stopping it, but some months later developed identical chorea again, without having re-started the use of the preparation. When examined it was clear that she was in the early stages of pregnancy.

Sydenham's chorea is uncommon in young adults these days, and when it does appear in otherwise healthy young women most careful inquiry should be made to determine if they have been taking one of the progestogen-oestrogen preparations, for, as these may be prescribed for purposes other than contraceptive, the women may not themselves consider that they are on the pill.—I am, etc.,

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Bronchodilator Aerosols

SIR,—In view of recent misgivings about the use of bronchodilator aerosols, I feel it may be important to report preliminary findings in this field. For some time I have been interested in the fall in arterial oxygen tension following the administration of these substances.¹ Although I do not suggest that it is the cause of death associated with the use of these aerosols, it may well be a contributory factor, especially in already hypoxic patients who have reached the steep slope on the oxygen-dissociation curve. I have therefore carried out an investigation on the changes in blood gases associated with six different aerosol bronchodilators.

	Number of Cases	Number with Blood Oxygen Fall	Average Oxygen Fall (mm. Hg)
Isoprenaline 1% ..	11	10	6.6
Isoprenaline 1%, papaverine 2% (Neo-Epine No. 2) ..	18	10	8.4
Papaverine 2% ..	8	6	6.6
Orciprenaline (Alupent)	8	4	7.6
Salbutamol (Ventolin)	12	10	6.3
Isoprenaline, phenylephrine (Medihaler-duo) ..	12	1	One case—3.0

All patients had chronic airways obstruction which excludes asthma. There was no significant change in the PCO_2 values and the average increase in the forced expiratory volume (F.E.V.₁) for each compound was about 11%.

As may be seen from the Table, with all bronchodilators tested except a combination of isoprenaline and phenylephrine (Medihaler-duo) there was a significant number of patients whose blood-oxygen tension showed a decrease. Using the latter substance only one patient showed a decrease (3 mm. Hg) and the average increase was 9.9 mm. Hg.

The fall in oxygen tensions is probably due to the powerful vasodilating properties of bronchodilators, particularly around hypoxic areas of lung, increasing the venous admixture. It would appear that the addition of an alpha-receptor stimulating drug—phenylephrine—causes constriction or prevents dilatation of the blood vessels and prevents this possibly dangerous side-effect. This may be an important consideration in the manufacture and prescribing of bronchodilators both for aerosol and for parenteral use

in the future. Further investigations are being carried out in this department.—I am, etc.,

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REFERENCE

- Chapman, T. T., and Dowd, D., *Pharmacologia Clinica*, 1969, 1, 107.

Death from Neostigmine Treatment

SIR,—Several points arise from the interesting case report of Dr. James C. Briggs and others (8 November, p. 344) of the child with megacolon who died of neostigmine overdose.

Should not atropine have been given to reverse the bradycardia and profuse salivation noticed on admission, characteristic of the muscarinic effect of acetylcholine? It is appreciated that this in itself would not have averted the fatal outcome.

More important, however, the immediate cause of death appears to have been the apnoea from muscular paralysis. No mention is made in the report of the ability of neostigmine in high doses to cause neuromuscular block by prolonged depolarization of the motor end plate;¹ surely it is well established that the treatment of apnoea due to muscular paralysis is artificial ventilation, of which again no mention is made.

Neostigmine, atropine, and artificial ventilation are in daily use by anaesthetists and "intensivists." Does this not reinforce the view that overdosage involving respiratory inadequacy is more often appropriately managed by physicians specializing in anaesthesia and intensive care?—I am, etc.,

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REFERENCE

- Churchill-Davidson, H. C., and Christie, T. H., *British Journal of Anaesthesia*, 1959, 31, 290.

Alternative to Neostigmine for Megacolon

SIR,—The death of a child on neostigmine therapy for megacolon (8 November, p. 344) is, of course, a tragedy, and I would like to bring to the attention of clinicians an alternative and safer drug than neostigmine—namely, bethanechol chloride.

Neostigmine is usually recommended as the cholinergic drug of choice in gut motility disorders, partly because it is to be found in every hospital pharmacy. However, its pharmacology is complex, as in addition to being primarily an anticholinesterase agent¹ it also has marked nicotinic actions at both parasympathetic and sympathetic ganglia.^{2,3} These latter actions increase its potential for producing toxic side-effects.

