis and preventive aspect of breast cancer would be justified, and this should no longer take second place to the expensive and heroic surgical and radiotherapeutic measures which of necessity are still in use and often still advocated indiscriminately for both localized and advanced disease.

We are in full agreement that a method of selection of subjects at high risk would greatly increase the pick-up rate in any mammography survey and make it much more feasible. Although hormone assays and buccal smears, as mentioned in your leading article, are both possibilities, we would point out that thermography might be a profitable line of approach. Further simple criteria already known can be applied and will substantially increase the yield. We would suggest from our experience of over 2,000 mammograms that these criteria are:

1. All patients who have had one breast removed for carcinoma should have the contralateral breast *x*-rayed regularly. Although simultaneous bilateral carcinoma is uncommon (probably about 1%), metachronous carcinoma in the remaining breast is far from uncommon and the incidence rate ranges from 7% to 9%.[8] It is unfortunate that more centres dealing with breast disease in this country and abroad do not use this simple mode of follow-up.

2. All patients who have a discharge from the nipple or develop pagetoid changes or retraction of it should have mammograms done. This can be most rewarding.[9]

3. Patients who have a family history of breast cancer or cancerophobia should have mammograms taken. We feel your leader writer's comment on this aspect of breast disease is misleading, as familial incidence in breast carcinoma has been reported[10]

4. Patients who have persistent pain or discomfort (possibly cyclical) or evidence of breast dysplasia, especially fibrocystic disease,[11 12] should be examined by mammography.

Your leading article "Lumps in the Breast" (2 July, p. 1) has given rise to a spate of correspondence. It is perhaps significant that not until eight weeks had passed did a letter tentatively suggesting mammography in such cases appear (27 August, p. 522). To most clinicians and surgeons carcinoma is almost synonymous with a lump, and the idea that carcinoma of the breast can have an impalpable *in situ* stage[13] is foreign to them. It has now been amply demonstrated that carcinoma at this stage can be either positively identified radiologically or a very high index of suspicion of its presence and position can be entertained.

Although we all subscribe to the dictum that all lumps of the breast must be biopsied, to accept the same ruling for an area in a breast under suspicion from mammography has yet to be accepted. But this is essential if we are to make full use of the early detection of breast cancer by surveys, and the development of operative techniques to identify these areas at operation and treatment by simple surgery are imperative.[14] Early detection of this malignancy is now a practical possibility. If we continue to be content to await the development of a lump we shall have to be content with a prognosis which has not materially altered over the last thirty years.—We are, etc.,

ERIC SAMUEL.
G. B. YOUNG.

Radiodiagnostic Department,
The Royal Infirmary,
Edinburgh 3.

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Self-perpetuation of Bromism

SIR,—The four cases of bromism reported by Dr. G. Nuki and others (13 August, p. 390) were of considerable interest to us. In this area many bromide-containing proprietary medicines continue to be available without prescription, and the complications of chronic intoxication present themselves in both general medical and psychiatric practice. A recent admission to the hospital is felt to be worthy of report for two reasons. Dr. Nuki observes that a bromide rash may be helpful in diagnosis. In our case the bromism had presented and initially been identified by the skin manifestations. Further we feel it to be an illustration of the dangers of dehydration in persons with bromide intoxication. Although prior to surgery the serum bromide levels in this man had fallen below the generally accepted toxic levels, a post-operative dehydration appears to have precipitated a florid delirium.

A 60-year-old man who had not worked regularly for 15 years because of weakness and aching limbs was admitted to hospital for an evaluation of chronic peptic ulcer disease and nodular skin lesions. There was an eight-year history of skin disorder, although the gross lesions had appeared only within the previous three months. On examination he appeared cachectic and chronically ill. The skin lesions, mainly over the anterior aspect of the legs, were multiple, crusty, and irregular verrucous lesions approximately 2 cm. in diameter. The tendon reflexes were reduced in the legs, and his behaviour was mildly confused.

