abbreviated letters, so long as I have no other symptoms than pulse irregularity, I ignore.

I gather that quinidine is "out" and lanoxin is "in" for these arrhythmias, but I note with interest Dr Grant's experience with disopyramide.

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Aetiology of appendicitis

SIR,—Mr F T deDombal and Dr A J Hedley (24 March, p 820) dispute the assertion by Mr D P Burkitt and others that "the geographical distribution of appendicitis indicates that it is a disease associated with Western culture" (3 March, p 620), and cite recent reports published from a number of non-Western countries attesting to the frequency of acute appendicitis, found to be the commonest cause of hospital admission for acute abdominal pain.

This is also our experience with Canadian Indians and Eskimos in recent years. "Epidemics" of acute appendicitis, the appendix often being ruptured by the time the patient reached hospital, were noted in northern Alberta Indians in the 1950s, sub-arctic Indians and Eskimos of the western Arctic in the 1960s, and eastern arctic Eskimos in the 1970s, corresponding in each population group to drastic changes in diet and life style. This contrasts sharply with our experience in the early 1950s, when I saw during two years caring for more than 3000 Eskimos and Indians in the western Arctic and lower Mackenzie River area only three cases of appendicitis—all in children at native residential schools—while none occurred in the majority of children and adults staying at home.

Similarly, not one case of appendicitis was observed from 1928 to 1958 in a mission hospital in Pangnirtung caring for 4000-5000 Eskimos in Canada's eastern Arctic. But in 1964, for example, in an eight-week journey aboard a supply ship visiting the same shores three emergency appendectomies had to be performed in addition to numerous cases shipped annually to the new Frobisher Bay Hospital, where appendicitis has become the most frequent operation and commonest cause of hospital admissions for acute abdominal pain just as a decade earlier in the western Arctic.

Our observations in northern Indians and Eskimos—spanning a generation—of a marked change in the epidemiology of appendicitis, linked in each population group to drastic changes in diet and life style, are in accord with the ideas of Mr D P Burkitt and others that differences in geographical distribution of a number of intestinal diseases—such as diverticulosis, cancer of the colon in the older, and appendicitis in the younger age groups—may be associated with diet and the way of living of modern man. There is, however, a noteworthy difference: northern hunting populations, especially the almost exclusively carnivorous Eskimos, ingested in their traditional diet no more fibre than modern Western man, in contrast to most non-Western population groups, which led Burkitt and others to their epidemiological deductions. We found that intestinal transit times were nevertheless much shorter in traditionally living Eskimos than in modern urbanised Eskimos owing both to dietary patterns (polyunsaturated fatty

acids in fish and game, especially sea mammals) and to activity patterns.

Considering the marked changes in the epidemiology of appendicitis as well as cholecystitis, diverticulosis, and cancer of the colon and rectum,² in Eskimos during the last generation, one must wonder if the relatively high incidence of appendicitis in non-Western countries cited from recent reports by Mr deDombal and Dr Hedley reflects new developments in the same way as in our northern native population groups.

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¹ Schaefer, O, et al, in *Proceedings of IV International Symposium on Circumpolar Health, Novosibirsk, October 1978*, in press.

² Schaefer, O, et al, *Canadian Medical Association Journal*, 1975, **112**, 1399.

SIR,—One aspect of the geographical distribution of appendicitis appears to be overlooked by Mr D P Burkitt and others (3 March, p 620). This is the undoubted decrease in the incidence of the disease in Britain and the West over the past few decades. I summarised the evidence for this decrease in 1976.¹ On the basis of published estimates of case-fatality rates in the British and North American literature it seems that the incidence of appendicitis in Britain increased from the late nineteenth century up to about 1940 (in accord with the dietary hypothesis), but the incidence has decreased since about 1940.

While part of the decrease may be due to changes in diagnostic criteria and nomenclature¹ it must be true that, as Mr F T de Dombal writes (24 March, p 820), the relation between appendicitis and modern Western culture is undoubtedly far more complex than any simplistic association.

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¹ Donnan, S P B, and Lambert, P M, *Population Trends*, 1976, **5**, 26.

Psoriasis and cancer

SIR,—I read with considerable interest the paper by Professor Sam Shuster and colleagues (7 April, p 941), and also the previous paper by Chapman et al.¹ The question has been raised² as to whether or not psoriatics are possibly relatively resistant to cancer in the same way as they seem to be less prone than average to solar keratosis³ and as some prokaryotes, for example, are less susceptible to radiation-induced mutational damage to the DNA. Naturally, considering only lesions induced in skin this, in a sense, could be a side effect, "trivial" but obviously useful—related perhaps to the enhanced skin cell turnover of psoriatics. On the other hand, if a more fundamental and possibly general cancer resistance were true, the relation of psoriasis to HLA haplotypes is of added interest and would need an explanation.² The observations on impaired aryl hydrocarbon hydroxylase activity in psoriatic skin¹ introduce a further special point in relation to HLA.

It would therefore be most interesting to know whether Professor Shuster and his colleagues have had an opportunity of HLA testing their psoriatic patients in whom they

have studied the aryl hydrocarbon hydroxylase. Even if numbers are small the data might be informative.

