serving its special purpose, produced further resemblances with Stoicism to lend support to a false interpretation.—I am, etc.

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Laryngitis and Aerosols

SIR,—A 39-year-old man was referred with a six-month history of progressive hoarseness. Biopsies of the right aryepiglottic fold and right ventricle of the larynx performed at the referring hospital showed a chronically ulcerated, hyperplastic squamous mucosa only. The inflammatory cell infiltration was predominantly plasma cell in type. Indirect laryngoscopy showed an oedematous larynx with a papilliferous lesion of the right aryepiglottic fold with extension into the medial wall of the right pyriform fossa. The larynx was fully mobile; there was no ulceration and no palpable lymph nodes. A repeat direct examination with multiple biopsies was again negative for carcinoma; the histological appearances being similar to the previous biopsy.

He was an asthmatic of seven years' duration, on low-dose steroids for four years. He originally used a pressurized aerosol of isoprenaline sulphate 4 mg./ml., but had changed to the stronger suspension containing 20 mg./ml. for the past 18 months. His asthma had worsened progressively over nine months to the extent that when seen he had been off work for five months, able only to manage one flight of stairs, or 200 yards on the flat as a maximum exercise at any one time, and unable to sleep without being woken three or four times each night by asthma. Coincident with the deterioration of his asthma, there had been an increasing use of the aerosol, so that a 400-dose aerosol was lasting only one week, equivalent to more than 50 doses per day. Patients have been warned that it is dangerous to exceed the recommended dosage of one to three doses, and that it should not be necessary for more than eight treatments a day.¹

One week prior to his readmission for a further direct laryngoscopy and biopsy, the patient changed back to the low dose isoprenaline aerosol which he had first obtained 18 months previously. There was a dramatic improvement in his voice over seven days and a considerable early improvement in his general condition. Subsequent follow-up on three occasions over two months confirmed that the improvement was maintained. He was back at work full time after two weeks and by two months his larynx and voice were normal; he was sleeping uninterrupted and had been swimming for the first time for seven years. Whereas he had previously become dependent on his aerosol he was now actively refraining from its use as much as possible. He had been changed at one month to an adrenaline aerosol and was using it only once or twice a week.

A presumptive diagnosis of carcinoma of the larynx had been made in this patient. However, because this seemed a strangely situated and small lesion to cause the severe degree of hoarseness he had, treatment was delayed until a positive biopsy could be obtained. A dramatic improvement in his laryngeal condition followed a reduction in the concentration and the frequency of use

of a pressurized aerosol containing isoprenaline.

There have been several reports of the dangers of excessive use of any sympathomimetic amine in bronchial asthma,^{2,4} and statistical evidence of a relationship between overdosage and mortality.^{5,6} The evidence for isoprenaline being the cause of this man's hoarseness must remain circumstantial. However, on clinical grounds alone it would seem a reasonable assumption.

I am grateful to Mr. H. J. Shaw for permission to report this case.

—I am, etc.,

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Pathogenesis of Pre-eclampsia

SIR,—It is true that research into pre-eclampsia has been bedevilled by lack of clinical definition of the large group of patients with hypertension and proteinuria in late pregnancy. Therefore it is of great interest to read Dr. Helen P. McEwen's claim that the presence of alpha₂ macroglobulin (alpha₂M) in the urine in organic disease of the kidney distinguishes chronic renal disease from pre-eclampsia (10 January, p. 111).

If this is so, it might be assumed that this characteristic urinary protein pattern of chronic renal disease is the result of a different degree of glomerular permeability to proteins, which should be identifiable by differential protein clearances. Sixteen patients were studied in this hospital; nine with a clinical diagnosis of severe pre-eclampsia, four with proved nephrotic syndrome, and three with an undetermined cause of proteinuria. The protein clearance was invariably unselective—that is, IgG/transferrin = 20-30%—and afforded no help in the differential diagnosis of these patients.

From these preliminary results we think it probable that with the exception of minimal change glomerulonephritis all proteinuria occurring in pregnancy will be unselective, and that the detectable presence of alpha₂M in the urine will be determined solely by the quantity of proteinuria. We have, for example, found alpha₂M in the urine of a severe pre-eclamptic with a protein loss of 13 g. per day and an absence of detectable alpha₂M in a nephrotic with a proteinuria of 4 g. per day. Nevertheless, we do believe that the presence of alpha₂M in the urine may have some prognostic value, as Dr. McEwen has recently claimed,¹ but considering the similarity of the protein clearance it would appear to us that this index of severity could be deduced more easily by accurate measurement of the proteinuria.

It is ironic that, while Dr. McEwen is rightly stressing the importance of detailed consideration of proteinuria in pregnancy, most obstetricians will entrust the

measurement of urinary protein to a nurse or medical student using Esbach's albuminometer. We have compared the results obtained from Esbach's test performed in the manner described by Varley² with the more accurate biuret method in 145 twenty-four-hour urine collections from 11 patients. Eight patients had severe pre-eclampsia and three had pregnancies complicated by the nephrotic syndrome. The proteinuria in all patients was unselective. The results are shown in the Figure below.

These data confirm the inaccuracy of the Esbach's technique at all levels of proteinuria. The use of this inaccurate method is particularly inappropriate in pre-eclampsia because if the hypertension has been successfully controlled by drugs the precise urinary protein loss may be the most important index of the severity of the pre-eclampsia available, and if it is true that appearance of alpha₂M macroglobulin in the urine in pre-eclampsia is a harbinger of fetal death¹ accurate measurement of urinary protein in pre-eclampsia must have a similar predictive value.—We are, etc.,

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Phage Treatment of Severe Burns

SIR,—Many methods of treating infected severe burns have been advocated, including immunization against the common infecting organisms, chiefly hospital-resistant staphylococci and *Pseudomonas pyocyanea*, which inhibit healing and are antibiotic resistant. In the first world war, I used this method of treating infected septic