pyrimidine monoadducts, by subsequent light irradiation.^{1,3}

The conversion of psoralen DNA-monoadducts to DNA-crosslinks is not without potential problems. For some as yet unknown period of time photosensitised skin may continue to be further damaged by exposure to either direct or indirect sunlight as the conversion of monoadducts to crosslinks occur. Physicians would be well advised to realise that the cessation of black light irradiation is not the end of the treatment unless the lesions are kept in the dark, perhaps for several weeks.

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¹ Ashwood-Smith, M J, and Grant, E, *Experientia*, 1977, **33**, 384.

² Ashwood-Smith, M J, et al, *Mutation Research*, 1977, **43**, 377.

³ Ben-Hur, E, and Elkind, M M, *Mutation Research*, 1973, **18**, 315.

⁴ Cole, R S, *Biochimica et Biophysica Acta*, 1971, **254**, 30.

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Remission of psoriasis during haemodialysis

SIR,—We read with interest the short report by Drs H L Muston and S Conceicao (25 February, p 480). We too have had experience with clearing of psoriasis during haemodialysis¹; however, the reports of fairly severe recurrence in case 2 and only incomplete clearance in case 1 are of special interest. This information corroborates the findings of both McEvoy and Anderson (personal communication).

Also of interest are the type of dialyser, heparinisation technique, and, in general, the methodology of haemodialysis used. Specific information of this type may help determine the most efficient mode of application of haemodialysis. We used the Lundia Optima 17- μ m disposable dialyser and patients were dialysed three times each week for six-hour periods. Heparinisation was accomplished through constant regional infusion in uraemics without an initial loading dose.² Initial loading heparinisation in non-uraemics was 100 U/kg just before dialysis.

Twardowski et al have reported successful treatment of psoriatics with peritoneal dialysis.³ They postulate removal of some noxious substance which may be filtered by the normal kidney but not excreted owing to tubular reabsorption. We intend to explore similar and alternative hypotheses. They include the possibility that psoriatic clearing after dialysis may be induced by one or a number of the following: (1) removal of pathological or physiological substances; (2) a sponge-sink effect binding effector substances; (3) removal of an inhibitor to epidermal chalone; (4) stimulation of a change in intracellular cyclic nucleotides or their prostaglandin modulators; (5) immunological activation, inactivation of substances, or alteration of feedback systems; (6) depletion or alteration of essential amino- or fatty acids; (7) stress-induced hormone production; (8) the production of an "unphysiological state" (for example, variations in osmolality, trace metals, or pH).

Immunological mechanisms are attractive. It has already been established that chemotaxis is decreased in uraemic patients and is further decreased during chronic haemodialysis.⁴ The procedure appears to activate complement and thus affect neutrophils irreversibly so that these neutrophils are less responsive to further chemotactic stimuli.⁵ White cell aggregation in the lungs and both thrombocytopenia and leucocytopenia have been documented during dialysis.⁶ Furthermore, one would expect trace-metal alterations depending on water delivery systems, and the general "unphysiology" of the dialysis technique has been documented as well.⁷ Documentation of prostaglandin and cyclic nucleotide alterations await further analysis, as do membrane accumulation, infusion or effusion of diffusible substances, and other immunological effects.

Elucidation of the possible changes induced by dialysis relative to these hypotheses may help in determination of the pathogenesis of the disease as well as the specific aspect of dialysis therapy which is effective in psoriasis.

We would be interested in the dialysis techniques used and any observations the authors or other readers might have regarding these or other relevant hypotheses.

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¹ Buselmeier, T J, et al, *Journal of the American Medical Association*. In press.

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³ Twardowski, Z J, et al, *Annals of Internal Medicine*, 1978, **88**, 349.

⁴ Greene, W H, et al, *Journal of Laboratory and Clinical Medicine*, 1976, **22**, 981.

⁵ Jacob, H S, *Archives of Internal Medicine*, 1978, **138**, 461.