On the whole, cholinergic drugs are more effective in enhancing intestinal motility than anticholinesterase agents, and studies have shown that the most promising of these is bethanechol chloride.⁴ The actions of this drug are purely muscarinic and side-effects are minimal. Its effect on the intestinal tract is more marked, relative to its other actions, than any other choline derivative, and it acts

on both innervated and denervated intestine.⁵ It has been shown to be of value in the management of ileus,⁶ and, as it can be taken orally, its effectiveness in megacolon would be well worth a try.—I am, etc.,

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Unusual Effect of Fenfluramine

SIR,—Dr. M. Y. Alvi's letter (25 October, p. 237) describing an unusual effect of fenfluramine prompts me to report the following cases:

A 45-year-old woman taking phenelzine 15 mg. t.d.s., and chlordiazepoxide 5 mg. t.d.s., developed severe headache, neck stiffness, and nausea within an hour of taking a 20 mg. fenfluramine (Ponderax) tablet. Shortly afterwards she "collapsed" and remained stuporous for approximately four hours. She remained clouded and drowsy for the rest of the day, and made a gradual recovery over the next 72 hours.

A 56-year-old woman on chlordiazepoxide 10 mg. t.d.s. began to take fenfluramine one tablet twice daily for weight reduction. After several days it was noted that she was perplexed and confused towards evening, and restless throughout the night. After approximately one week on fenfluramine she became acutely agitated towards evening, misidentified people about her, and expressed vague paranoid ideas. On examination she was distressed, overactive, showed pupillary dilation, and her consciousness was clouded. On phenothiazines and sedation she settled, the fenfluramine was stopped, and there has been no recurrence.

An 18-year-old youth with a long history of drug abuse was of particular interest because under the influence of amphetamine and related drugs he manifested a distinct facial dyskinesia both while "going up" and "coming down." Ashcroft¹ *et al.* have reported "a physical sign widely recognized among the amphetamine fraternity. This takes the form in addicts receiving the drug of continuous chewing or teeth-grinding movements, with rubbing of the tongue along the inside of the lower lip, often leading to trauma to the tongue and lip with ulcers visible to inspection at both sites." This boy, however, showed a distinct pattern of movement similar to the bucco-linguo-masticatory dyskinesia described by Sigwald² and recently reviewed by Crane.³ On one occasion he was seen chewing gum as his usual means of disguising the facial movement, and complained that on the suggestion of some friends he had had "half a dozen or so" Ponderax (fenfluramine) tablets, which they had been successfully using to obtain "trips" or "highs," but got nothing from it but his teeth-grinding and movements. He said, "Except for the grinding, which has gone on all night, I wouldn't have known they were pep pills."

Thus, a drug interaction with monoamine-oxidase inhibitors similar to that which occurs with amphetamines, and acute confusion

episodes, dyskinetic movement disorder, and adoption as a drug of abuse, may all be added to the record of a drug which has already been associated with a small number of fatalities. As with other drugs introduced as substitutes for the amphetamines, claims have been made that fenfluramine is a drug of low toxicity which does not stimulate the central nervous system. These assertions can no longer be sustained, and it is imperative that the same caution be exercised in the use of this drug as would be appropriate to other central nervous stimulants.—I am, etc.,

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- 2 Sigwald, J., Bouttier, D., and Courvoisier, S., *Revue Neurologique*, 1959, **100**, 553.
- 3 Crane, G. E., *American Journal of Psychiatry*, 1968, **124**, Supplement 40.

SIR,—I read with interest Dr. M. Y. Alvi's report of nightmares described by a patient who had been taking fenfluramine as an aid to reducing weight (25 October, p. 237).

Today I saw a female patient aged 45 for whom I had prescribed fenfluramine to be taken morning and evening five days ago. She complained bitterly of extreme sleepiness and lethargy during the three days that she persisted in taking it, and indeed she claimed that apart from brief waking spells she slept for 24 hours after the first day's tablets, and was totally unable to get up to prepare her husband's breakfast and lunch on the other two occasions. On stopping the tablets at her own discretion she experienced a normal night's rest with a return of her normal daytime alertness. I would point out that she is a well-balanced, rather phlegmatic individual and has never exhibited any symptoms of anxiety, depression, or hysteria.—I am, etc.,

Leeds,
Yorks.

GERALD ELLIS.

Avian-Battey Mycobacteria Infection

SIR,—In view of the increasing interest in atypical mycobacterial infections and the recent article on Avian-Battey group infection in England and Wales (17 May, p. 412) and the evidence from Western Australia (2 August, p. 300) our considerable experience with Battey infection in Florida may be of some interest, and I enclose a Table derived from our register of excretors since 1962.

The marked increase in the number of excretors was due to the replacement of the old sputum digestion technique by the much less abrasive Zephiran trisodium phosphate

sputum digestion technique in June 1964. In 1965, the first full year with the new technique, a 200% increase in the total number of excretors occurred. It will be noted that there was only a small increase in the number of *M. kansasii* group I excretors, as indeed there was in the number of *M. tuberculosis* excretors. The increase in atypical mycobacterial cultures was from 1.6% to 6.2%, and in *M. tuberculosis* cultures from 3.8% to 4.8%. An additional significant finding was that 8.4% of specimens yielding negative smears gave positive cultures, indicating the unreliability of the negative smear report. Battey infection is not uncommon in Florida and accounts for some 4% of tuberculosis hospital admissions, although many cases are treated privately. Battey infections are largely resistant to normal therapy, but in-vitro tests suggest that Rifampin may be more effective.

