Side-effects of Phenindione

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

Another variety of rash should be recognized because it may harbinge the rather frequent serious toxic ("side") effects of phenindione on the kidneys, bone marrow, and liver. The three patients I reported (31 July 1965, p. 305) were women in hospital who had developed, without warning, widespread ichthy emacous 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. In these two, fever and biochemical evidence of liver damage were noted. One patient died.

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 Jopling test was found 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.

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, then it can be looked upon as a "useful" phenomenon and an urgent warning to stop treatment.—I am, etc.,

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1 Silber, W., Amer. J. Dig. Dis., 1968, 13, 252.
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Chloramphenicol and Tetracyclines

Sir,—Your expert contributor's excellent essay on chloramphenicol and tetracycline (6 June, p. 607) was a unfair to tetracycline. He states that "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 tetracycline has been compared to other tetracyclines. Whitby and Black compared the effect of one capsule of tetracycline (204 mg. equal in assay to 162 mg. of tetracycline hydrochloride) to one capsule of tetracycline hydrogen succinate (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 Bienenstock gave similar doses and found a difference in side-effects favouring tetracycline 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 capsules of tetracycline hydrochloride 2 g. daily or tetracycline 1,630 mg. daily for two weeks showed significant advantages for tetracycline with regard to side-effects. A criticism by Strasford's, quoted, is not valid, but was admitted, and is unaccountably still quoted. In a later comparison tetracyline 1,630 mg. was compared to 1,200 mg. demethylchlortetracycline and 1,200 mg. methacycline, all given daily for two weeks. Again tetracycline was tolerated significantly better than the other compounds. In all four trials, tetracycline was equal in clinical effect to the other compounds—tested—that is, capsule for capsule.

We conclude that tetracycline is better tolerated than the older tetracyclines, especially when a higher dose has to be given. Recently we found that 12 capsules of tetracycline (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 was used.

In view of these results, how often must such trials be repeated to convince your expert contributor?

We are, etc.,

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REFERENCES


Anemia and Hiatus Hernia

Sir,—The article concerning iron absorption in hiatus hernia (6 July, p. 22) was of particular interest to me, but the subsequent letter (9 July, p. 185) cannot go unchallenged. It is true that patients with sliding hiatal hernia may present with haematemesis, melena, 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 anaemia. Further, there is no categorical proof that a sliding hiatal hernia is a precarious condition. This is substantiated by a recent prospective study of 628 cases of hiatal hernia which I have investigated and followed up since 1957. 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 regarded as virulent and irreversible, have been over exaggerated. The incidence of "strictures" is distinct from stenosis due to spasm of the oesophagus which 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, suggested histological investigation, 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 of 40% of cases with hiatus hernia an intact abdominal lesion, which very often was the primary cause of the patients' symptomatology, I am, etc.,

W. SILBER.

Unexpected Reaction to Anthelminthic

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 hoarse throat and whitlow infestation, diagnosed from examination of the stools. She had been given benzoxyprazaphosphate 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, delirious, 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, but there have been no reports of psychiatric disturbances.—I am, etc.,

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REFERENCES


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