ever, the advice to continue increasing the dose "until intolerable side-effects are provoked or a total daily dose of about 8 g. is attained" should be modified. Experience in starting three to five new patients weekly on treatment with L-dopa has shown that many months are needed to become familiar with the drug's actions, its foibles, and the range of patients' responses to it. Some of our patients have done well on as little as 1.5 g. per day, and only rarely was it necessary to exceed 6 g. per day. In a group of 88 patients we found the average effective therapeutic dose to be 4.5 g. per day. This is in agreement with the average dose used by Barbeau,¹ and was 1.3 g. less than that used by Cotzias, Papavasiliou, and Gellene.²

The therapeutic results of the first reported clinical studies in which large doses of L-dopa were used were so dramatic that, when using the drug for the first time, physicians now tend to overdose patients. During the first few months of our trial we aimed at increasing the dose gradually to an arbitrary upper limit of 8 g. per day, but even patients who were able to tolerate such a high dose without excessive nausea showed a high incidence of other severe effects, particularly involuntary bulbar and limb-muscle dyskinesias, which necessitated cutting back the dose. The dose was reduced from 6-8 g. per day to 2-3 g. per day in some patients without loss of therapeutic effect. It would therefore appear either that the maintenance dose of L-dopa is less than that required initially to achieve a therapeutic result, or a lower dose than the average of 5-6 g. per day reported in early papers becomes equally efficacious when taken over a prolonged period. As is the case with other chronic diseases, there is much individual variation in the drug requirements of Parkinsonian patients; furthermore, it is often necessary to adopt a compromise between a larger dose to attain a maximum therapeutic response and a lesser dose to avoid side-effects. In view of these facts, it is both untherapeutic and unkind to force the dose of L-dopa to an arbitrary maximum of 8 g. per day.

Improvement of Parkinsonian symptoms may continue for many months, so it is reasonable to delay increasing the dose of L-dopa beyond say 5 g. daily in any patient in whom significant improvement occurs within the first month. These individuals tend to show progressive and gratifying lessening of disabilities, and the dose can always be increased later in those with residual symptoms or signs but who have not developed disabling side-effects. Following preliminary laboratory studies, including an electrocardiogram, the majority can be started on L-dopa quite safely as outpatients. Small increments may give a lower incidence of side-effects, but increments of less than 250 mg. are rarely necessary, provided the rate of increase is not too fast. We start outpatients on 250 mg. tablets or capsules with food, as follows:

Day	Breakfast	Lunch	Supper
1st-3rd	1	1	1
4th-6th	1	2	1
7th-9th	1	2	2
10th-12th ..	2	2	2
13th-15th ..	2	3	2
16th-18th ..	2	3	3

and so on, adding 250 mg. every fourth day.

New increments are begun with the second, then the third, and finally the first

dose, because experience shows that patients adapt poorly to the first dose of the day. Patients who become nauseated on this regimen are advised to divide the daily dose of L-dopa into four or more parts, and take each one with food. One to three non-phenothiazine anti-emetic tablets (dimenhydrinate, cyclizine, etc.) may be taken half an hour or more before taking the L-dopa. Many patients find it useful to take one tablet prophylactically each morning on rising.

Both trifluoperazine and haloperidol are useful antidotes to the involuntary movements in some patients, but it is essential to prescribe them in minute doses. When patients are given more than 1 or 2 mg. per day Parkinsonian symptoms tend to recur. If these are mild they may be acceptable, provided the involuntary movements are also alleviated, but in one patient an excellent therapeutic response to L-dopa was completely vitiated by only 1 mg. per day of either of these drugs.—I am, etc.,

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REFERENCES

- 1 Barbeau, A., *Canadian Medical Association Journal*, 1969, **101**, 791.
- 2 Cotzias, G. C., Papavasiliou, P. S., and Gellene, R., *New England Journal of Medicine*, 1969, **281**, 272.

Severe Dermatitis and "Biological" Detergents

SIR,—Acute oedema of the penoscrotal skin area of young boys in the absence of demonstrable infection or intra-scrotal pathology, while not a common condition, is probably better known to surgeons and casualty officers than mention in textbooks would suggest. It is described in three recent textbooks dealing with the surgery of childhood, but labelled "idiopathic".¹⁻³ To the best of my knowledge the possibility of an association with detergents has not been raised.

Over the last 12 years I have seen over 50 patients with this condition. Without exception their underclothes had been washed with one of three leading detergents. The association has been predominantly with one brand, to the extent that one may predict its use with considerable accuracy. In most instances the suspect detergent has been used for the family wash for more than a week before the episode of oedema, but there is some evidence to suggest that inadequate rinsing may have been a factor. Constitutional predisposition to allergic reactions has not been a feature of the affected patients. The suspicion that contact with certain detergents has been a factor has been strengthened by the absence from the case histories of any other common contact or systemic agent; the absence of known recurrence following advice to substitute a soap-based preparation for the detergent in washing undergarments; the recurrence, in two instances, following the re-introduction of the suspected brand into the wash, after more than a year; and positive results on patch-testing three recent subjects.

"Biological" detergents have been freely

available, and no doubt extensively used, in Northern Ireland for several months, but it is only during this last week that I have seen a patient with severe penoscrotal oedema whose clothes had been washed in one. The oedema was unusually severe affecting the scrotum, penis, upper medial thighs, and suprapubic region, but predominantly (and characteristically) affecting one side of the scrotum and penis, the skin of which appeared thickened to almost $\frac{1}{2}$ in. (1.25 cm.) and almost translucent. A dull carmine, macular rash extended from below the umbilicus to mid-thigh, and he had pyrexia (38.5°C) and vomiting and complained of headache and general malaise. It was quite the most severe reaction of this type I have seen, and for this reason he was given a single dose of hydrocortisone in addition to the anti-histamines and bed rest usually employed. Signs and symptoms rapidly subsided to near normal in less than 48 hours. Like Dr. G. A. G. Peterkin (28 March, p. 818) I was reluctant to risk provocation of reaction by patch testing.

Impression and suspicion are not enough to establish a clear relationship of cause and effect, and more information is required to establish or refute the relation of detergents to this condition. The present incidence of penoscrotal oedema would not constitute an argument for restriction in the use of strong detergents even if they were proven to be a cause, but I feel it is only prudent to advise the parents of affected children against the use of detergents for underclothes in these children until more is known about the cause.

It seems to me that the incidence of penoscrotal oedema is increasing, and that the condition should be known to doctors concerned in the emergency treatment of children to a greater extent than it is at present, so that parents can be reassured and advised and unnecessary treatment (including surgery) avoided. There must be, however, no doubt about the diagnosis, for it can never be emphasized enough that torsion of the testes (or the rare epididymo-orchitis of childhood) may present with very considerable unilateral scrotal oedema.—I am, etc.,

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REFERENCES

- 1 Nixon, H. H., O'Donnell, B., *Essentials of Paediatric Surgery*, p. 102. London, Heinemann, 1961.
- 2 Dennison, W. M., *Surgery in Infancy and Childhood*, 2nd Ed. p. 304. Edinburgh, Livingstone, 1967.
- 3 Johnston, J. H., in *Paediatric Urology*, Ed. D. I. Williams, p.45, London, Butterworth, 1968.

Corticosteroids and Pituitary-adrenal Function

SIR,—Dr. J. R. Daly points out in his letter (14 March, 1970) that the depression of plasma cortisol levels which is seen following the injection of methylprednisolone is a normal consequence of corticosteroid administration, and therefore one may question the interpretation of pituitary-adrenal function tests during this period. This argument implies that amounts of exogenous steroid sufficient to inhibit