matic response to the initial course (see case 2). Such a course should prevent perforation, and this maintenance dose regimen has also been shown to reduce the recurrence rate of the ulcers.[1 5]

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Acne induced by PUVA treatment

Recently there has been a rapid development in the world-wide use of oral and topical methoxsalen (8-methoxypsoralen; 8-MOP) with long-wave ultraviolet light (UVA) for treating patients with psoriasis. This form of photochemotherapy is known as PUVA treatment, and is effective in clearing and maintaining a remission of psoriasis in most patients treated.[1-3] It is currently being evaluated at various centres in the UK to define the indications for its use and to determine the short- and long-term side effects. Acute side effects such as erythema, nausea, pruritus, and dizziness, though rare, are well recognised.[4] We report a hitherto unrecognised side effect of PUVA treatment: the development of an acneiform eruption in one of our patients.

Case report

The patient, a 37-year-old man with extensive psoriasis for over 30 years, was started on PUVA treatment in April 1977. He was treated initially three or four times weekly, taking by mouth 40 mg methoxsalen two hours before being irradiated by arrays of high-intensity UVA fluorescent tubes arranged in two modules (Dermatron-48). The irradiance as measured at skin surface varied from 3-6 mW/cm^2. The treatment dose was gradually increased by 0·5 J/cm^2 twice weekly from an initial dose of 2·0 J/cm^2. After six weeks (20 treatments) his psoriasis was clearing, but he developed an acneiform eruption on the chest and back that consisted mainly of small, red, dome-shaped papules and a few comedones and pustules. He had never had acne vulgaris and there was no history of exposure to industrial oils. Treatment with topical corticosteroids had been discontinued in January 1977.

A biopsy specimen of a papular lesion showed a dilated pilosebaceous follicle filled with inflammatory debris and keratin. At one point the follicular epithelium was necrotic and ruptured with a sparse surrounding dermal infiltrate. We considered that his acneiform eruption was induced by the PUVA treatment. We did not discontinue treatment because the patient regarded the eruption as much less of a problem than his psoriasis. By the end of July (34 treatments) his psoriasis had almost completely cleared apart from a few residual plaques on the elbows and lower legs. His acneiform eruption on the chest, upper back, and deltoid regions persisted.

Comment

Acneiform eruptions may occur after prolonged periods of sunbathing. In 1972, Hjorth *et al*[5] described 40 patients who developed an acneiform eruption which they termed "acne aestivalis," and because it often followed a Mediterranean holiday in the sun, "Majorca acne." Studies on a case of acne aestivalis[6] have not helped in disclosing its cause, though the histopathological findings resembled those in cases of steroid acne[7]—namely, necrosis of a segment of the follicular lining with a sparse neutrophil infiltrate. Histological evidence of this type of monomorphic acne was found in the biopsy specimen taken from our patient. The papular lesions he developed were like those described in acne aestivalis,[5 6] but he also had pustules and comedones such as occur in the sun-aggravated common acne.

Though acne usually improves during the summer with exposure to sunshine, it may be aggravated in some patients,[8] particularly in a hot and humid climate. It is probably related to excessive sweating.[8 9] Patients undergoing PUVA treatment are usually irradiated in enclosed cabinets and cubicles in rather confined areas. Despite powerful extractor fans and fans incorporated in the cabinets and modules used, the temperature and humidity in these units are often high, and some patients sweat profusely. We consider that these factors including the UVA light contributed to the development of the acneiform eruption in our patient, and would be interested to know if others have seen this side effect of PUVA treatment.

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Disopyramide and warfarin interaction

Disopyramide is an antiarrhythmic compound, with activity against supraventricular and ventricular dysrhythmias.[1 2] Recent work has suggested that it may be particularly useful in ectopic atrial tachycardia.[3] We describe here an interaction between disopyramide and warfarin that may be of clinical importance.

Case report

A 58-year-old marine engineer, who had previously enjoyed good health, was admitted to the coronary care unit on 9 May 1977 suffering from an acute anteroseptal cardiac infarction. Complications included left ventricular failure on presentation and an episode of atrial tachycardia at 12 hours. The latter was immediately treated with an intravenous bolus dose of disopyramide phosphate (1·5 mg/kg body weight), with a rapid and sustained reversion to sinus rhythm. The patient was digitalised and started on a maintenance regimen of disopyramide base administered by mouth (100 mg every six hours). The policy of the coronary care unit is to use prophylactic intravenous heparin in the absence of contraindications. Heparin was administered for 48 hours, after which it was replaced by oral anticoagulation with warfarin.

The patient's further recovery was uneventful and he was eventually discharged after two weeks in hospital on the following treatment: digoxin 0·25 mg/day, frusemide 80 mg/day, potassium supplements, warfarin 3 mg/day, and disopyramide base 100 mg every six hours.

