say that it is easy for me to wear shorts both because I live and work in the Provinces and, as a community physician, I am not a "real doctor." Well, we do have sartorial standards in the Provinces—indeed, they are often higher than in London—and we community physicians have our standards also. I am often called on to pronounce on some policy in housing or social service debates in which my status as doctor is all-important. Will the sight of my knees reduce my credibility?

Society changes and we must change with it. It is not so much decaying as melting under our climatic change. I was in Covent Garden Opera House last week and by the end of "Don Giovanni" every man was without jacket and tie (except, interestingly enough, Mr B Levin). Even MCC members are now allowed to shed their jackets.

If doctors do adopt short trousers it is wise to let every registered practitioner wear them without considering the effect that the sight might have on some patients. Should the General Medical Council develop a supplementary register of approved short-wearers or would this infringe medical freedom? Should community medicine study the effects of short-wearing before any action is taken or is this the thin end of the wedge of medical audit by the administration?

Now is the time to debate such issues. We have nothing to lose but our trousers.

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T Lymphocytes in kidney allograft recipients

SIR,—Dr T Tursz and others (3 April, p 799) report the results obtained with spontaneous sheep erythrocyte (E) rosette test carried out on lymphocytes from 14 renal allograft recipients on the occasion of 17 rejection episodes. They observe that most (12/17) rejection crises were associated with a rapid decrease in E rosettes before steroid treatment and that clinically successful steroid pulses induced an increase in E rosettes.

We have determined the absolute number and the percentage of T and B peripheral blood lymphocytes 1-3 times a week for 2-5 months in 30 patients with renal transplant (480 observations). T cells were identified by E-rosette formation¹ and B cells by EAC-rosette formation² and by immunofluorescent staining of surface immunoglobulins (Ig).³ Twenty-five rejection episodes occurred in 21 patients. Contrary to the findings of Dr Tursz and his colleagues no significant change was found in the relative and absolute numbers of T cells during rejection before steroid-pulse therapy.

Intravenous pulses of methylprednisolone, 1 g every 48 h, used in the management of acute rejection, induced profound effects on the circulating lymphocytes. There was a steep though transient fall in the total lymphocyte count, maximal at 12 h after steroid administration, when, on average, only $49 \pm 17\%$ of the cells initially present remained in circulation ($P < 0.001$). This lymphocytopenia was, however, selective in that, despite a fall in the absolute numbers of both T and B lymphocytes, there was a proportionately greater depletion of circulating T lymphocytes, $40 \pm 16\%$ of the initial number of E rosettes remaining at 12 h, whereas $72 \pm 30\%$

of Ig⁺ lymphocytes were still present at that time ($P < 0.01$). Thus the proportion of T cells declined after methylprednisolone (from $62.1 \pm 10.7\%$ to $48.6 \pm 8.7\%$, ($P < 0.01$)) whereas the proportion of B cells actually rose (from $24.1 \pm 7.7\%$ to $36.7 \pm 6.8\%$, ($P < 0.005$)). The lymphocytopenia and T-cell depression were still present, though less marked, at 24 h, but the counts had returned to the original levels 48 h after methylprednisolone administration. The most likely explanation of this steroid-induced lymphocytopenia could be a redistribution of cells from the circulation to other body compartments (bone marrow?), as suggested by experimental models^{4,5} and studies in human beings.⁶

Our results confirm the "need for caution" suggested by Dr Tursz and his colleagues in using the E rosette test and, more generally, B and T cell markers for monitoring anti-graft immunity in renal allograft recipients. However, our findings are different in that in most rejection episodes the number of E rosettes remained stable and steroid pulses induced a profound though transient lymphocytopenia. This latter finding may be explained by the fact that in our patients the determinations were performed every 12-24 h after steroid pulses.

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Further thoughts on hypnotics

SIR,—Dr John R Bennett's "Personal View" (May 29, p 1338) was most illuminating, especially his comments in the first and last paragraph—for example, "all hypnotics have been forbidden on my wards, except on my personal direction." It would be enlightening to know if other consultants engender similar attitudes or whether they turn a blind eye while innumerable housemen, either on their own initiative or egged on by nursing staff adept in the art of "pharmacological overkill," hand out Welldorm (dichloralphenazone), "Moggies" (nitrazepam), or the inordinately expensive Heminevrin (chlormethiazole) with thoughtless abandon.