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¹ Chapman, P H, Rawlins, M D and Shuster, S, *Lancet*, 1979, **1**, 297.

² Polani, P E, in *Human Genetics: Possibilities and Realities* (discussion), Ciba Foundation Symposium No 66, ed R Porter and M O'Connor. Amsterdam, Excerpta Medica, in press.

³ Koscard, E, *Australian Journal of Dermatology*, 1976, **17**, 65.

* * * We sent a copy of this letter to the authors, whose reply is printed below.—ED, *BMJ*.

SIR,—We have done HLA studies on most of the patients with psoriasis in whom we showed a decrease in epidermal aryl hydrocarbon hydroxylase activity.¹ The results, which we will publish shortly, show an increase in BW17 frequency. In our paper we also suggested that the same abnormality of aryl hydrocarbon hydroxylase activity with its consequences for cancer protection is a possibility requiring testing in other organs; but, unlike Professor Polani, we would consider protection against cancer of the skin as major enough—if only because 2% of the population could be a little more optimistic about the future of photo-chemotherapy for psoriasis.²

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¹ Chapman, P H, Rawlins, M D, and Shuster, S, *Lancet*, 1979, **1**, 297.

² Rogers, S, et al, *Lancet*, 1979, **1**, 455.

Defects in copper winding of intrauterine devices

SIR,—During recent months we have been concerned at finding apparent breakage and loss of the copper winding from Gravigard intrauterine devices removed from patients attending family planning clinics. In each of our cases the intrauterine device had been inserted more than three years previously. The amount of copper winding lost has varied from a small deficiency to almost total loss.

We would be interested to know if others have found similar defects in the copper winding of devices left in situ for more than two years.

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Estimating gestational age

SIR,—I would like to support Professor C J Roberts and others in a plea for accurate obstetric dating (14 April, p 981). Dating is so important, not just for such screening programmes, but also in distinguishing "small-for-dates" gestation from mistaken dates and, of course, for reducing unnecessary induction of incorrectly diagnosed prolonged pregnancy. Most tests of fetal well-being likewise depend on an accurate knowledge of gestational age.

I was surprised at the high error in these workers' ultrasound dating until I realised that the biparietal diameter was measured on a static B scan display. Greater accuracy may be obtained by combining this static display with the A scan display using the method described by Campbell.¹ A further advantage of using an A scan display is that fetal life may be confirmed from 7 weeks from the last menstrual period onwards.

I would like to make an appeal for far more extensive ultrasound screening—hopefully, of all pregnancies in those referred sufficiently early. This could be done in the first trimester by the method described by Robinson² using crown-rump length measurement. I feel that the "spin off" obtained by early routine ultrasound examination would be of extreme help not only to the obstetricians but also to the paediatricians who have to care for the patient next.

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¹ Campbell, S, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1968, 75, 568.
² Robinson, H P, *British Medical Journal*, 1973, 4, 28.

Sauna habits of Finnish women during pregnancy

SIR,—The possible teratogenic effect of hyperthermia has been discussed in a leading article (9 December, p 1586). It is evident that in animals maternal hyperthermia can cause malformations in the fetus.¹ The role of hyperthermia as a cause of congenital malformations in man has not yet been elucidated.^{2,3}

Sauna bathing (10-30 min at 70-100°C) raises the body temperature by 0.5-1.3°C for 10-30 min.⁴ This short-term hyperthermia has been claimed to be able to cause congenital malformations, especially anencephalus.² In Finland the frequencies of the congenital malformations which may be caused by hyperthermia are low, the incidence of anencephaly being only 0.32/1000 births.^{5,6} Furthermore, pregnant women in Finland regularly take sauna baths. However, exact data on the sauna habits of these women are lacking.

To get some numerical data we made a questionnaire survey of 100 women a few days after delivery, inquiring about the sauna habits before and during the first and second halves of the pregnancy. Eighty-nine women took saunas regularly before pregnancy, so that their body temperature should have risen by 0.5-1.3°C.⁴ During the first and second halves of pregnancy the numbers of women were 84 and 59 respectively, as shown in the table. During the pregnancy there was a clear trend to shorten the visits to the sauna and to reduce its temperature. Only 16 women did not mentally and physically enjoy sauna during pregnancy as much as before pregnancy.

It is evident that so-called hyperthermia-associated congenital malformations are rarer in Finland than in other parts of the world.⁶ Finnish people take, and have taken for at least 2000 years, hot sauna baths once or more weekly. Our study shows similar behaviour

also during pregnancy. We think that there are no scientific reasons to change the habits of Finnish women who enjoy the mentally and physically refreshing effects of sauna also during pregnancy.

