mediators—for example, histamine.³ Paracetamol, however, has no appreciable anti-inflammatory effect when used in therapeutic doses and has been used safely in patients who react with bronchospasm to anti-inflammatory analgesics.⁴ Moreover, in two of the cases reported to the Netherlands Centre for Monitoring of Adverse Reactions to Drugs (cases 2 and 3) the use of drugs with a strong anti-inflammatory action did not cause this kind of reaction. Hence the reactions to paracetamol are presumably mediated immunologically.

In view of the worldwide use of paracetamol and the paucity of reports of hypersensitivity reactions the incidence of these reactions to paracetamol is presumably low. Nevertheless, since anaphylactic reactions are serious and may be fatal medical practitioners should be aware of their possible occurrence after the ingestion of tablets containing paracetamol.

We thank the National Drug Monitoring Centres of Australia (Dr J McEwen), Canada (Dr E Napke), Finland (Dr E Alhava), Israel (Professor H Halkin), New Zealand (Professor I R Edwards), Norway (Dr L Kjeldas), Spain (Professor J R Laporte), Sweden (Dr B E Wiholm), the United Kingdom (Dr J C P Weber), and the United States (Dr J K Jones) for permission to use their data.

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(Accepted 10 July 1985)

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Photosensitivity during treatment with azapropazone

Azapropazone is a non-steroidal anti-inflammatory drug and was first launched in 1970. We have found only one published case report of photosensitivity during treatment with azapropazone.¹ Neither *Martindale: The Extra Pharmacopoeia* nor the *Side Effects of Drugs* series mentions this adverse reaction. The product information for azapropazone in some countries now mentions photosensitivity as an occasional adverse effect.^{2,3} The experience of the World Health Organisation's programme for monitoring adverse reactions indicates, however, that reports of photosensitivity as a proportion of reports of all reactions is higher for azapropazone than for almost all other non-steroidal anti-inflammatory drugs.

Methods and results

This study was based on 190 reports of photosensitivity thought to be associated with azapropazone. The reports were submitted by doctors to their national drug monitoring centres in Belgium, Denmark, Ireland, the Netherlands, Sweden, and the United Kingdom and forwarded to the WHO Collaborating Centre for International Drug Monitoring before September 1984. Eighteen reports already mentioned in publications from two of the national drug monitoring centres were included in the study.^{4,5}

The possibility of a causal relation between azapropazone and photosensitivity was assessed at the national centres for 154 reports. A causal relation was considered to be certain in six, probable in 138, and possible in 10. Of the patients affected, 117 were women, 72 were men, and in one case sex was not stated. Ninety seven patients were aged 60 or more. Information on age was lacking in 17 reports.

The table shows the number of cases of photosensitivity by year. The greatest number of reactions occurred in April (43 cases) followed by May (42), March (24), and June (18). The doses given to patients who developed photosensitivity were generally within the recommended range of 600-1200 mg daily, although 40% of the reports analysed lacked information about dosage. In 116 reports no drug other than azapropazone was mentioned.

Twenty seven patients experienced the reaction within the first week of treatment, 104 after one to five weeks of treatment, and 36 patients after more than five weeks' treatment.

In most reports the adverse effect was described only as a photosensitivity reaction, reversible by withdrawal of treatment. A few reports included more detailed descriptions of the reactions such as oedema, eczematous eruptions, maculopapular rashes, or dermatitis. In general the photosensitivity did not seem to affect the patients seriously.

Comment

The scarcity of published reports of photosensitivity induced by azapropazone suggests that this phenomenon is rare. Systems for spontaneous reporting of adverse reactions are not well suited for estimations of incidence, particularly when, as in this case, no estimate of drug consumption is available. The main factor indicating that photosensitivity is a fairly frequent reaction to azapropazone was the number of reported cases as a proportion of the total number of suspected reactions. This fraction was higher for azapropazone than for any other non-steroidal anti-inflammatory drug except benoxaprofen, according to reports of adverse reactions from the six countries that contributed to this survey. The table shows that this proportion rose from around 10% in 1976-9 to more than 20% in 1980 and subsequent years. This may reflect a heightened awareness among doctors of photosensitivity reactions related to drugs, created by the publicity given to benoxaprofen.

The finding that April and May were the months in which reactions most commonly occurred contrasts with results of a corresponding study based on all reports of photosensitivity, irrespective of the incriminated drug, submitted to the WHO from countries in the northern hemisphere, which shows a symmetric distribution around June and July.

In view of our data we recommend that prescribing doctors advise patients taking azapropazone to limit their exposure to direct sunlight.

We thank all the doctors who reported the reactions, the national drug monitoring centres for supplying the data, and all those who provided useful comments on criticism of the analysis—namely, Mr B Huyghe, Belgium; Ms I Kovacs, Denmark; Dr A Scott, Ireland; Dr K van Dijke, the Netherlands; Dr B-E Wiholm, Sweden; and Dr P Weber, United Kingdom. This article expresses the views of the authors and does not necessarily represent those of the World Health Organisation.

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(Accepted 5 July 1985)

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Yearly number of reports of adverse reactions in which azapropazone was the drug implicated and proportion of these adverse reactions that were photosensitivity

	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	Total
Total No of reports	12	5	4	21	38	136	128	99	77	126	159	112	917
No (%) of reports of photosensitivity	1 (8)		1 (25)	2 (10)	4 (11)	16 (12)	8 (6)	18 (18)	17 (22)	45 (36)	48 (30)	30 (27)	190 (21)