

Side-effects of Phenindione

SIR,—Dr. I. S. Menon states (8 June, p. 622) that "Minor side-effects, such as fleeting skin rashes during the first 10 days . . . [of phenindione therapy], can be ignored." Of course, more dramatic urticarial, purpuric,¹ and haemorrhagic necrotic lesions² may also occur during this early stage as with other hypoprothrombin-inducing drugs. Therefore, all eruptions seen during phenindione treatment, although common,¹ are potentially important.

Another variety of rash should be recognized because it may harbingering the rather frequent serious toxic ("side") effects of phenindione on the kidney,³ bone marrow,⁴ and liver.⁵ The three patients I reported (31 July 1965, p. 305) were women in hospital who had developed, without warning, widespread itchy eczematous eruptions. The eruption persisted in two of them for several months despite energetic treatment; one of them had mild exfoliative dermatitis (erythrodermia), a sequela that has been reported.⁶ In these two, fever and biochemical evidence of liver damage were noted. One patient developed anuria.

Last year I watched a fourth patient, a woman aged 50 (with a deep vein thrombosis that occurred during inpatient treatment for a leg ulcer), develop such a rash during the second week of treatment with phenindione. There was no active eczema around the leg ulcer. Unlike the other patients, she had had some eczema in the past, but this new eruption had occurred in a different distribution, affecting particularly the axillae and groins. The anticoagulant was changed 36 hours after the onset of the rash. A low grade proteinuria was found on the following day and persisted for one week. She never developed fever or any significant alterations in blood urea, blood count, or liver function tests. She became partially bald from the coumarin treatment.⁷

To develop a primarily eczematous response from a drug administered systemically is unusual. In patients taking phenindione, it may be important to recognize this type of rash, because, if it is indeed a precursor of the dangerous toxic actions of the drug, as noted in another patient,⁸ then it can be looked upon as a "useful" phenomenon and an urgent warning to stop treatment.—I am, etc.,

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Anaemia and Hiatus Hernia

SIR,—The article concerning iron absorption in hiatal hernia (6 July, p. 22) was of particular interest to me, but the subsequent letter (20 July, p. 185) cannot go unchallenged.

It is true that patients with sliding hiatal hernia may present with haematemesis, mel-

aena, or both, or with an anaemia, but in all these cases it is mandatory to look for another cause for the haemorrhage. It is very rare for a sliding hiatal hernia *per se*, as distinct from a paraoesophageal hernia, to be the cause of this complication.¹ Further, there is no categorical proof that a sliding hiatal hernia is a precancerous condition. This is substantiated by a recent prospective study of 628 cases of hiatal hernia which I have investigated and followed up since 1957.² The statement that "The complications of hiatus hernia, of which anaemia is only one, are potentially so serious . . ." likewise cannot be accepted. In the past the complications of gastric reflux, which have often been stated to be virulent and irreversible, have been overexaggerated. The incidence of "strictures" as distinct from stenosis due to spasm of the oesophagus is very low in sliding hiatal hernia. There are many other benign oesophageal lesions which have to be differentiated from "strictures."

In symptomatic hiatal hernia the treatment, based upon a full investigation, consisting of cine-radiography, manometry, augmented histamine tests, and oesophagoscopy, is essentially conservative. Only if persistent and diligent therapy fails is surgery indicated, and the logical approach is the abdominal one. This is important, as in my series over 40% of cases were associated with an intra-abdominal lesion, which very often was the primary cause of the patients' symptomatology.³—I am, etc.,

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Chloramphenicol and Tetracyclines

SIR,—Your expert contributor's excellent essay on chloramphenicol and tetracycline (8 June, p. 607) was a little unfair to lymecycline. He states that "not all observers have reported a lower incidence of side-effects" than with the older tetracyclines. We believe this statement is misleading unless amplified.

We are aware of four British "blind" trials in which lymecycline has been compared to other tetracyclines. Whitby and Black¹ compared the effect of one capsule of lymecycline (204 mg. equal in assay to 162 mg. of tetracycline hydrochloride) to one capsule of tetracycline hydrochloride (250 mg.), four times daily for eight days. There was no difference in side-effects, but the authors themselves drew attention to shortcomings in their study. McGill and Bienenstock² gave similar doses and found a difference in side-effects favouring lymecycline and significant nearly at the 1% level. With a double dose of these drugs given for twice the time, which we require for our patients, side-effects would be higher. A comparison of patients treated with tetracycline hydrochloride 2 g. daily or lymecycline 1,630 mg. daily for two weeks showed significant advantages for lymecycline with regard to side-effects.³ A criticism by Stratford⁴ was shown to be invalid,⁵ but unaccountably is still quoted.⁶ In a later comparison lymecycline 1,630 mg. was com-

pared to 1,200 mg. demethylchlortetracycline and 1,200 mg. methacycline, all given daily for two weeks.⁷ Again lymecycline was tolerated significantly better than the other compounds. In all four trials, lymecycline was equal in clinical effect to the other compounds tested—that is, capsule for capsule.

We conclude that lymecycline is better tolerated than the older tetracyclines, especially when a higher dose has to be given. Recently we found that 12 capsules of lymecycline (equal in clinical effect to 3 g. of tetracycline hydrochloride) was as well tolerated as ampicillin in a dose of 4 g. daily, an experience which would have been unlikely if tetracycline hydrochloride had been used.⁸ How many more times must such trials be repeated to convince your expert contributor?—We are, etc.,

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Unexpected Reaction to Anthelmintic

SIR,—I would like to draw attention to an acute psychiatric reaction occurring during treatment with thiabendazole.

The patient, a 57-year-old West Indian, was admitted with hookworm and whipworm infestation, diagnosed from examination of the stools. She was given bphenium hydroxynaphthoate 5 g. daily for four days, and after three days started on thiabendazole 1.5 g. twice daily. After two days of treatment with thiabendazole she became paranoid, deluded, agitated, and violent. She physically assaulted a member of the nursing staff and threw articles about the ward. She was transferred to a psychiatric hospital, where she recovered completely in a few days.

As thiabendazole has only recently become generally available for the treatment of worm infestations, the possibility of such reactions should be kept in mind. Dizziness and disturbance of colour vision have been previously noted,¹ but there have been no reports of psychiatric disturbances.—I am, etc.,

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Ultrasound in Diagnosis

SIR,—In answer to Dr. D. Gordon (24 August, p. 500), who has done so much on the technical side for medical ultrasound in this country, I think the reasons why this method of investigation has not become