revealed a characteristic alteration of the ganglion cells with many intracytoplasmic membranous structures which are possibly phospholipids (see Figure). The close morphological resemblance between these inclusions and those described in amaurotic familial idiocy is apparent when comparing the electronmicrograph of a human cerebral ganglion

Electronmicrograph of rat ganglion cell from a chloroquine-treated hooded rat (100 mg./kg. daily for 12 months). The cytoplasm contains many membranous structures.

cell in Tay-Sachs disease⁵ with our own observation. The striking similarity between the two entities at both the macroscopic and ultrastructural levels suggests the possibility of common features in the pathogenesis of these specific lesions.—We are, etc.,

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Children with Asthma

SIR,—Dr. B. Dalton (30 March, p. 838) advocates the early use of steroids in the treatment of asthma which may be “psychologically determined” in children. Dr. Anne Tothill (p. 837) suggests that the action of isoprenaline may be disadvantageously modified in states of anxiety, and notes that it is not known if it is altered when given with steroids. Dr. M. J. Greenberg (p. 838) suggests that the use of disodium cromoglycate (Intal) may assist reduction of dosage of prednisone.

I should like to comment on those letters as a result of my experience as a psychiatrist working with a paediatric team in a special clinic for severely ill asthmatic children, many of whom are treated with steroids because they have failed to respond to all other forms of treatment. During a three-year period 32 children under 13 years of age received 5 mg. prednisone twice daily. At the start of our survey I might have been tempted,

in agreement with Dr. Dalton, to advocate the early use of steroids in those asthmatic children who showed emotional disturbance, as it was notoriously difficult to get parents to accept psychotherapy for them. The initial response of the whole group of 32 children on prednisone was excellent, and those children who were obviously emotionally disturbed responded as well as the rest of the group. Physical symptoms abated, reactive anxiety disappeared, and long-standing symptoms of emotional disturbance caused less distress than before treatment. The children were not distressed by side-effects of prednisone and developed no replacement symptoms.

Unfortunately a minority failed to sustain this improvement. Of course, physical determinants are of critical importance, but some categories of psychological disturbance were prominent in the case histories of those who failed to sustain a good response. Eleven out of 32 children became dependent on maintained use of steroids, and five of those were among those whose emotional disturbance appeared to play a decisive role in the severity of their asthmatic condition. In four other children personality development showed modifications in character organization, often socially acceptable, but clinically disadvantageous when viewed in relationship to the perpetuation of the asthmatic wheeze and its recurrence during steroid withdrawal. It is possible that this group shows most clearly the complexity of relationship between experience of eczema and asthma, psychological modification of the personality, and response to treatment by steroids.

Three children subsequently died, including two of these severely emotionally disturbed children. We suspect that all three used aerosols excessively during the period of great anxiety which preceded their death. Hence my interest in Dr. A. Tothill's and Dr. M. J. Greenberg's letters. We noted the high incidence of dependency upon comfort habits and failure to resolve infantile dependencies on the mother. These psychological problems were reactivated during the withdrawal stage, and the children became acutely distressed if forbidden to use their inhalers. Research into the safety of these is essential. I suggest that physicians and psychiatrists should co-operate and explore all methods of treatment before resorting to steroids. But if these become necessary they can provide a “breathing space” in which renewed efforts can be made to tackle psychological and physical problems and modify dependency on the use of aerosols.

The cases reported are part of a study conducted by Dr. A. P. Norman at the Hospital for Sick Children between 1961 and 1964.

—I am, etc.,

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Deaths from Asthma

SIR,—Your correspondent Dr. Anne U. Tothill (30 March, p. 837) suggests that the bronchodilator action of isoprenaline could be reversed to bronchoconstriction in asthmatic patients using excessive amounts of this catecholamine. Further, the bronchodilator action of adrenaline secreted during an asthmatic attack might induce

bronchospasm in the presence of excess isoprenaline. We have studied the interaction of catecholamines on bronchial smooth muscle in the anaesthetized guinea-pig measuring bronchoconstriction and bronchodilation with a transducer system. A full account of our experiments will be published elsewhere at a later date, but in the meantime one of the findings is of relevance to Dr. Tothill's point.

The bronchodilator effect of adrenaline was measured as reduction of the bronchoconstriction produced by histamine. Injection of either adrenaline or isoprenaline 20 seconds before the injection of histamine reduced the histamine bronchospasm. Infusions of either catecholamine also reduced histamine bronchospasm. If the injections of one catecholamine were repeated during an infusion of the other the effects of the two catecholamines in reducing histamine bronchospasm were additive. Even though the infusions were prolonged the bronchodilator effects of injections persisted. This is in contrast with the effects of injections on the cardiovascular system during infusions: the tachycardia and the effects on blood pressure of injections of isoprenaline, adrenaline, and orciprenaline were reduced or abolished during the infusion of any one of these drugs.¹ In fact the depressor effects of injections of isoprenaline or of low doses of adrenaline were reversed by infusions. However, no reversal of the bronchodilator actions of adrenaline or isoprenaline occurred during infusions. From these findings it is clear that interactions of drugs on one system do not necessarily apply to another.—We are, etc.,

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REFERENCE

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SIR,—As a postscript to the lengthy correspondence (6 April, p. 50 and others) on this topic, we should like to make a brief comment on the type of cardiac arrest we have observed in patients with status asthmaticus, and on the treatment of this complication. It is widely assumed that cardiac arrest in status asthmaticus is usually due to ventricular fibrillation, and this could conceivably be the main cause of death in those patients who die in their homes, and in whom ventricular fibrillation may have been induced by the excessive self-administration of isoprenaline. In this unit, however, ventricular fibrillation has been responsible for cardiac arrest in only one of the four inpatients with status asthmaticus who have developed this complication, and the patient was an elderly man who may have had an inadequate coronary circulation. Electrocardiographic recordings showed that the cardiac arrest in the other three patients was due to ventricular asystole, preceded by progressive bradycardia, and we suspect that this may be a more frequent cause of cardiac arrest in status asthmaticus than ventricular fibrillation, particularly in hospital inpatients, who are usually spared the potential hazards of adrenaline and isoprenaline.

In our first case of cardiac arrest caused by ventricular asystole external cardiac