Balkrishnan for help in the statistical analysis of the data on liver-function tests.

ADDENDUM.—I have realized since this paper was written that my assumption concerning the lower cost of sequential oral contraceptives may be incorrect. It is possible that the increased cost of packaging and ensuring that the right tablets are always packed may more than offset any saving in cost of materials. If this is the case, the most economical oral contraceptive for a national family planning programme may still be a low-dose combination tablet.

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Medical Memoranda

"Collagen Disease" due to Carbamazepine (Tegretol)

Brit. med. J., 1966, 2, 1434

The toxic effects of carbamazepine (Tegretol) hitherto reported included drowsiness, dry mouth, nausea, and vomiting, which appear to be infrequent and not severe. There have been two cases of jaundice, which recovered, and two fatal cases of aplastic anaemia. Generalized erythema, resolving without sequelae on cessation of the drug, occurs in an estimated 3–4% of those taking it, and one case of photosensitivity has been reported. Coombes (1965) reported a case of Stevens–Johnson syndrome from this cause. The following case report illustrates another reaction affecting chiefly the skin, which appears to have been provoked by carbamazepine.

CASE REPORT

A woman aged 63 was seen in December 1963 with a nummular, partly lichenified eczema of nine months' duration involving the neck, the backs of the forearms, and the left wrist. Subsequently, other patches appeared elsewhere on the trunk and limbs. There were good reasons for thinking that the eruption was due to stress, and it settled gradually with rest, sedation, and topical application of steroid creams and fractional x-ray therapy. All signs and symptoms had gone by March 1964. Her only previous dermatological history was of pruritus ani 10 years earlier, for which she received an injection, which was followed by a widespread rash persisting for several months.

Towards the end of 1964 she experienced intermittent pain on the right side of the face, which was not relieved by dental extractions and for which no other cause could be found. During September and October 1965 she took carbamazepine, 200 mg. t.i.d., continuing on 200 mg. b.d. in November and December. Her skin had remained well until the middle of September 1965. On 1 October she was seen again with an eruption which was identical in character and similar in distribution to her previous eczema, and which responded rapidly to similar treatment within four weeks. She remained well apart from slight loss of weight and indigestion until, early in January 1966, she suddenly developed a non-irritant rash of entirely different character, associated with malaise and pain in the right scapular region. On 6 January she presented a discrete eruption of a peculiar dusky heliotrope colour affecting the eyelids, which were slightly oedematous, eyebrows, backs of the elbows, lumbo-sacral region, and wrists. On the dorsal surfaces of

the hands and carpometacarpal and interphalangeal joints the lesions were slightly infiltrated and covered with fine superficial grey scales. The same heliotrope colour was found on the paronychia folds, where capillary dilatation could be recognized with a lens. There was no muscular weakness or wasting, but the clinical picture suggested a diagnosis of either lupus erythematosus or dermatomyositis. All treatment was stopped and she was admitted for intensive investigation, particularly in view of the fact that dermatomyositis at this age is often associated with an internal malignant neoplasm.

Clinical examination by a general physician and a gynaecologist revealed no abnormality apart from the skin. Blood count, E.S.R., midstream urine, serum proteins, S.G.O.T., and urinary creatine were all normal. Skiagram of chest, intravenous pyelogram, and barium-swallow, meal, follow-through, and enema revealed no abnormality.

Before the end of January the rash had completely disappeared and the patient was free from all symptoms. She remained so until 5 March, when the rash, malaise, and pain in the back all recurred. On 4 March she had taken one tablet of carbamazepine and continued on 200 mg. t.i.d. until 7 March. When seen on 10 March the eruption was similar in all respects to that which she had presented in January. The symptoms and signs again resolved spontaneously within three weeks.

COMMENT

The patient had experienced two previous episodes of skin disease, and was perhaps for that reason more liable than usual to react in this way. The recent eruption, however, was totally different in character and was certainly not a recurrence of the endogenous eczema observed in 1963–4 and in October 1965. Its spontaneous recovery on stopping the drug and prompt recurrence on resuming it, followed again by spontaneous recovery, leave no doubt that it was caused by carbamazepine.

Lupus erythematosus, or a syndrome closely resembling it, has been reported in association with the ingestion of hydralazine, derivatives of hydantoin, griseofulvin, sulphonamides, and penicillin. To this list carbamazepine must now be added.

I am grateful to Dr. A. W. Galbraith, of the Medical Department of Geigy Ltd., who kindly supplied me with the relevant literature.

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