

must be given (and this is partly why the service is expensive) to allow the couple to express any fears and anxieties they may have about the methods, and to help them choose the method best suited to them. Also, poorly motivated couples need constant encouragement and reassurance if they are to persevere with contraception as they are less tolerant of side effects. In Haringey special problems exist (found also in Birmingham and Wandsworth) in that there is a large immigrant population, mostly West Indian, Irish, and Greek Cypriot, with differing cultures which have to be taken into account when birth control advice is given.

Domiciliary family planning should be regarded as preventive medicine—families where it is successful are better able to care for the well-being of their children. While it is to be hoped that the increasing liberalization of attitudes will continue there will still be a need for “individual and sympathetic family planning advice,” to use Dr. Wilson’s words, to be brought to the homes of a small but disproportionately problem-ridden section of the population.—I am, etc.,

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Crystals in Skeletal Muscle

SIR,—In reply to Dr. G. H. Hitchings (27 November, p. 555), the possibility that the crystals which were observed in frozen sections of muscle tissue from gout patients who had been treated with allopurinol for from six months to three years were attributable to the freezing process was carefully considered by us and investigated experimentally in our laboratory.¹ Your leading article (23 October, p. 185) refers to the paper in which these experiments are reported but Dr. Hitchings does not. This experimental evidence may be summarized as follows:

It was not possible to induce crystal formation by soaking fresh human muscle in aqueous or plasma solutions of hypoxanthine, xanthine, or oxipurinol; by soaking either fresh or ethanol fixed rat muscle in human plasma containing uric acid 9.8 mg/100 ml. Furthermore, no crystal formation was observed in a piece of human muscle which had been stored at -6°C for 25 days. During this time the hypoxanthine content increased from 36 $\mu\text{g/g}$ wet weight to 408 $\mu\text{g/g}$ wet weight, the inosine content reaching a concentration of 336 $\mu\text{g/g}$ wet weight. Inosine monophosphate (IMP) and adenosine monophosphate (AMP) were present in the stored muscle whereas adenosine triphosphate (ATP) had decreased from 1,047 $\mu\text{g/g}$ wet weight to zero.¹

These experiments provided strong evidence that cooling was not a factor in the formation of the crystals. We concluded that the presence of hypoxanthine and xanthine crystals in muscle tissue is related to lack of xanthine oxidase activity and not to gout. This was in agreement with our previous observation on two patients with congenital xanthine oxidase deficiency or xanthinuria.² In these studies 120 sections of muscle tissue from 13 normal untreated subjects (one of whom in fact had asymptomatic hyperuricaemia; serum uric acid was 10 mg/100 ml) had been examined as controls and found to contain no more than two hypoxanthine crystals and no xanthine or other crystals in any of the sections. It was also shown

that gout patients who had not received allopurinol also showed no excess of hypoxanthine or xanthine crystals in their muscle. The presence of oxipurinol crystals in the muscle of the allopurinol-treated gout patients was also reported, and it is of interest that it has been shown that allopurinol can be converted to oxipurinol in vivo in the absence of xanthine oxidase activity.³

In summary, we have demonstrated differences on microscopic examination between two groups of patients—namely, those who were treated with allopurinol and those who were not so treated—and we have presented experimental evidence for the view that these differences are not associated with the cooling procedure needed to produce frozen sections which are suitable for examination by refined optical methods. Thus, Dr. Hitchings’s contention that we ignored this possibility is untrue. It is not justifiable to regard striated muscle as a simple aqueous solution, and to relate concentration of solutes per unit volume of muscle to their concentrations and solubility in an equal volume of water. Dr. Hitchings related 12 nanograms of hypoxanthine/mg wet weight of muscle to the saturation of 1,150 nanograms/ml of plasma. But in 1 mg of muscle the volume of free water in which the hypoxanthine can be dissolved is a minute fraction of that weight of muscle, most of which is occupied by protoplasm and by protoplasm-bound water. Striped muscle may be particularly liable to induce the formation of crystals because of its high degree of molecular orientation.¹

Knowing the complex physicochemical environment which prevails within cells, it is, in our opinion, naive to argue that observed phenomena cannot occur because they appear to contravene preconceived patterns of behaviour which have been derived from a consideration of simple aqueous systems.—We are, etc.,

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- 1 Watts, R. W. E., Scott, J. T., Chalmers, R. A., Bitensky, L., and Chayen, J., *Quarterly Journal of Medicine*, 1971, 40, 1.
- 2 Chalmers, R. A., Watts, R. W. E., Bitensky, L., and Chayen, J., *Journal of Pathology*, 1969, 99, 45.
- 3 Chalmers, R. A., Parker, R., Simmonds, H. A., Snedden, W., and Watts, R. W. E., *Biochemical Journal*, 1969, 112, 527.

Cost and Speed of Medical Publication

SIR,—Dr. David Pyke’s Personal View (5 February, p. 371) is surely echoing the feelings of the medical profession as a whole when he criticizes the publication of conference proceedings as these usually appear: too late and too expensive. But he is incorrect in implying that the International Diabetes Federation is breaking new ground in publishing abstracts only. The Seventh European Rheumatology Congress held at Brighton in June 1971 omitted the customary post-conference proceedings in favour of a bound handbook of abstracts given to each participant on arrival. Copies of this abstract handbook are available for £2 at the address below. They bear study by any student of

“congressology.” Each of the 542 abstracts appears in English as well as in one of the other official languages, and the method of photographic reproduction allowed authors to revise their abstracts up to the very last moment, even those in Cyrillic script. Further, appropriate grouping of abstracts enabled our printer to run off separate sections of the handbook for advanced mailing to participants in individual sessions.—We are, etc.,

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Chairman, Scientific Subcommittee

M. C. G. ANDREWS
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Generalized Pustular Psoriasis

SIR,—We are disappointed at the final conclusion of your leading article on “Generalized Pustular Psoriasis” (29 January, p. 262) that corticosteroids should continue to be used until a bacteraemia is found and its response to antibiotics confirmed. The papers that you quoted give a strong hint that corticosteroids are concerned aetiologically in many cases, and it would seem undesirable to give them on this score (except as a last resort) even though they may suppress the symptoms and signs temporarily. We would certainly prefer to rely on your alternative suggestion, methotrexate, under these conditions.

The point of our paper¹ was that the six weeks’ course of cloxacillin and cephaloridine that we recommended was the safest effective means of controlling generalized pustular psoriasis that we had found. If faced with a case, having taken initial blood cultures, we would not recommend waiting for the result before starting this treatment. As your leader rightly suggests, the significance of the positive blood cultures in our cases is difficult to interpret, but the fact of clinical response to appropriate antibiotics is to us beyond doubt.—We are, etc.,

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- 1 McFadyen, T., and Lyell, A., *British Journal of Dermatology*, 1971, 85, 274.

Unusual Type of Postanaesthetic Jaundice

SIR,—The Dubin-Johnson syndrome, also known as the Dubin-Sprinz disease and as constitutional hyperbilirubinaemia, is a rare condition. Usually seen in young people, it presents as a chronic or intermittent jaundice characterized by an increased concentration of conjugated bilirubin in the serum (but also some increase in unconjugated bilirubin) and by inadequate excretion of bromosulphalein. The aetiology is obscure, but it may be due to an inborn deficiency or deficiencies in the liver cell which result in an inadequate excretion of bilirubin, bromsulphalein, and the dyes used in cholecystography.¹ Investigations in the following case of postanaesthetic jaundice, at first attributed to halothane, suggested that it was probably due to the Dubin-Johnson syndrome.

The patient was a healthy man aged 37