induced by oestradiol in the endometrial stroma and myometrium. 3

The simultaneous presence of an atrophic mucosa, dilated cystic glands, and a dense oedematous stroma can be due to a dissociated effect of tamoxifen, which varies according to the endometrial tissue components. Tamoxifen might exert weak oestrogenic stimulation on glandular epithelium secretion, thus increasing the volume of fluid inside the glands and, therefore, their size. This contrasts with the absence of any stimulatory effect on growth of the epithelium, which remains thin and atrophic. Finally, the thick and oedematous stroma could be due to an oestrogenic effect of tamoxifen.

The action of tamoxifen on the human endometrium seems to be more complex than a simple oestrogenic effect inducing hyperplasia. Our results suggest dissociated antioestrogenic and weak oestrogenic effects of tamoxifen on various components of the endometrium. Practitioners should be alerted to tamoxifen’s effects on the endometrium to avoid misinterpretation of results of ultrasound investigation and to investigate misleading aspects of hyperplasia by hysteroscopy and biopsy.

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Treatment of genital chlamydial infection

Sir—Alary and colleagues (Nov 26, p 1461) report a failure rate of 12% in a group of 99 pregnant women with urogenital Chlamydia trachomatis infection who received erythromycin 500 mg four times daily for seven days. They state that it was not known if a longer course of twice daily erythromycin would cause fewer side-effects. Our clinic policy is to give erythromycin 500 mg twice daily for ten days. The action of the drug is to prevent the growth of the organism, so treatment failure defined as positive chlamydia culture at test of cure or cessation of treatment because of side-effects.

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<table>
<thead>
<tr>
<th>Total number</th>
<th>Cured</th>
<th>Treatment failure*</th>
<th>Lost to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-pregnant</td>
<td>255</td>
<td>224 (88-5%)</td>
<td>15 (5-9%)</td>
</tr>
<tr>
<td>Pregnant</td>
<td>12</td>
<td>9</td>
<td>3</td>
</tr>
</tbody>
</table>

Treatment failure defined as positive chlamydia culture at test of cure or cessation of treatment because of side-effects.

Table: Results of treatment with erythromycin 500 mg twice daily for ten days

Eliciting P300 in comatose patients

Sir—Event-related brain potentials reflect stages of information processing associated with consciousness and cognition. Some of these potentials (P300 and mismatch negativity) have been evaluated in comatose patients for prognostic purposes. 1, 2 Passive auditory odd-ball paradigms have been used to evoke P300. A possible criticism of this method, however, is that it elicits a low percentage of P300 responses even in normal subjects. 3 Conditioning techniques make it easier to evoke P300 or P300-like waves in normal and in non-collaborative subjects, such as autistic and mentally retarded patients 4 or animals. We have recorded auditory P300 in comatose patients by use of conditioned stimulii in an attempt to improve the detection of surviving mental processes and so to enhance the prognostic value of such tests.