Taking Dr Bennett's initial comments a step further I would suggest that hypnotics are being prescribed quite uncritically in the institutions which ought to know better, with little thought given to specific indications or long-term effects. The great majority of prescriptions for hypnotics are based on invalid indications, the main one being noise, the most inexcusable reason of all. The noise is created by the chattering of animated, thoughtless night staff together with the flinging of metal bed pans around a sluice room accompanied by a symphony of plumbing; jack-booted night ward rounds by doctors conversing in anything but discreet tones; and the use of ward lighting after hours in a way which would put Piccadilly Circus to shame. The remedy is self-evident, but woefully the alternative, damping the patients'

responses, is seen as a convenient, natural method.

Solicitous insistence on eight hours plus of slumber for hospital inpatients with their mundane daily timetable is evidently pointless, as their nocturnal spells are bound to be shortened at times. Old age precludes the hours of sleep we take as normal and it is consequently ludicrous to compel prolonged nights on such patients artificially by means of drugs. The occasional irregular night is insignificant, except to those individuals who regard sleep in the same light as the desirability of opening their bowels by the clock. And, finally, the practice of issuing hypnotics on request I find reprehensible.

Hospitals are moving, and being moved, steadily to a situation where every aspect of mental and physical performance in hospital is catered for pharmacologically. Where we should be making efforts to reduce poly-pharmacy and the size of the patient's drug chart, with its inherent problems of side effects and drug interactions, we are needlessly adding to it.

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What do community physicians do?

SIR,—Dr W S Parker (26 June, p 1588) has told us what the medical officer of health used to do. Dr P H M Carson (12 June, p 1469) and many other members of the profession are anxious to know what community physicians do now, especially as Dr Parker informs us that Whitehall has tied their hands behind their backs.

A ROBERTS

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Compulsory seat belts

SIR,—I read with interest Dr John Knight's letter from Victoria (5 June, p 1391). Their improved road accident statistics following the compulsory wearing of seat belts is encouraging in view of our Government's pending legislation. Here too there is a strong lobby against the Bill on several grounds, including the infringement of liberties. The views of statisticians and politicians are being voiced but not those of road accident victims, particularly those who have been cut by windscreen glass. I have found it rewarding to study 20 such patients. None of them had been wearing a seat belt at the time of the accident. They are 12 men and 8 women of average age 22 years. Eighteen of them had been on short journeys—within 20 minutes of home—and only two were on longer journeys. Twelve were drivers and eight front-seat passengers.

Eighteen of the 20 volunteered the information that the wearing of seat belts would probably have prevented the injury caused by their contact with the windscreen and fascia—only two patients disagreed. Sixteen of these 18 patients attributed their non-wearing of seat belts to laziness, their hurry to get somewhere, or the late hour. None found seat belts uncomfortable. The remaining two of these 18 patients did not have seat belts fitted in their cars.

Now, many months and years later, only 10 of these patients regularly wear seat belts. Thus many of this select group of road

accident victims don't wear seat belts, although they believe in their effectiveness to prevent injuries and have been injured through not wearing them. So what hope do we have in convincing the rest of the public to wear seat belts, short of Government legislation?

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Mechanism of the asthma attack

SIR,—The classical theory of asthma suggests that an asthma attack is due to a contraction of the bronchial musculature directly caused by chemical mediators locally liberated by sensitised bronchial mast cells following the interaction of antigen and antibody fixed to the mast cell membrane. This traditional concept has been challenged by some recent studies: (a) atropine can block the antigen-induced bronchoconstriction in asthmatic patients¹; (b) vagal blockade (with vagotomy, cooling, or atropine) markedly reduces the bronchoconstriction in experimental asthma in allergic dogs²; (c) in guinea-pigs sensitised to the tracer protein horseradish peroxidase and challenged with an aerosol of the antigen a significant diminution of airways resistance has been observed, although it was not possible to demonstrate any penetration of the tracer protein beyond the basement membrane of the bronchial epithelium.³

Two hypothetical suppositions conflicting with the classical theory follow from a consideration of these findings. Firstly, that the bronchoconstriction characteristic of the asthma reaction is mainly due to a vagal reflex triggered by chemical mediators liberated by the sensitised mast cells on contacting the antigen. Secondly, that the interaction between the antigen and the antibody fixed to the mast cells, with the resulting liberation of chemical mediators, occurs (at least in the first phase of the asthma reaction) in the bronchial epithelium, as this, because of its firm attachments, does not allow the passage of the antigen molecules as far as the subepithelial connective tissue where, according to the traditional concept, the antigen-antibody interaction has hitherto been thought to occur.

In the hope of verifying the possible presence of mast cells in the bronchial epithelium, I have

examined sections of biopsy specimens obtained from the bronchi of chronic bronchitics and asthmatics and stained by a selective method for mast cells (alcian blue 8 GX at pH 0.2 after permanganate oxidation). In all cases I have observed the presence of scattered mast cells among the epithelial cells and at the surface of the epithelium. These cells were rich in granules in chronic bronchitics and in asthmatics in remission, while they were practically degranulated and therefore often hardly identifiable in asthmatics in the active phase (see figure).