A biopsy of the nodules showed marked acanthosis of the hyperkeratotic dermis consistent with diagnosis of bromaderma. The serum bromide level was found to be 93 mg./100 ml. and questioning revealed that a "sleep mixture," which he had taken for many years, sometimes consuming 3 to 4 oz daily, contained approximately 4.5 g. of bromide per fluid ounce. Treatment with sodium chloride and mercurial diuretics reduced the serum bromide to 53 mg./100 ml. over the next four days, and it was felt safe to prepare the patient for surgery of his chronic duodenal ulceration. Three days later he underwent a pyloroplasty and vagotomy. Forty-eight hours after the operation he was restless, paranoid, and combative, making his medical management very difficult. He had removed his wound dressing and also the intravenous catheter from his arm. He appeared clinically dehydrated with characteristic halitosis and sordes of bromism. Serum electrolytes were not grossly disordered nor was his fever severe (99° F). The serum bromide estimation at this juncture was 13 mg./100 ml. He was sedated with chlorpromazine and rehydrated by intravenous infusion, upon which his delirium cleared. Retrospectively he spoke of confusion, delusional fears, and hallucinations extending over several years. Ironically, with each exacerbation of his "nervousness" he had been prone to increase his self-medication with his "sleeping mixture."

This patient's bromide poisoning only came to light after he developed associated skin lesions. He had experienced mental symptoms for some years but had been able to cover these up prior to hospitalization and surgery. Dehydration then precipitated an acute delirium despite a falling serum bromide level. Although other factors may have been at work, this case suggests that following prolonged bromide intoxication the serum levels may not accurately reflect the residual central nervous system involvement,

in this situation magnified by the post-operative complications. Further, the point is made that the taking of bromides is frequently a self-perpetuating cycle, the patient medicating the symptoms of intoxication with further doses of the bromide mixture.—We are, etc.,

PETER C. WHYBROW.
JOHN A. EWING.
University of North Carolina, U.S.A.

Protective Response to Revaccination

SIR,—In the abridged report of Dr. D. Thomson's comprehensive Milroy Lectures (20 August, p. 427) it is stated that with smallpox vaccination "early protection ensures a much quicker response, with little risk of complications, when secondary vaccination is needed as a result of possible exposure to smallpox in later life." It would be valuable to have the evidence that a "much quicker response" occurs. As has been said,[1] everybody would like this to be true, but revaccination is not like giving a reinforcing immunizing injection, when the level of existing antibody will be rapidly "boosted," for the virus has to grow in the skin in order to produce immunity. This is more difficult, not less difficult, in those who have been previously vaccinated.

It might be expected from first principles that successfully revaccinated individuals show an accelerated production of antibody as compared with that following primary vaccination. There is, as far as I know, one small laboratory study by K. McCarthy *et al.*[2] which supports this view, but unfortunately there are no data on the relationship between levels of antibody and protection against smallpox in man, nor of the time interval between primary vaccination and revaccination when an accelerated antibody response might be expected to take place. It is certainly unlikely to outlast the period of partial protection—say, 25 years after primary vaccination. It is of interest to note that "when secondary vaccination is needed as a result of possible exposure in later life" the data published by the Ministry of Health[3] in the 1961–2 outbreak show that the protection of contacts by vaccination in the incubation period was "apparently unaffected by the previous vaccinal state."

Perhaps Dr. Thomson in his lecture provided the data which shows that early protection ensures an accelerated protective response on revaccination. This would be most welcome in formulating a rational vaccination policy.—I am, etc.,

Middlesex Hospital, London W.1. GEORGE DICK.

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Inheritance of Diabetes

SIR,—Dr. A. M. Cooke and others (17 September, p. 674), in their valuable survey of diabetes in children of diabetic couples, have dispelled the fears generated by previous theories, which assumed a single recessive mode of inheritance of diabetes, by showing that only a relatively small minority of children born to diabetic couples become diabetic in turn. They, in common with others, accept that heredity plays a role in diabetes because, compared with those cases the incidence of diabetes is less in children with only one diabetic parent, and less still when neither parent is diabetic; but while expressing their doubt about the likelihood of diabetes being transmitted as a single recessive gene, are still prepared to admit the possibility of such a gene only with low penetrance. Recent thought on the matter favours the idea that not one but a number of factors may be concerned in this metabolic disorder, and the high incidence of early diabetes among the offspring of those who themselves develop the disease early in life is in favour of such an assumption.

The paper raises many questions which it may be possible to answer by yet more extensive and detailed surveys, and in this connexion it would be of interest to take special note of the outcome of first-cousin marriages among diabetics, whose children might be expected to show the disease in a frequency lying somewhere between that observed in identical twins and that found in the offspring of unrelated diabetics.—I am, etc.,

Selly Oak Hospital, Birmingham 29. A. M. NUSSEY.