Four weeks later he returned because of general malaise and was found to be hypotensive (80/60 mm Hg). The disopyramide was discontinued in view of its potential negative inotropic effect. There was a good clinical response over 24 hours. Over the next few days we noticed that his previously stable prothrombin time fell considerably, requiring incremental doses of warfarin (see table). At no time was there any evidence of hepatic or renal dysfunction in this patient.

Comment

We are unaware of any reported interaction between disopyramide and warfarin in vivo. There is, however, some suggestion of an in-vitro synergism in animal studies (personal communication, Searle Laboratories). The mechanism is unknown but unlikely to be due to displacement of warfarin by disopyramide from plasma protein binding sites, as disopyramide is only 27% protein bound.[4] Coumarin metabolism occurs in hepatic microsomal mixed function oxidase systems,[5] and the apparent interaction between disopyramide and

Prothrombin values after withdrawal of disopyramide and their response to warfarin

Day:	1 (disopyramide stopped)	2	3	4	5	6	7	8	9
Warfarin dose (mg) ..	3	3	5	5	6	5	6	8	6
Prothrombin time (s)..	24		16	15			19	22	28

warfarin might be explained by a competitive phenomenon at the receptor site if disopyramide is metabolised at the same site.

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Pleurisy and methotrexate treatment

The association between adverse pulmonary reactions to cytotoxic agents such as busulphan, cyclophosphamide, and methotrexate is now well documented.[1] A syndrome of cough, dyspnoea, fever, and diffuse pulmonary infiltration has been described both in children with acute leukaemia[2] and in patients with psoriasis[3] on maintenance treatment with methotrexate. We wish to report the occurrence of pleuritis in patients treated with methotrexate for trophoblastic tumours, since this complication has not been a notable feature of reviews on the subject.[3 4]

Patients

We studied patients with trophoblastic tumours who were attending the medical oncology department at Charing Cross Hospital. Between 1958 and 1975, 317 patients were successfully treated with drug regimens including 50 mg methotrexate given as a single intramuscular dose, followed after 30 hours by folinic acid. This treatment was repeated to a total of 120 mg in eight days. Of these patients, 20 (6%) developed pleurisy. We excluded six of the 20 patients who had clear evidence of pulmonary metastases, from the series studied. The remaining 14 patients had no evidence of pulmonary disease or metastases but developed pleuritic chest pain, which occurred in association with the first treatment in some and up to the fifth in others (see table), but not necessarily with every course of treatment. In all but one of the patients studied the human chorionic gonadotrophin concentration was abnormally high when pleuritic pain developed. No patient had pleuritic pain associated with use of other cytotoxic agents. The eosinophil counts remained normal in all patients. In four there was radiological evidence of pleural effusion or basal shadowing compatible with localised collapse of lung. Pulmonary disease was not subsequently detected in any patient.

Comment

Treatment with methotrexate was associated with an acute pleural reaction in 20 of 317 patients with choriocarcinoma—an incidence of 6%. This relatively common and disturbing side effect has not been reported. It appeared to be directly associated with treatment, occurring immediately after administration of methotrexate; it is not clear why it occurred in some patients during the first course of treatment and in others after several treatments, nor why only some patients were affected. We have found that pleuritic pain does not occur in patients with pulmonary metastases from breast cancer treated with smaller doses of methotrexate, and that it is not apparently associated with intermittent high-dose (>200 mg) intravenous methotrexate in patients with trophoblastic tumours.

Association of development of pleurisy with course of treatment of methotrexate and folinic acid in patients with trophoblastic tumours, but without radiological evidence of metastases

Patient No	Course of treatment (No)	HCG concentration
1	5	Abnormal
2	5	Normal
3	2	Abnormal
4	2	Abnormal
5	2	Abnormal
6	4	Abnormal
7	2	Abnormal
8	3	Abnormal
9	3	Abnormal
10	2	Abnormal
11	5	Abnormal
12	3	Abnormal
13	2	Abnormal
14	3	Abnormal

HCG = human chorionic gonadotrophin.

The immediate association with treatment suggests a hypersensitivity response, but there was no eosinophilia, leucocytosis, wheezing, or rash in any of our patients. The pleural reaction may be associated with necrosis of tumour deposits on the pleura; this does not explain, however, the absence of pleural reaction to other cytotoxic agents which may be equally effective in reducing trophoblastic tumour mass. Trophoblastic embolism after treatment might be responsible for the pleural reaction,[4] but there is little evidence of pulmonary embolism in connection with methotrexate treatment.[5] Methotrexate may have a harmful effect on serosal cells lining the pleura or peritoneum.

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