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⁷ Kjellstrand, C M, et al, *Kidney International*, 1975, **7**, suppl 2, p 30.

Intended place of delivery and perinatal outcome

SIR,—In a field where statistics are notably lacking, Jean Fedrick and Professor N R Butler's contribution (25 March, p 763) is to be welcomed, but it must be seriously doubted that their evidence justifies their uncompromising conclusion. May I give four of the reasons why?

(1) The highly significant difference in perinatal mortality rates in favour of NHS consultant hospitals depends entirely on attributing to the original place of booking the relatively great number of deaths associated with maternal transfers. The attribution of such deaths poses a very difficult methodological problem. All possible solutions are open to objection, but the one adopted here would be logical only if it were known for certain that the risk attaching to delivery in hospital was not greater than in other places, which is precisely the issue which is in question. The proof that a proposition is true cannot depend on the prior assumption that it is true.

(2) In the three low-risk groups identified consultant hospitals are shown to have consistently the lowest mortality rates for booked cases; the χ^2 significance test permits the conclusion at a very high level of confidence ($P < 0.001$) that the differences in rates between the four listed places are real, though by itself it can prove no more than that. These are useful findings. It is, however, pertinent that while the level of significance is as high as this for the aggregate of the three groups and for group A considered separately, it falls to about $P < 0.05$ for group B and far below $P < 0.05$ for group C. In other words, for this group which

is at lowest risk of all and makes up nearly half of the cases studied there is no significant difference in death rates between the different places of booking. It is pertinent also that the very high level of significance is the result of including "private wards and nursing homes" and residual places. Without these the level of significance falls to about $P < 0.02$ and, if only hospital and home are compared, to far below $P < 0.05$. In other words, for the aggregate of groups A, B, and C there is no significant difference in death rates between hospital and home bookings (χ^2 calculated approximately from data in the article).

(3) Various factors conducive to increased risk are measured in table III of the article, while table IV shows their distribution by place of booking for group A (which, as indicated above, may not be completely representative). It is, of course, obvious that the factors are not additive but overlap considerably—for example, mothers of light weight tend to be of low stature also. The death rate associated with mothers born light and short is likely to be little higher than if they had only one of these characteristics. The home-booked cases were not free of high-risk factors, but the hospital-booked cases had more, yet had the lower death rates nevertheless. In itself this is evidence to be respected, but can the evidence of this one group legitimately be taken as applying to all groups? I have drawn attention elsewhere¹⁻³ to the arithmetic principle that an average death rate is determined by the sum of the products of the proportion of cases in each subgroup multiplied by the death rate in that group. Further analysis of data is required to establish that hospitals have a proportion of cases at high predelivery risk sufficiently greater than at other places of delivery to account for the great excess of their overall death rate—the issue in question.

(4) As the authors accept, conclusions based on 1958 data have limited relevance in 1978. To meet this weakness they quote from the Registrar General's annual analyses of stillbirths and point to the rising trend in the home stillbirth rate since 1970. Those readers who were not thoroughly misled by the deceptive scales used in the graph will have noticed that, even so, the home rate remained far below the overall rate: the original statistics show that in 1973 it was, in fact, still less than half the rate in consultant hospitals.

The rising stillbirth rate at home does indeed appear an extraordinary deviation from the general downward trend. If domiciliary deliveries are becoming less safe than they used to be for mothers of the same predelivery risk this is a serious indictment of official policy in dismantling the once very efficient domiciliary maternity service. More likely, the mothers are not of the same predelivery risk: those of them at lowest risk, from choice or lack of choice rather than medical need, are increasingly being delivered in hospital, and it is this dilution with low-risk cases which is the main contributor to the decline in the hospital stillbirth rate.