The procedure consisted of 12 successive trials. In the initial 2 trials, only conventional tone bursts were administered (passive odd-ball phase). These were followed by 6 trials in which verbal stimuli with an emotional or neutral content were coupled to the tones (conditioning phase). Finally, 4 further trials were given by use of the simple passive odd-ball paradigm to determine whether the responses ceased once reinforcement was withdrawn (extinction phase). The tone bursts were presented at 90 dB intensity with a duration of 50 ms. The rare stimuli comprised 2000 Hz tones presented on 20% of trials. The frequent stimuli were 500 Hz tones presented on 80% of trials. Moreover, 2 types of prerecorded verbal stimuli of similar length were associated with them by use of a voice synthesiser during the conditioning trials. These were: words with an emotional content particular to the subject (the patient’s name or short phrases spoken by a member of the family), associated with the rare stimulus; and meaningless words (spoken by unfamiliar voices), associated with the frequent stimulus. The verbal stimuli followed the tones with a delay of 900 ms. In each trial, 200 stimuli were presented binaurally with an inter-stimulus interval of 3 s. The verbal stimuli comprised 2000 Hz tones presented on 20% of trials. The frequent stimuli were 500 Hz tones presented on 80% of trials. Moreover, 2 types of prerecorded verbal stimuli of similar length were associated with them by use of a voice synthesiser during the conditioning trials. These were: words with an emotional content particular to the subject (the patient’s name or short phrases spoken by a member of the family), associated with the rare stimulus; and meaningless words (spoken by unfamiliar voices), associated with the frequent stimulus. The verbal stimuli followed the tones with a delay of 900 ms. In each trial, 200 stimuli were presented binaurally with an inter-stimulus interval of 3 s. The electroencephalogram was recorded from Cz, Pz, C3, and C4 (locations in the international 10–20 system) with respect to linked ear lobes as the common reference. It was filtered between 0·3 and 70 Hz. The sampling rate for the successive average was 1 point every 2 ms. Electro-oculograms (EOG) were monitored and trials with large EOG were rejected.
probability of damage to receptive language mechanisms. All patients had a Glasgow coma scale (GCS) score ranging between 3 and 8 and had previously been investigated by electroencephalography, brain-stem auditory evoked potentials, and computed tomography. P300 was obtained in 9 of 16 patients. It was recorded in all three phases (passive odd-ball, conditioning, and extinction) in 2 cases. It was present in both the first passive odd-ball and in the conditioning phases but not in the extinction phase in 4 cases. In 3 cases P300 occurred only in the conditioning phase. Over all trials the P300 latency and amplitude ranged between 308 and 870 ms, and 7 and 255 μV. The 2 patients who showed P300 in all the trials had a GCS of 6 whereas those who had P300 only in the conditioned phase had a mean GCS of 4-3 (range 3-6). Of the 9 patients who showed P300 waves, 7 survived, with a return to normal reaction times and normal Raven progressive matrices (PM47) scores in 5 cases. The 2 patients with P300 who died had secondary non-neurological complications. By contrast, only 3 of the 7 patients who did not show any P300 potential 3-6 days after trauma survived. Of these 3 patients, 2 developed a P300 3 weeks later, while still unconscious but with GCS improved. These results show that emotional conditioning increases the chances of obtaining P300 in comatose patients. Responses were obtained in 56% of patients. This high percentage of responses was due to the fact that the conditioning technique evoked P300 in patients with a lower GCS rating. Moreover, the effectiveness of the conditioning reflects a learning process involving more complex mentation than is probed by the passive odd-ball paradigm. Our work also confirms other studies that show a positive correlation between the existence of P300 waves and the probability of awakening from coma.1

Dietary polyunsaturated fatty acids and aortic plaques

Sir—Felton and colleagues’ report (Oct 29, p 1195) describing an association, in 9 people, between the composition of some fatty acids in serum and adipose fat has three serious failings. First, they report a correlation between polyunsaturated fatty acids in the diet and adipose fat, serum, and plaque. They then claim that these associations “reflect a direct capacity of the omega-6 and omega-3 fatty acids to promote the atherosclerotic process” and that some protection may be “afforded by monounsaturated fatty acids”. The latter claim is contradicted by their findings since palmitoleic and oleic acids, the two monounsaturated fatty acids, correlate just as highly as the omega-6 and omega-3 fatty acids. Second, they claim that plaque and adipose tissue are correlated. So will not the Swedes, with a higher adipose content of omega-6 fatty acid (mainly linoleic acid as in this case) compared with Edinburgh people, have a higher plaque content of omega-6 fatty acids? According to Felton and colleagues’ thesis, the Swedes should have a higher mortality than the Scots from heart disease—but their mortality is lower. Felton and co-workers report total fatty acids, which mainly would derive from triglyceride in adipose tissue, a mixture of lecithin, cholesterol ester, and triglyceride in serum, and we know not what in the plaque or intima that they examined. Without such data it is difficult to draw conclusions about the extent to which their findings were due to post-mortem equilibration with serum.

Third, there are no control data. In a study of 80 patients with aorto-iliac/femoropopliteal atherosclerosis Kingsbury and colleagues showed that plasma cholesterol esters contained less linoleic acid and more oleic acid in those who had an acute infarct or vascular death than in 40 patients who were alive and well. Their work suggests a deficiency of essential fatty acids without which cellular integrity is known to be put in jeopardy. In prospective or retrospective case-control studies significantly lower levels of linoleic and arachidonic acids have been recorded in patients with myocardial infarction, and there is good experimental and intervention evidence favouring a protective role for omega-3 fatty acids. Phylactos and co-workers noted an increase in mitochondrial superoxide dismutase activity in response to increased membrane polysaturation. I suggest an alternative hypothesis. A correlation between serum and plaque, if true, merely means that the plaque takes up lipid from the serum in some form. Contrary to Felton and colleagues’ suggestion, this uptake might be advantageous. A supple coronary artery can respond to the stress of movement and high pressure waves. A polysaturated plaque would be more supple and the endothelium consequently less easily damaged than a plaque filled with rigid saturated fatty acids and cholesterol. Hence the protective effect of polysaturated fatty acids might have been understated rather than overstated.

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