that the first phase of any compulsive action which the doctors take must be mild but definite. I would advocate a graded strike commencing with refusal to sign all death certificates, sick notes, and Health Service prescription forms. I have no doubt that the Government has already plans in hand for lay officials to take over these duties, and some little time would elapse before their incompetence became fully evident. During this time doctors could achieve the cohesion that is required and the knowledge that all were taking part in the action.

The next step would be to close down all the non-emergency treatment—clinics, investigation, and diagnosis would continue. It is a dreadful thing to find myself, a doctor who willingly put life and freedom at the disposal of the R.A.M.C. in 1939 on behalf of my country, so disgusted by the treacherous and vote-grabbing manner in which politicians have handled the National Health Service that I am prepared to advocate the abandonment of this service in favour, once again, of total private medicine.

The present stage is climacteric and only a return of the Ministry to loyal and truthful adherence to the original conditions of service should persuade us to continue to deal with it. But it must be remembered that we can deal with it only from a position of strength which it will respect and indeed fear.—I am, etc.,

RANDLE LUNT

Boylestone, Derbyshire

Metaclopramide and Prolactin

SIR,—The report by Dr. A. S. McNeilly and others (29 June, p. 729) that metaclopramide is a potent stimulator of prolactin release may be a matter of serious consequence in the treatment of patients with breast cancer. It has been shown¹ that the growth of breast cancer is sometimes dependent upon the presence of prolactin. Metaclopramide is often used to treat the sickness induced by radiotherapy or cytotoxic chemotherapy in patients with breast cancer. It now appears that by releasing prolactin this drug could stimulate the growth of the cancer. I suggest that this drug should never be given to a patient with breast cancer. It has previously been reported² that prochlorperazine is equally effective in treating radiation sickness.—I am, etc.,

H. W. C. WARD

Radiotherapy Department,
Queen Elizabeth Hospital,
Birmingham

¹ Salih, H., et al., *Lancet*, 1972, 2, 1103.

² Ward, H. W. C., *British Medical Journal*, 1973, 2, 52.

Drugs for Gastric Ulceration

SIR,—Your leading article on the above subject (27 April, p. 186) leaves one with an impression that all currently available drugs for the treatment of gastric ulceration either suffer from side effects or are not very effective in accelerating ulcer healing. The reference to a "carefully conducted Scandinavian trial which showed no demonstrable effect at all" with carbenoxolone is interesting. A recent clinical trial with this compound carried out on Chinese subjects in

Singapore resulted in a similar conclusion.¹

It appears likely that once again the ubiquitous prostaglandins might fill the gap. The gastric antisecretory effect of naturally occurring prostaglandins E_1 , E_2 , and A_1 in man has been recognized for several years.^{2,3} However, these compounds are effective only when administered by continuous intravenous infusion and the gastric inhibitory effect is accompanied by unacceptable side effects. Of all the naturally occurring prostaglandins only PGA_2 is active by mouth, but inhibition of gastric secretion is transient.⁴ In laboratory animals some naturally occurring prostaglandins have an ulcer-sparing effect, but the drugs have to be given by subcutaneous infusion for many hours.⁵

The lack of effect of orally administered natural prostaglandins is most likely due to their rapid metabolism and inactivation. Results obtained with some synthetic analogues of prostaglandins are more encouraging; 15 (R) 15-methyl prostaglandin E_2 methyl ester, 15 (S) 15-methyl PGE_2 methyl ester, and 16, 16-dimethyl PGE_2 methyl ester and free acid are all potent inhibitors of gastric secretion in man⁶⁻¹⁰ when given by mouth. Of all these analogues 15 (R) 15-methyl PGE_2 methyl ester appears to be the most promising, and six-hourly oral doses of this compound for two weeks in normal volunteers are well tolerated. Repeated administration of the other analogues is associated with gastrointestinal side effects.¹¹

Some of the interesting and useful properties of 15 (R) 15-methyl PGE_2 methyl ester are: (1) A single oral dose of 150–200 μ g of this compound results in complete inhibition of acid secretion in man. The volume of gastric juice does not alter significantly but there is a marked elevation in pH of gastric juice from around 2 to 7. (2) A similar inhibition of pepsin secretion has been observed.¹² (3) After a single dose the inhibitory effect on acid and pepsin secretion lasts for over three hours. (4) Given orally, it has a potent stimulant effect on mucus-secreting cells.¹³