This is clearly illustrated by the experience of the group at minimal risk—mothers aged 20-29 having their second or third legitimate baby. In 1969⁴ 66% of this group gave birth in consultant hospitals; their stillbirth rate was 11.7 per 1000 births, while the rate for the remaining 34% in all other places combined was 4.2. By 1975⁵ 83% gave birth in hospital; their stillbirth rate had fallen to 8.8 per 1000, while for the 17% remaining outside the rate fell to 3.4. If the 17% who moved over to hospital had the average experience of this group in hospital, then their stillbirth rate per 1000 births rose from 4.2 (1969) to 8.8 (1975)—a worrying deterioration. If, on the other hand, they fared no worse than the 17% remaining outside, their stillbirth rate in 1975 would have been 3.4 per 1000; but in that case, since the overall average in hospital was 8.8 the other mothers in the group must have

had a stillbirth rate of 10.1 per 1000. A decline in the hospital stillbirth rate for this minimal-risk group from 11.7 to 10.1 per 1000 is relatively less than that achieved outside, from 4.2 to 3.4—hardly an impressive vindication of the current policy of moving towards hospitalisation for all.

Thus the more recent evidence on stillbirths fails to support the conclusion drawn by Mrs Fedrick and Professor Butler from 1958 data. The need for further research is as great as ever.

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¹ Tew, M. *New Society*, 1977, **39**, 120.

² Tew, M., *Journal of the Royal College of General Practitioners*, 1977, **27**, 689.

³ Tew, M., in *The Place of Birth*, ed S Kitzinger and J Davis. London, Oxford University Press, 1978.

⁴ Office of Population Censuses and Surveys, *Registrar General's Statistical Review of England and Wales for 1969*. London, HMSO, 1971.

⁵ Registrar General, unpublished return for 1975.

Hospital laboratory computing

SIR,—Your leading article (18 February, p 387) and Professor I D P Wootton (1 April, p 851) are right in saying that medical computing systems that can easily be transferred to other sites are highly desirable. I would, however, like to question whether we yet have such systems for hospital laboratory computing in Britain. Dr M D Buckley-Sharp (4 March, p 577) lists a number of recipient laboratories of the excellent Phoenix system from the Hammersmith Hospital, but he does not say if any of them are actually being served by their computer system on a routine basis. As I have said before,¹ we should not accept that a system is a general one until it has proved itself in routine use at a number of recipient sites.

Simple transfer of medical computing systems has proved an elusive goal in the past, but it is still one which we should try to achieve. Success in overcoming the problems it presents should be carefully and accurately recorded for the benefit of others trying to achieve it. May we know, therefore, how many laboratories now routinely use Phoenix (or a derivative of it) and for how long they have done so?

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¹ Coles, E C, *Journal of the Royal College of Physicians of London*, 1974, **8**, 355.

Drug information services

SIR,—The total number of inquiries received by the regional drug information centres, as reported by Dr F N Leach (25 March, p 766), represents only a small percentage of the total number of inquiries made annually to drug information centres and, if taken alone, underestimates the advisory role of these services. The results of a small survey will illustrate this point.

The survey was conducted during a two-week period in 1976 and detailed all inquiries received across a teaching district of 1700 acute beds serving most specialties. There is an active ward pharmacy programme at each of the hospitals within the district and a department of clinical pharmacology and therapeutics at the hospital in which a specialist

pharmacy-based district drug information service has been developing over four years. The extrapolated district total of inquiries for 1976 was 5800 compared with a total of 8584 from the eight regional centres listed by Dr Leach. During the survey period the drug information pharmacist dealt with 13% of all inquiries, the rest being answered by pharmacists in the course of their work; 10% were made directly to the centre and 3% referred. However, within the hospital in which it is based the centre answers 33% of inquiries. During the survey period 8% of inquiries arose outside the district.

The types of inquiry made to the district drug information service were very similar to those quoted by Dr Leach. The highest proportion came from hospital pharmacists as a result of clinical problems met on the ward rounds. This demonstrates the interception of inquiries by district and area centres. Non-clinical staff accounted for nearly as many inquiries as clinicians. A multidisciplinary approach is required for the provision of a comprehensive drug information service, which includes clinical, pharmaceutical, and scientific problems.