It is of course true that thanks to chemotherapy the community now includes old tuberculous cases, many with a residual fibrosis, itself a predisposing factor to the acquisition of atypical infections. A recent analysis of Battey cases in Florida revealed that, apart from *M. tuberculosis* infection, emphysema, chronic bronchitis, asthma, bronchiectasis, diabetes, and gastrectomy were predisposing causes actually diagnosed in well over 30% of cases. In some areas silicosis would increase this percentage. Similar figures were obtained for the *M. kansasii* cases.

It would seem obvious, therefore, that although *M. tuberculosis* infection may be a considerable predisposing cause to the acquisition of atypical infection it is so in only some 30% of atypical cases. The other causes of pulmonary fibrosis, idiopathic and otherwise, together account for the majority of cases. The aetiological relationship of the atypical infection to the pulmonary fibrosis is largely undetermined, and the incubation period for these infections is quite unknown. Schaefer (personal communication) has recently confirmed two strains of *M. intracellulare* (Battey bacillus) isolated from Florida soil as Boone and Yandle serotypes, both frequently implicated in cases of human pulmonary mycobacteriosis.

Further information on the biochemical tests differentiating the potential pathogens and common saprophytes in each of Runyon's groups of atypical organisms will shortly appear in the *Southern Medical Journal*.

These concluding Florida studies have been supported in part by Grant 5R01, CC00062-10, Department of Health, Education and Welfare.

—I am, etc.,

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Management of Infants with Cerebral Palsy

SIR,—The balanced discussion by Dr. J. Wilson on the management of children with cerebral palsy (18 and 25 October, pp. 152 and 211) is obviously intended for the guidance of the family doctor. May I ask for clarification of several points arising from his discussion?

What immediate plans have been made for setting up and medically staffing the urgently needed district assessment centres (as distinct from one or two research centres)? It is obvious that highly skilled specialists are essential to appraise the complex neurological and mental problems which are so commonly found associated with the palsy.

Where does one find the centres he mentions, where it is "usually possible to make arrangements for . . . a preschool programme of treatment" to provide "passive stimulation and movement and an awakening of interest in under-used limbs"?

Where neither of these facilities are available, why are parents of such infants discouraged (as Dr. Wilson admits they usually are) from seeking the highly specialized treatment methods which provide sensory stimulation, play, and functional patterning? Such treatment must, at the very least, provide general stimulation of a child whose "inability to explore his environment may add sensory and social deprivation to his physical problems." I am sure that Dr. Wilson, like myself, must have seen good results from two well-known methods of such treatment, which aim at return to normality in some cases with the help of intensive therapy by the parents. (Neither of these methods is unrealistic enough to claim return to normality as its usual goal.)

Does objection to the methods exist as a consequence of the involvement of parents in the treatment? A sense of guilt may indeed be felt by parents who have been persuaded to undertake a laborious method and become discouraged. In other parents the advice of folded hands while awaiting spontaneous progress or institutionalization may fit in with deep-seated rejection feelings. Nevertheless, there is a considerable number of parents (particularly those who have seen a capacity to learn in their child) in whom a policy of inactivity encourages a deep sense of suspicion of their advisers, and of impotent unease. This can be even more frustrating than the sense of guilt felt by those who have tried and failed. Surely we should assess the emotional attitudes of both parents as carefully as we should make a realistic neurological assessment of the infant's capacity to progress.

May I take the liberty of quoting Dr. Wilson's words in a somewhat different context: "exchange of correspondence, even if faithfully undertaken, is only second best, and

Identified Florida Excretors of Unclassified Mycobacteria. Analysis by U.M. Group and Year

U.M. Group	1962		1963		1964		1965		1966		1967		1968	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
I	24	4.3	26	5.1	22	2.6	26	1.7	46	2.8	39	3.7	66	10.0
II	138	25.0	135	26.3	391	45.5	728	46.2	880	53.1	364	34.6	228	34.8
III	274	49.7	264	51.5	249	28.9	510	43.4	410	24.7	225	21.5	155	23.6
IV	99	17.9	72	14.0	161	18.7	263	16.7	276	16.7	365	34.7	175	26.7
Unknown	17	3.1	16	3.1	37	4.3	47	3.0	45	2.7	58	5.5	32	4.9
Total	552	100.0	513	100.0	860	100.0	1,574	100.0	1,657	100.0	1,051	100.0	656	100.0

June 1964, Zephiran trisodium phosphate sputum digestion technique instituted.
January 1, 1967. Excretors of Tween hydrolysis positive organisms of Group II and Group III dropped from register.