forced without any consultation or choice to make this change. Diabetic patients of long standing should still be able to obtain animal insulin (their doctor permitting). I suppose that the manufacturers make more money this way.

Flat 19,
50 Leinster Gardens,
London W2 3AT PHYLLIS BARHAM

MAKING INSECT REPELLENTS SAFE

SIR,—Your Sept 10 editorial suggests withdrawal of preparations that contain more than 75% of the insect repellent diethyltoluamide (DEET) to reduce the risk of side-effects. However, whatever concentration of alcoholic solution is applied, the solvent will presumably evaporate to leave concentrated DEET on the skin. Furthermore people using preparations that contain lower concentrations are likely to apply larger volumes to obtain the desired insect repellency. A safer way to use DEET would be via impregnation into cotton jackets[1] or anklets[2] from which the vapour is slowly released with little or no skin contact. One impregnation remains effective for several weeks if the clothing is stored in a plastic bag or hat tin and only worn when insects are biting.

London School of Hygiene
and Tropical Medicine,
London WC1E 7HT C. F. CURTIS

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CEREBRAL VASOSPASM AND UNRUPTURED ANEURYSM IN THUNDERCLAP HEADACHE

SIR,—Dr Clarke and colleagues (Sept 10, p 625) plead that cerebral angiography should still be considered in patients with sudden and unusual headache but without evidence of subarachnoid haemorrhage on computerised tomography and lumbar puncture. They report a patient with severe generalised headache, vomiting, photophobia, and mild neck stiffness, in whom angiography revealed aneurysm of the internal carotid artery with vasospasm despite a normal computerised tomogram and clear cerebrospinal fluid. Day and Raskin had previously described a similar patient.[1] In contrast, in our follow-up of 71 patients with "thunderclap" headache, we failed to identify a single episode of subarachnoid haemorrhage in the subsequent years. The headaches could not be distinguished from those in patients with subarachnoid haemorrhage. Doubtful neck stiffness was observed in some patients. "Pseudo-subarachnoid haemorrhage", as suggested by Dr Pearce (Sept 10, p 625), or "crash migraine"[2] might be equally appropriate terms.

Vasospasm on the angiogram is the feature that led to the belief, in both reported cases with aneurysms, of a causal relation with the headache. The aneurysm would have suddenly enlarged, but without rupturing. We think that migraine is a more probable explanation for both the headache and the vasospasms. Call et al[3] drew attention to the occurrence of segmental and fully reversible vasospasm in patients with severe headache but without a concomitant aneurysm. We caution that a few adults harbour asymptomatic aneurysms[4] and that indiscriminate angiography is bound to uncover some of these. We agree that angiography cannot be avoided when patients with a suggestive history are seen after a long interval. Angiography was done for this reason in 2 of our 71 patients, with negative results.

Department of Neurology,
University of Utrecht,
3511 GV Utrecht, The Netherlands E. F. M. WIJDICKS
H. KERKHOFF
J. VAN GIJN

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CARBON DIOXIDE AND ACUTE MOUNTAIN SICKNESS

SIR,—Dr Harvey and colleagues (Sept 17, p 639) provide evidence to support the use of carbon dioxide in acute mountain sickness. In 1971, because of several deaths caused by high-altitude pulmonary oedema, officials of the Mount Kenya National Park asked the department of medical physiology at the Nairobi Medical School to investigate the problem. We came to the conclusion that low levels of carbon dioxide were a key factor. In addition to the findings of Harvey et al, we argued that the paradoxical vasodilatation in the pulmonary bed produced by low levels of pCO_2 might contribute to the pulmonary oedema.[1] Moreover, we could find no recorded case of high-altitude pulmonary oedema below 2743 m (9000 feet) above sea level. This is the critical altitude above which arterial pCO_2 begins to fall.[2] We therefore recommended that gas cylinders for acute resuscitation at high altitude should contain 2% carbon dioxide.[3] The recommendation was never followed because of the fears of cerebral oedema discussed by Harvey and colleagues.

Efamol Research Institute,
Kentville, Nova Scotia, Canada B4N 4H8 DAVID F. HORROBIN

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TUMOUR CELL MORPHOMETRY AND RESPONSE TO CHEMOTHERAPY IN OVARIAN CANCER

SIR,—The prediction of response to chemotherapy in ovarian cancer by in-vitro tests does not reliably correlate with clinical courses.[1] We have investigated the value of tumour cell morphometry in predicting response in 63 patients who had been referred for palliative surgery for advanced epithelial ovarian cancer (FIGO-stage III,IV); 17 patients responded to postoperative chemotherapy, 46 were non-responders. Tumour reduction of at least 30% was designated a response. There was no significant difference in the responder/non-responder ratio when tumour stage, cell type, and drug regimen were evaluated separately (χ^2 test). For each case, seventeen morphometric variables were taken from two representative photographs (1000 × magnification) of the tumour with an interactive digital analyser system ('MOP 30', Zeiss Kontron); the mitotic index was also counted. Of these eighteen variables, eight had a p value below 0·2 in a U test of responders against non-responders and were further analysed. Three of the eight were highly correlated to two other variables of this group (the mean and median nuclear area to the nuclear area at the 10th percentile and the nuclear area at the 90th percentile to the standard deviation of the nuclear area; correlation coefficient greater than 0·95). These three variables were excluded due to a higher p value in the U test. The remaining five variables and their p values were: nuclear hypokaryotic area (nuclear area at the 10th percentile, $p < 0·05$), nuclear anisokaryotic index (standard deviation of the nuclear area, $p < 0·09$), nuclear ovality factor (median value of the nuclear ovality, $p < 0·11$), nuclear density factor (number of cells per area, 0·04), and mitotic index (number of mitotic figures in 10 fields at 400 × magnification, $p < 0·03$). On the assumption that the combination of several morphometric variables enhances the value of the information, these five variables were entered into a multiple linear discriminant analysis with stepwise selection.[2,3] All five were accepted in the selection procedure ($p = 0·0013$). 76% (13/17) responders and 80% (37/46) non-responders were correctly classified (79% efficiency). The discriminant function is given by: $D = -0·0856 \times \text{mitotic index} - 0·0459 \times \text{nuclear hypokaryotic area} + 0·0671 \times \text{nuclear area standard deviation} + 14·7 \times \text{nuclear ovality factor} + 397 \times \text{nuclear density factor} - 12·2$. Values of D greater than zero imply allocation to the response group, values below zero to the non-response group.

To assess the reliability of the discrimination formula when applied to new cases, the "leave one out" method was used (each