treatment of asthma where there is a history of the excessive use of aerosol bronchodilators.—I am, etc.,

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Pressurized Aerosols in Asthma

SIR,—Recently correspondents have suggested that excessive amounts of sympathetomimetic drugs cause cardiac arrhythmias in asthmatics (4 March, p. 563, 25 March, p. 756). In this context I think the following case is of interest.

The patient, a man of 46, has suffered with asthma for 20 years. He was first admitted to this hospital in September 1966, with severe bronchial asthma and a pulse of 160 a minute. An electrocardiogram showed atrial flutter with 2:1 block.

The asthma responded to steroids. When free from bronchospasm sinus rhythm was restored with direct-current shock. He admitted to refilling his "Rybar" inhaler 10 times a day during the three days preceding this admission. This means he was inhaling approximately 200 mg. of adrenaline a day. When discharged he was advised to use inhalers sparingly. He was seen in outpatients a month later. There was considerable bronchospasm but he was in sinus rhythm.

He was readmitted on 2 March this year with a further attack of asthma. Again an electrocardiogram showed atrial flutter with a 2:1 block. In the week prior to admission he had used three "Bronchilator" inhalers—one in the preceding 24 hours (ten times the recommended maximum dose). Direct-current shock has again converted the flutter to sinus rhythm.

I thank Dr. R. D. Blachford for permission to publish this case.

—I am, etc.,

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Traveller's Oedema

SIR,—During the recent flights of man in space, where gravity is non-existent, travellers' oedema was not observed, although the astronauts remained in the capsules up to 14 days.¹

The genesis of traveller's oedema is believed to be due to immobility and orthostasis. In the absence or reduction to a minimum of movements of the legs contractions of muscles which normally aid the flow of blood are non-existent, and a state of comparative venous stasis ensues. This is greatest in the lowest venules because of the greater hydrostatic pressure of the column of venous blood.² Thus oedema starts to form as soon as the lower extremities become inactive and continues to increase during the inactivity. It has been pointed out³ that the static filling pressure of the venous circulation in the vertical posture is chiefly determined by the size of the total blood volume of the venous

trunk and the potential capacity of the whole vascular bed.

Orthostasis is not a factor in the case of astronauts, since the hydrostatic pressure is nullified in the zero gravity environment. Regarding the factor of immobility, this is also neutralized owing to pneumatic cuffs used for massage of the legs and the programmed isometric muscular exercise performed by the astronauts.

Ideal conditions for a separate study of the immobility factor were expected to be present in experimental animals put in orbit round the earth. In effect, neither pneumatic cuffs to serve as a substitute of the muscle-pump nor any kind of muscular exercise imposed on the animals in space has been used in these experiments. Nevertheless, these animals, as seen in televised pictures, although apparently quiet, were alert and standing upright with their legs stretched.⁴ It is evident that the factor of immobility was absent in these cases too, and in a weightless environment, with the muscle-pump continuously working, the lack of hydrostatic pressure on the venous system facilitated fluid transfer from the extravascular spaces, thus preventing oedema.

It would be interesting to assess the effect of the immobility factor alone in the production of oedema in an animal kept under long-lasting anaesthesia during a long space flight.—I am, etc.,

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Treatment of Choriocarcinoma

SIR,—Professor W. S. H. Tow and Dr. W. C. Cheng's paper "Recent Trends in Treatment of Choriocarcinoma" (4 March, p. 521) touches the issue of how research into uncommon diseases can be effective. Before chemotherapy was applied to choriocarcinoma no clinician ever saw more than a few cases; there was no progress and the disease was almost invariably fatal. When a 23% recovery rate was reported¹ it became clear that cytotoxic chemotherapy had achieved its first major success, and gynaecologists quickly recognized the need for systematic studies. Treatment centres for choriocarcinoma evolved with the purpose of providing surgical, medical, nursing, and specialized investigatory facilities. In these units accumulated experience feeds back continuously into patient care, systematic evaluation of new therapeutic measures is facilitated, and knowledge gained from choriocarcinoma is applied to other neoplasia. Recovery of 70 to 80% of patients with trophoblastic neoplasias is now achieved, and, if diagnosed within four months of the antecedent pregnancy, is probably always curable. Much improvement in the treatment of cerebral metastases and advanced diseases is needed, however, and these improvements will probably come if systematic studies are maintained. If it were shown that the results of treatment in specialized centres were equalled by those in non-specialized units, the case for

specialized treatment would be weakened but not demolished.

Tow and Cheng write that they have safely and successfully managed the chemotherapy of choriocarcinoma with hysterectomy, fresh blood, and simple assays of human chorionic gonadotrophin. Modestly discounting the value of their own considerable experience, they suggest that other general gynaecological units can do the same for local cases. The reader is led to believe that some workers have claimed that hysterectomy is valueless and that sterile wards are essential. Such claims have not, I think, been made and they should not distract attention from the dissociation between Tow and Cheng's conclusions and their evidence.

The proposition that the Singapore results equal those obtained elsewhere should be based on sound comparisons. Tow and Cheng omit these, perhaps because their pathological classification, which admits hydatidiform mole and invasive mole into the category of "choriocarcinoma," precludes it. The least arbitrary basis for assessment of their results is the ratio of molar to non-molar pregnancies anteceding choriocarcinoma. Pre-chemotherapy studies^{2,3} found that for fatal cases this ratio was about 1:2. An epidemiological study found no evidence that mole was a relatively more frequent antecedent to choriocarcinoma in S.E. Asia than in the U.S.A.⁴ Most chemotherapy series include an excess of post-molar cases, but the Singapore series ratio is 4:1, and in the last 25 cases it is apparently 12.5:1. Accordingly, the expected number of fatal cases without treatment would be about 24. The reported figure of 30 deaths with treatment indicates either that the disease is different in Singapore or that treatment of potentially fatal disease there is ineffective. Despite the excess of benign lesions treated as choriocarcinoma, Tow and Cheng's fatality rate is twice that of a somewhat larger series at Fulham Hospital.

Hysterectomy is not valueless in choriocarcinoma, but Tow and Cheng do not do this problem justice. In Singapore more than three-quarters of the patients have more than three children;⁵ in our series a half are childless. Tow and Cheng do not hysterectomize young nulliparous women or those with widespread metastases; since no one has condemned hysterectomy in elderly multiparous women without evident metastases, all they are asserting is its value in patients with a few distant metastases. Their case for hysterectomy appears to be the belief, not any evidence, that it promotes spontaneous regression of metastases; the onus of proving such a case rests on its advocates, not its critics.

Tow and Cheng, advocating hysterectomy, write it "eliminates once and for all the source of tumour emboli and thus aids the body defence mechanism," and "its value has been amply demonstrated." This follows a discussion which explains why hysterectomy often delays appropriate treatment. They also compare a surgically fit hysterectomized group having a few metastases with a non-hysterectomized group which includes all their patients "with widespread metastases." The comparison is audacious, but the difference in results is not significant ($P = < 0.05$). The only clue to their conclusion lies in Table I of Tow⁶ and Table II of Tow and Cheng. Twenty-five recent additions to the series have included 12 further hydatidiform moles and no addition to the total number of deaths. Deaths in their "no chemotherapy" group have, however, increased and the total number of deaths in the "hysterectomy-chemotherapy" group have, by inference, decreased. Spontaneous resurrection? Or did the