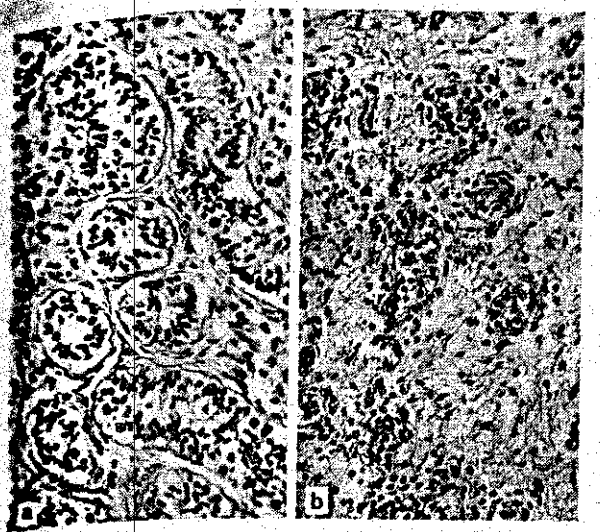

Microscopic appearance of testicular morphology in prepubescent boys.

(a) Normal: immature tubules lined by Sertoli cells and containing spermatogonia; connective tissue shown is scanty; hæmatoxylin and eosin, ×250 (reduced to two-thirds). (b) testis of the 6-year-old boy treated with cyclophosphamide: abundant fibroconnective-tissue stroma with distortion and disarray of small testicular tubules; hæmatoxylin and eosin, ×250 (reduced to two-thirds).

Comment

Fairley et al.[5] described azoospermia and oligospermia in 31 males aged 24–44 years who had received cyclophosphamide. Testicular biopsy revealed no spermatogenesis in 4 of 5 of these patients. Testicular atrophy was also observed. Kumar et al.[6] studied testicular biopsies in 8 males aged 17–48 who had received cyclophosphamide for nephrotic syndrome. Again, testicular atrophy was observed in all patients. Our patient is the first prepubescent male with apparent cyclophosphamide-induced testicular atrophy to be reported. Possibly other prepubescent males treated with this drug may not show as striking testicular changes as observed in this one case, and studies of more cases are needed. Although it is difficult to predict the long-term effects of cyclophosphamide on testicular morphology and function in prepubescent males, the changes observed in this patient would suggest that, with the severe degree of atrophy and fibrosis present, regeneration to functional capacity at puberty would be unlikely.

We agree with Cameron and Ogg [6] that the risk of sterility in addition to other complications of immunosuppressive therapy in such renal lesions as membranous glomerulonephropathy, focal glomerulosclerosis, membranoproliferative glomerulonephritis, and lupus nephritis may justify a vigorous search for other more effective modes of treatment. Further review of dose and duration of cyclophosphamide in prepubescent males is indicated. In the "steroid-resistant" nephrotic syndrome of minimal-change glomerulopathy of childhood, drugs which apparently do not injure reproductive function, such as azathioprine and mercaptopurine, merit trial.

L. R. H. is supported by U.S.P.H.S. special fellowship AM-53086.

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6. Cameron, J. S., Ogg, C. S. *Lancet*, 1972, i, 1174.

CYCLOPHOSPHAMIDE PLUS EMETINE IN LUNG CANCER

SIR,—One of us (K. M.) has seen some of the cases described by Dr. Street (Aug. 19, p. 381) and has been most impressed by case 4 (male, 64, oat-cell carcinoma), whose "quality of life" has been very considerably enhanced. Unfortunately, in our hands treatment with cyclophosphamide 400 mg. intravenously daily for ten days and emetine 1·5 mg. per kg. intravenously on alternate days for ten days has not led to any improvement, but this may well be because we have treated only patients who have already had radiotherapy.

If emetine in some way sensitises the tumour to antitumour therapy—either radiotherapy or chemotherapy—it would be reasonable to give the drug at the time of radiotherapy, and a trial in conjunction with Dr. Brinkley in the radiotherapy department has begun. Concurrently, work to try and confirm Dr. Street's results with cyclophosphamide is also in progress.

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MYXŒDEMA—POSSIBLE SIDE-EFFECT OF LITHIUM?

SIR,—Dr. Myers's communication (June 10, p. 1287) prompts us to report five cases of myxœdema which arose during lithium treatment.

Case 1.—A 47-year-old woman with no family history of thyroid disease had, since 1953, been admitted several times with endogenous depression and had been treated with imipramine and amitriptyline. In August, 1970, prophylactic lithium carbonate was commenced, and in March, 1971, she complained of tiredness, weight-gain, sensitivity to cold, dry and peeling skin, and hoarseness. No goitre could be found. P.B.I. was 0·08 μmole per litre (normal 0·32–0·58); T_4 18 nmole per litre (normal 60–148); radioactive-iodine uptake 4·6% after 24 hours. She was treated with thyroxine, and lithium treatment was continued. Both treatments were discontinued in August, 1971, when the patient complained of effort angina. In October, 1971, thyroxine treatment was recommenced, and in June, 1972, the P.B.I. was 0·64 μmole per litre, T_4 165 nmole per litre, and T_3 0·084 (rel. molc.) (0·7–0·12).

Case 2.—A 63-year-old woman with no family history of thyroid disease had been admitted six times since 1955 with a depressive type of manic-depressive psychosis. She had been treated with E.C.T., chlorpromazine, meprobamate, chlorprothixene, and methyprylone. In December, 1970, prophylactic lithium was commenced. In July, 1971, she complained of tiredness, hoarseness, dry and peeling skin, loss of hair, and weight-gain. No goitre could be found. P.B.I. was 0·07 μmole per litre; T_4 13 nmole per litre; and radioactive iodine uptake 11·4% after 24 hours. After T.S.H. stimulation uptake values were still low. Lithium treatment was discontinued and she was treated with thyroxine. Thyroid-function tests were soon normal and the patient became euthyroid.

Case 3.—A 50-year-old woman with no family history of thyroid disease had been treated since 1969 for manic-depressive psychosis. In November, 1969, prophylactic lithium was commenced, supplemented with chlorprothixene, imipramine, and clomipramine. In January, 1971, the patient complained of dullness of mind, constipation, dry and peeling skin, effort dyspnœa, and weight-gain. No goitre could be found. P.B.I. 0·18 μmole per litre; T_4 22 nmole per litre; radioactive iodine uptake 25·3% after 24 hours. There was only minimal response to T.S.H. stimulation. The patient was treated with thyroxine and lithium was continued. The thyroid-function tests soon became normal and the patient euthyroid.

Case 4.—A 43-year-old woman with no family history of thyroid disease had, since 1961, been admitted eight times for manic-depressive psychosis, six times in a manic phase and twice in a depressive phase. She had been treated with E.C.T. and with neuroleptics. From July to November, 1971, she had