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¹ Edwards, M J, *Archives of Pathology*, 1967, 84, 42.
² Miller, P, Smith, D W, and Shepard, T H, *Lancet*, 1978, 1, 519.
³ Leck, I, *Lancet*, 1978, 1, 671.
⁴ Hasan, J, Karvonen, M J, and Piironen, P, *American Journal of Physical Medicine*, 1966, 45, 269.
⁵ Rapola, J, Saxén, L, and Granroth, G, *Lancet*, 1978, 1, 1162.
⁶ Granroth, G, Hakama, M, and Saxén, L, *British Journal of Preventive and Social Medicine*, 1977, 31, 164.

Naproxen and renal impairment

SIR,—I refer to a short report by Drs Robert D Brandstetter and Dexter D Mar (28 October, p 1194), in which the statement is made that the propionic-acid-derivative non-steroidal anti-inflammatory drugs (NSAID) fenoprofen and naproxen have been associated with renal papillary necrosis. The reference for this statement is a paper by Wiseman and Reinert.¹

I have checked the Wiseman and Reinert reference and find a mention of fenoprofen and other NSAID (not naproxen) as having produced renal papillary necrosis in rats, but also the statement that definite evidence linking NSAID to renal papillary necrosis in man is lacking. That article also presents data linking sudoxicam with renal papillary necrosis in rats. Naproxen, however, is not mentioned at all in that article. Unpublished Syntex data do document papillary necrosis in mice and rats similar to that seen with other NSAID, but only as toxic changes following extremely high dosage levels.

Since the above-quoted inaccurate statement from your article by Drs Brandstetter and Mar may cause unwarranted concern about the safety of naproxen—to the best of my knowledge there has been no publication linking naproxen to renal papillary necrosis in man—we at Syntex would appreciate it if a correction could be printed.

S JOHN INGRAM

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¹ Wiseman, E H, and Reinert, H, *Agents and Actions*, 1975, 5, 322.

* * * We sent a copy of this letter to the authors, whose reply is printed below.—ED, *BMJ*.

SIR,—Dr Ingram's letter is correct in stating that the paper by Wiseman and Reinert does not mention naproxen. In the process of limiting the number of references, the second reference for the statement that naproxen has been associated with renal

papillary necrosis was deleted. This reference was to a paper by Feldman.¹

The usefulness of animal toxicity studies in detecting vulnerable organ systems depends on the similarity of drug metabolism in the test animal or animals and in man. Although the predictive value of these tests is by no means absolute, their results can create an awareness of potentially vulnerable organs in man. This potential can be illustrated by phenylbutazone toxicity studies that indicated nephrotoxic action in animals, which was later confirmed by a case of phenylbutazone-induced papillary necrosis in man.²

Furthermore, and more in keeping with the emphasis of our report, Kimberly *et al*³ have reported the reduction of renal function in patients with systemic lupus erythematosus who were taking propionic-acid-derivative NSAID, including naproxen. No such NSAID is known to cause papillary necrosis in man; however, their adverse renal effects are now well established owing to warranted concern about their effects and their safety.

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¹ Feldman, D, *Naprosyn® (naproxen): Monograph and Clinical Practice Handbook*. Palo Alto, Syntex Laboratories Inc, 1976.

² Morales, A, and Steyn, J, *Archives of Surgery*, 1971, 103, 420.

³ Kimberly, R P, *et al*, *American Journal of Medicine*, 1978, 64, 804.

Anaphylactic reactions to wasp and bee stings

SIR,—Supplementing your expert's answer given on this subject (17 March, p 726), I would like to suggest that for a patient threatened with anaphylaxis from insect stings the easiest and fastest method of emergency treatment is with a Medihaler-Epi, which contains free adrenalin.

Adrenalin is indeed the drug of choice in anaphylaxis¹ as it controls both the respiratory and the circulatory manifestations; it is therefore preferable to salbutamol. Ideally adrenalin should be given by injection, and indeed for many years the allergy clinic at St Mary's Hospital advised the use of subcutaneous adrenalin for severe reactions to bee and wasp stings. Patients were supplied with syringes and adrenalin and instructed and supervised in their use. To the ordinary layman the giving of an injection remains a traumatic and difficult procedure. Moreover, in severe cases the onset of respiratory and central nervous system symptoms may be so swift (45-60 seconds) that there will barely be time to draw up the adrenalin. Now a Medihaler-Epi is prescribed and old patients returning to the clinic are delighted when they are offered an inhaler for emergency treatment. Many say that the syringe and ampoule were too cumbersome to carry at all times and most doubt whether, in the fear and panic following a sting, they could have given themselves an injection efficiently—or at all. Patients who are acutely sensitive are therefore advised to carry their inhaler at all times and to take three puffs immediately if they are stung; this can be repeated in 20-25 minutes if necessary.

Although insect venom sensitivity can appear quite unexpectedly, it usually increases with each successive sting until the frightening occasion when visual disturbances, vomiting, and unconsciousness occur. As a rule of thumb, it is adequate to

Sauna habits of 100 Finnish women before and during pregnancy

	No of women						
	Time in sauna (min)		Temperature in sauna (°C)		Visits per week		
	10	≥10-30	70	≥70-100	0	1	2
Before pregnancy	8	92	11	89	0	43	51
During first half	16	84	14	86	0	46	45
During second half	35	59	19	75	6	45	37
							12