The national usage of drug information resources and the contribution of local drug information pharmacists is greater than Dr Leach's paper, concentrating on the regional centres only, would suggest.

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British standard insulin syringe

SIR,—Let us stop, look, listen, and think—let us not be stampeded and corralled into accepting U-100 (100 U/ml) insulin as the only one, with all other strengths banned (Drs B F Brearley and J Mackie, 18 March, p 713). This would irrevocably condemn all insulin-dependent diabetics to one system of varying (expensive) syringes and all its drawbacks. One system, like a monopoly, could become a tyranny.

Let the positive aim of this country be the acceptance of U-100 as a new factor for assessment for improved insulin administration to patients and not be abused as a weapon to remove the possibility of better techniques. One technique I suggest is to combine the use of U-20 and U-100 using the present standard syringe only, with its 20 graduation marks. For U-100 one graduation mark would measure 5 U and for U-20 1 U of insulin, this information to be precisely engraved on the syringe.

Thus the largest part of one injection could be measured from U-100 in multiples of 5 U and the balance of less than 5 U from U-20, which would give accurate end-point measurement to 1 U per graduation for the dose. For several reasons precision measurement of dose is of great importance. Small doses would be measured from U-20 insulin up to 20 U. I have used this simple technique on myself for many years with U-80 and U-40. These would be withdrawn when U-100 and U-20 became available.

The advantages for the patient are the lower volume given by U-100 and great precision of measurement by U-20; the use of one syringe only for all doses of insulin, and therefore no added stress; and for the NHS and our country

no massive additional cost for multiple differing syringes and holders.

Adopting the American technique, banishing all insulin concentrations except U-100, excludes this suggested (British) technique. Adopting the suggested (British) technique of one standard insulin syringe and of two insulin concentrations, U-100 and U-20, does not prevent anyone adopting the American technique, but in the beginning they should have to buy the special syringes required.

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Outpatient chemotherapy for breast cancer

SIR,—We wish to comment on the letter from Dr R Bell and others (1 April, p 857) concerning the oral administration of 400-mg doses of methotrexate.

The statement that the patients' supreme effort of swallowing 10 tablets every hour for 16 h results in similar blood levels to those achieved by infusion of the drug is not supported by hitherto published evidence. Although doses of less than 30 mg/m² have been shown to be nearly completely absorbed from the gastrointestinal tract,^{1,2} absorption is protracted and incomplete with doses of 80 mg/m² or more, leading to plasma levels less than one-tenth of those achieved after intravenous administration.^{3,4} If this is, in fact, the case it is not surprising that in the study by Dr Bell and his colleagues toxicity was relatively mild. However, the cytotoxic efficacy of the drug may well be open to question.

In answer to the request for a higher-strength tablet, may we point out that we are in the process of developing a 10-mg tablet? In addition we can supply a formula from which a 2 mg/ml syrup preparation can be made. Preliminary pharmacological and stability data for this formulation have been published.⁴

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¹ Henderson, E S, *et al*, *Cancer Research*, 1965, **25**, 1018.

² Huffman, D M, *et al*, *Clinical Pharmacology and Therapeutics*, 1973, **14**, 572.

³ Wan, S H, *et al*, *Cancer Research*, 1974, **34**, 3487.

⁴ McVie, J G, *British Journal of Cancer*, 1977, **36**, 417.

Intra-articular steroids

SIR,—Your recent leading article on this subject (11 March, p 600) presented highly agreeable and balanced advice to clinicians, since many previous reports concerning this subject have been paradoxical at least to some extent. However, it seems to us that the excess use of intra-articular corticosteroid injections in sports medicine as "pain-killers," especially in knee injuries, should be criticised.

A recent experimental study on rabbits¹ suggested that intra-articular betametasone seemed to have a protective effect against early articular cartilage degeneration in the knee joint when the rabbits were subjected to strenuous exercise. However, the protective effect of both intra-articular and intramuscular glycosaminoglycan polysulphate injections