Inhibition of pepsin and acid secretion and increase in mucus production could provide an ideal milieu for the healing of gastric ulcers. Two clinical studies with this compound in ulcer patients have been carried out so far. (a) In eight out of 10 subjects with gastric ulcers oral administration of a single dose of 150 μ g 15 (R) 15-methyl PGE_2 methyl ester resulted in elevation of gastric pH from 1.5 to 7 accompanied by a reduction in epigastric pain and tenderness lasting for over three hours.¹⁴ (b) In another study the effect of this compound on the healing of gastric ulcers in 10 patients was evaluated and compared with that in a similar group prescribed an antacid and bed rest. It was given orally in doses of 150 μ g every six hours for two weeks. Gastric ulcer healing in both groups was assessed endoscopically with a duodenofibrescope. In the prostaglandin group complete healing was seen in three cases, considerable healing in six cases, and slight healing in one case. In the control group complete healing was seen in none, considerable healing in two cases, slight healing in four cases, and no healing in three cases. The difference was statistically significant.¹⁵

These preliminary encouraging results warrant further clinical trials with 15 (R) 15-methyl PGE_2 methyl ester which may

provide a much-needed compound for the treatment of gastric ulceration.—I am, etc.,

SULTAN M. M. KARIM

Department of Obstetrics and Gynaecology,
Kandang Kerbau Hospital,
University of Singapore,
Singapore

- 1 Fung, W. P., et al., *Annals of the Academy of Medicine, Singapore*, 1973, 8, 359.
- 2 Classen, M., et al., *Klinische Wochenschrift*, 1970, 48, 876.
- 3 Wilson, D. E., Phillips, C., and Levine, R. A., *Gastroenterology*, 1970, 58, 1007.
- 4 Bhana, D., et al., *Prostaglandins*, 1973, 3, 307.
- 5 Robert, A., Nezamis, J. E., and Phillips, J. P., *Gastroenterology*, 1968, 55, 481.
- 6 Karim, S. M. M., et al., *Advances in Biosciences*, 1972, 9, 255.
- 7 Karim, S. M. M., et al., *British Medical Journal*, 1973, 1, 143.
- 8 Carter, D. C., et al., *British Journal of Surgery*, 1973, 60, 828.
- 9 Karim, S. M. M., et al., *Prostaglandins*, 1973, 4, 71.
- 10 Robert, A., Nylander, B., and Andersson, S., *Life Sciences*, 1974, 14, 533.
- 11 Karim, S. M. M., Sivasuboo, R., and Ratnam, S. S., *Prostaglandins*, 1974, 6, 349.
- 12 Salmon, J. A., et al., *Prostaglandins*. In press.
- 13 Fung, W. P., Lee, S. K., and Karim, S. M. M., *Prostaglandins*, 1974, 5, 465.
- 14 Fung, W. P., and Karim, S. M. M., *International Research Communication Systems*, 1974, 2, 1001.
- 15 Fung, W. P., Karim, S. M. M., and Tye, C. Y., *Lancet*. In press.

Hepatitis B Antigen in Papular Acrodermatitis in Children

SIR,—In your leading article (9 March, p. 407) you suggested that there were alternative interpretations to my observations^{1,2} on the association of hepatitis B antigen (HBAG) with papular acrodermatitis in children (P.A.C.). From our 20 years' study of P.A.C. I must emphasize that diagnosis of the disease depends on the presence of (1) non-relapsing, non-itching erythematopapular dermatitis localized to the face and limbs and lasting 20–25 days; (2) a reactive reticulohistiocytic lymphadenitis; (3) an acute hepatitis, usually anicteric, which lasts for at least two months and may persist for several months or years; and (4) HBAG in the serum after the first few days of the dermatitis. These diagnostic criteria distinguish cases of P.A.C. from those of papular-vesicular-acrodermatitis syndrome.

HBAG can be shown in the serum of all cases of P.A.C. by immunodiffusion, electrophoresis, or radioimmunoassay and may be seen on electron microscopy as pleomorphic spherical, tubular, and double-shelled particles identical with those found in the serum of patients with serum hepatitis or polyarteritis nodosa. We and others³ have seen some cases of P.A.C. where one or more members of the family were HBAG carriers. We and others³ have also seen cases where a few weeks before or after a child had developed P.A.C. another member of the family showed symptoms of icteric hepatitis.

We believe that P.A.C. is more common than it is thought to be. The diagnosis is often missed because neither the relatives nor the doctor pay much attention to the only symptom—the non-itching eruption without fever. Acute hepatitis, usually anicteric, is unsuspected, for there is little constitutional upset and only moderate hepatomegaly. We consider P.A.C. to be the clinical manifestation of the primary infection with HBAG (the causative virus of long incubation hepatitis) in childhood via the mouth or mucous membranes. It is true, as your leading article pointed out, that the characteristic rash and lymphadenopathy of