These findings suggest that the prime mover in the chain of events leading to an asthmatic crisis is situated in these intraepithelial mast cells, degranulation of which liberates histamine, which, stimulating the intraepithelial lung irritant receptors, causes a reflex vagally mediated bronchoconstriction.⁴ The constriction of the bronchial wall stimulates in turn, through a mechanism of positive feedback, the irritant receptors, in this way creating a vicious circle⁵ so that an intense bronchoconstriction could be triggered by a comparatively light stimulus.

In a second phase the damaged epithelium tends to flake off, as is often observed in bronchial specimens from asthmatics in the active phase.⁶ This facilitates the penetration of the antigen into the subepithelial connective tissue rich in mast cells,⁷ which become involved in the reaction, degranulate, and liberate chemical mediators, causing further bronchoconstriction.

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Sodium valproate and platelet function

SIR,—We have read with great interest the letter from Dr S G N Richardson and others (24 January, p 221). The minimal platelet dysfunction which they observed in vitro after incubation of citrated plasma with sodium valproate and the absence of significant effects in 23 patients taking sodium valproate do not agree with our results.

Examination of coagulation factors and platelet function tests were carried out on 20 children with seizures. The patients were under treatment with sodium valproate and the effectiveness of administration was ensured by determination of serum levels of the drug. In the five patients in whom coagulation studies gave normal results before treatment was started abnormalities were found during treatment in tests which included thrombelastography,¹ platelet adhesiveness,² retention,³ spreading,⁴ thrombin-induced aggregation,⁵ bleeding time,⁶ platelet count, and prothrombin consumption. Because of these findings we investigated 15 further patients who had been receiving sodium valproate for periods ranging up to two years; six of them had developed clinical signs of haemorrhagic disease, including petechiae, epistaxis, otorrhagia, and prolonged bleeding after surgery. In these 15 patients and the five previously investigated the total numbers of abnormal findings were as follows: thrombelastography, 15; platelet adhesiveness, 14; retention, 11; spreading, 10; thrombin-induced aggregation, 10; bleeding time, 6; and platelet count, 7. Partial thromboplastin

time (2), Quick's prothrombin time (5), and prothrombin consumption (4) were decreased in some patients.

Our in-vitro investigations with platelet-rich plasma confirmed the assumption that sodium valproate influences platelet function, resulting in liberation of platelet factor 3 after adding adenosine diphosphate,⁷ decreased spreading of platelets, and inhibition of thrombin-induced aggregation. Furthermore, we have found that thrombin-induced lipid peroxidation⁸ in platelets is inhibited by sodium valproate. To explain this last observation we postulate that sodium valproate may have an antithrombotic effect similar to that of acetylsalicylic acid. Inhibition of lipid peroxidation was also observed in normal adults after ingestion of sodium valproate.

It is our clinical impression that platelet dysfunction caused by sodium valproate cannot be ruled out with certainty by determination of the bleeding time and platelet count. According to our results thrombelastography appears to be a more reliable method of excluding haemorrhagic side effects of sodium valproate.

It should be emphasised that some of our patients were receiving other convulsive drugs in addition to sodium valproate—for example, primidone, ethosuximide, and phenytoin. In patients who were treated with these drugs alone platelet function tests gave abnormal results only rarely.

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Death from asthma

SIR,—In 1786 William Withering sen wrote: "However distressing the disease [asthma] may be at the time it does not cut short the normal period of Life."¹ In the nineteenth century Oliver Wendell Holmes in America called spasmodic asthma "a slight ailment that prolongs longevity"² and at about the same time the not less famous Trousseau bestowed on the disease the accolade "le brevet de longue vie."³ In 1906 Sir William Osler maintained that "death during the attack is unknown."⁴

I was reminded of these famous sayings when I read the excellent and timely paper by Dr J B Macdonald and others (19 June, p 1493). It seems that the misstatements by the above three great men, excusable at their time, are still in the minds of some doctors today.

I believe that it is inexcusable to discharge an asthma patient from hospital without a follow-up period of at least five years or, even worse, not to refer him or her for specialist supervision at all. The admirable "Edinburgh scheme" referred to by the authors—that is, the possibility of self-referral to hospital and

Sections of biopsy specimens showing: (a) granulated mast cell (arrowed) in bronchial epithelium of chronic bronchitis; and (b) degranulated mast cell (arrowed) in bronchial epithelium of asthmatic patient ($\times 500$).