Disease Spectrum of Arthritis

SIR,—In common with their earlier communications, the recent letter from Dr. P. R. J. Burch and Dr. N. R. Rowell (6 August, p. 362) is both stimulating and based on plausible reasoning, but certain assumptions are involved and these have not been adequately examined.

The essential building blocks used by Drs. Burch and Rowell are the age and sex distributions of clinical assessments of inflammatory polyarthritis (I.P.) and interpretations of erosive changes on radiographs, erosive arthritis (E.A.). In using these data they make the same assumptions that have hitherto been made about the American Rheumatism Association (A.R.A.) criteria for the diagnosis of rheumatoid arthritis (R.A.)—that is, that they are describing meaningful and homogeneous entities. Drs. Burch and Rowell suggest that the A.R.A. criteria for R.A. refer to a complex of diseases and conditions, a point for which there appears to be fairly widespread acceptance, judged by the decisions at the recent Third International Symposium on Population Studies in the Rheumatic Diseases in New York.

On the other hand, Drs. Burch and Rowell do not seem to approach I.P. and E.A. with the same critical faculty. The gradings of both I.P. and E.A. were derived empirically from preconceived notions about disease patterns. This was a valuable pragmatic approach, but one that requires validation. Admittedly the very regularity of the data could encourage them in their belief that I.P. and E.A. both represent meaningful entities, but more detailed analyses, which were not available to Drs. Burch and Rowell, hardly support this view, nor do they permit the conclusion that I.P. and E.A. are different entities just because their age and sex distributions appear to differ.

Although some healing may occur, the nature of erosive changes on radiographs is such that an *x*-ray at any given time will reveal the cumulation of all past as well as present E.A. In contrast, the ability of the clinical observer to detect past inflammatory polyarthritis is less sensitive, as previous involvement does not necessarily leave residual physical signs. Thus some of the differences between the patterns of I.P. and E.A. may reflect this difference in sensitivity, the lesser increase in the age-specific prevalence of I.P. at older ages, when compared with E.A., representing some degree of healing that is not apparent on the radiographs. A discrepancy in the opposite direction may occur in early cases, in which I.P. may be observed before erosions have had time to develop. On the other hand, neither of these factors would explain the sex differences.

There is an inconsistency in the implications of some of the existing data on E.A. that has not been emphasized. The prevalence of E.A. shows an almost linear increase with increase in age, and reaches a value approaching unity (at the grade 1+ level) at about the end of a normal life span. This might be interpreted as suggesting that almost 100 per cent. of the population were susceptible to the development of erosive changes, if only they lived long enough. On the other hand, in family studies both in Wensleydale and in the Manchester region[1] E.A. was the characteristic that showed the highest degree of familial aggregation (about three or four times the expected rate in neighbouring population samples). This would certainly be surprising if the majority of the population were at risk to developing this characteristic.

Perhaps a more disturbing observation for clinicians is the lack of sex differential in the distribution of E.A., whereas R.A., as observed in hospital patients, and I.P., observed in the population, both show a marked female preponderance. The assessments of E.A. were a composite, the worst grade observed in radiographs of different regions, which potentially could introduce heterogeneity. In fact when one considers the separate distributions of E.A. by the site of its occurrence[2] one is struck by the following:

(i) Mild degrees of E.A. showed an almost linear increase in prevalence with increase in age at each of the three separate regions surveyed—the cervical spine, the feet, and the hands—although the prevalence in any one region at the end of a normal life span was very far from unity. In addition, there was usually no relation between the occurrence of mild E.A. in one region and in either of the other two regions. This suggests that what has been described as E.A. of mild degree (grade 1 and many grade 2 changes) is an age-related trait, perhaps with different subpopulations susceptible to its occurrence in each of the different regions. The lack of a sex differential and the absence of any correlation with I.P. or with rheumatoid factor makes one wonder whether E.A. of this degree is related in any way to R.A.

(ii) A small group differed by showing coincident changes in both hands and feet considerably more frequently than would be expected from random occurrence (the analyses for coincidence have not so far been extended to include the neck). The individuals with coincident changes had more severe degrees of abnormality (55% showed grade 3 or 4 changes at both sites), and they also showed a highly significant correlation both with I.P. (at the grade 2+ level) and with seropositivity for rheumatoid factor (sheep cell agglutination test). Even more interesting, a female preponderance similar to that